A TEXTBOOK OF THE PRACTICE OF MEDICINE

XFORD MEDICAL PUBLICATIONS

A TEXTBOOK OF THE PRACTICE OF MEDICINE

By VARIOUS AUTHORS

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THIS BOOK IS DEDICATED

TO

THE MEMORY OF

THE RIGHT HON. SIR CLIFFORD ALLBUTT

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PREFACE TO SIXTH EDITION

THE continued rapid advance of medical science, and the extending use and appreciation of this textbook, have made necessary the publication of this, the sixth edition, within four years of the appearance of its predecessor. It will readily be understood that the production, under wartime conditions, of a volume of this character and magnitude, has been a somewhat formidable task, which has been successfully accomplished only through the self-sacrificing labours of the contributors and the co-operation of the publishers.

The extent of the revision may be judged by the details set forth below, which are generally noted in the order of appearance of the respective articles throughout the work. It will be a source of satisfaction that, notwithstanding the very extensive revision, the size of the volume is practically the same.

The purpose and scope remain the same as when the work was originally conceived twenty years ago, namely, the presentation of a comprehensive survey of the practice of modern medicine in the form of a textbook, each subject being dealt with in an essentially practical manner, prominence being given to diagnosis, treatment, and prognosis, rather than to ætiology or pathology, although both these latter are dealt with in sufficient detail for ordinary reference.

In the new edition, the principal alterations in the general arrangement, classification, and nomenclature include: The sub-section on Diseases due to Filtrable Viruses is placed immediately after that on Bacterial Diseases. The articles on Acute Anterior Poliomyelitis, Lethargic Encephalitis, Herpes Zoster, and Rabies have been transferred from the sub-section due to Filtrable Viruses to form a sub-section of Diseases of the Nervous System, and the article on Multiple Myeloma from the section on Diseases of the Blood to that on Diseases of the Skeleton. Oroya Fever and Verruga Peruviana are included under the general term Bartonellosis. There is a new classification of Typhus and the Typhus-like Fevers; a re-arrangement regarding Toxic and Infective Diseases of the Liver; a re-classification of the Hæmorrhagic Diseases; a modification of the classification of Diseases of the Arteries; and a new arrangement regarding Meningeal Hæmorrhage and Chronic Subdural Hæmatoma. Changes in nomenclature are: Lymphopathia Venereum for Climatic Bubo; Upper Dysphagia with Anæmia (Paterson's (so-called Plummer-Vinson) Syndrome) for Dysphagia with Anæmia and Glossitis (Plummer-Vinson Syndrome); Methæmoglobinæmia and Sulphæ-

moglobinæmia for Enterogenous Cyanosis; and the Motor Neurone Disease for Progressive Muscular Atrophy.

New articles have been added on the following: The Common Cold, Leptospirosis, Epidemic Myalgia, Pink Disease, Injuries from X-rays, Injuries from Radio-active Substances, Manganese Poisoning, Poisoning by Coal-Tar Derivatives, Poisoning by Chlorinated Hydrocarbons, Adiposity, Diabetes Tenuifluus, Antihormones, Acute Suprarenal Deficiency, Virilism, Feminisation, Pseudo-Hermaphrodism, Sexual Precocity, the prescribing and administration of Hormone Preparations, Idiopathic Steatorrhœa, Tuberculosis of the Spleen, Chronic Tuberculous Lymphadenitis, Functional Bundle-Branch Block, the Heart in Hypothyroidism, Allergy, Adenoma of Bronchus, Congenital Cystic Disease of the Lung, Pneumonitis, Focal Osteitis Fibrosa, Dyschondroplasia, Sarcoidosis, Benign Aseptic Meningitis, Hypertensive Encephalopathy, Acute Disseminated Encephalomyelitis, Kernicterus, Rupture of the Intervertebral Disk, Acute Febrile Polyneuritis, Progressive Hypertrophic Polyneuritis of Dejerine and Sotta, and Neurofibromatosis.

Other new matter has reference to the use of the sulphonamide group of drugs in the treatment of acute infections, the use of a toxoid in the prophylaxis of Tetanus, skin tests and capillary fragility in Scarlet Fever, the classification of the Organisms causing Bacillary Dysentery, specific treatment in Oroya Fever, Verruga Peruviana, Malaria, American Dermal Leishmaniasis, Trypanosomiasis, Giardia Intestinalis, and in Thread Worms, the pathology and complications of Mumps, the symptoms and diagnosis of Amœbic Dysentery, the diagnosis and prophylaxis of Louse-Borne Typhus, Mercurial Poisoning, the use of the new insulins Protamine and Protamine Zinc Insulin, the treatment of Infantile Scurvy, the ætiology of Rickets, the Sub-Scurvy State, the Red Blood Cells, Clinical Electro-Cardiography, including the Fourth or Chest Lead, Chronic Miliary Tuberculosis, Epituberculosis and Hilar Flare, Oleothorax, Thoracoplasty and Extrapleural Pneumothorax in the treatment of Pulmonary Tuberculosis, the Superior Pulmonary Sulcus or Pancoast Tumour, the prognosis of Acute Nephritis, Familial Hæmorrhagic Nephritis, Sodium Diaphenyl hydantoinate (dilatin, epanutin) in the treatment of Epilepsy, Migraine, and the effects of the stress of war upon the mental health of soldiers and others.

The following portions have been entirely rewritten: The sections on Diseases of the Endocrine Glands and Diseases of the Joints and Inflammatory Diseases of the Fibrous Tissues. The articles on Lymphopathia Venereum, Spirochætosis Icterohæmorrhagica, Introduction to Rickettsia Diseases, Alcoholism, Lead Poisoning, tests for Hepatic Function, Acholuric Jaundice, Acute Infective Hepatitis, Aplastic Anæmia, Methæmoglobinæmia and Sulphænoglobinæmia, Melæna Neonatorum, the Aetiology of Agranulo-

cytosis, Niemann-Pick's Disease, Hand-Schüller-Christian's Disease, Irritable Heart of Soldiers, Primary Cardiac Strain, Auriculo-Ventricular Nodal Rhythm, Ventricular Fibrillation, Sino-Auricular Block, Chronic Adhesive Pericarditis, Tuberculosis of the Pericardium, the Surgical Treatment of Angina Pectoris, Hypertension, Raynaud's Disease, Hæmoglobinuria, the Pathology of Toxæmic Kidney, Osteitis Deformans, Leontiasis Ossea, Osteomalacia, Osteogenesis Imperfecta, Oxycephaly, Achondroplasia, Multiple Myeloma, the ætiology of Ménière's Disease, the treatment of Spasmodic Torticollis, the ætiology and pathology of Polyneuritis and Hæmatomyelia.

The following articles have been partly rewritten: Infection, Immunity, the treatment of Coliform Bacillus Infections, the methods of immunisation and of prophylaxis in Diphtheria, Yellow Fever, Syphilis, Yaws, Flea Typhus, Mite Typhus, Tick Typhus, the Clinical Aspects of Glandular Fever, Arsenical Poisoning, Beriberi, Pellagra, Tropical Macrocytic Anæmia, the pathology of Chronic Œsophageal Ulcer, the ætiology of Anorexia Nervosa, the surgical treatment of Ulcerative Colitis, Acute and Subacute Hepatic Necrosis, the Blood Volume, Symptomatic Hæmorrhagic States, the Treatment of Splenic Anæmia, Heart Failure, Auriculo-Ventricular Block, Pulsus Alternans, Chronic Valvular Disease, Acute Simple Myocarditis, Chronic Mycardial Disease, Hypertrophy and Dilatation of the Heart, Acute Pericarditis, Syphilitic Affections of the Aorta, the Heart, and the Pericardium, the treatment of Bell's Palsy, the signs of Local Lesions within the Skull and Brain, the pathology of Hydrocephalus and Craft Palsy.

An important innovation has been made in connection with the names of drugs. It was thought that a useful purpose would be served by the following: The English names in the *British Pharmacopœia* of 1932, or in one of its addenda, or in the *British Pharmaceutical Codex* are used. On the first occasion on which the official name is mentioned in the section on treatment of any particular disease, it is followed immediately by the name used in the *United States Pharmacopœia* when there is a material difference between the two. Next follow, almost always in brackets, the names of the more widely known of any proprietary preparations of corresponding composition, the British products usually being given priority, and, in the case of both the British and the foreign preparations, usually in alphabetical order. In the prescribing of drugs, following the recommendation in the *British Pharmacopœia*, grains and ounces for solids, and minims and fluid ounces for liquids, are used instead of the conventional symbols. It is a pleasure to express my indebtedness to Mr. H. Davis, Ph.D., A.I.C., Ph.C., for his valuable technical assistance in this connection.

There are 12 new illustrations (Figs. 51, 68, 82, 85, 86, 87, 89, 90, 92, 93, 94, and 95).

Drs. W. S. C. Copeman, Donald Hunter, Alan Moncrieff, and S. L.

Simpson are new contributors, and to them I desire to offer a warm welcome.

Since the appearance of the last edition Medical Science and Practice have suffered a great loss in the death of three of the contributors, namely, Otto Leyton, Edward Mapother, and William Henry Willcox, the last since this edition went to press. I desire to pay to their memory a profound tribute of regard and gratitude.

It may be considered not inappropriate if I offer a few remarks on this occasion. From the inception of this textbook, it met with a notable degree of appreciation from the class of readers for whom it was intended, and each successive edition has been received with an ever-growing measure of approval. Its circulation to-day is greater than ever in all English-speaking countries, and it is interesting to observe that its popularity abroad has increased in even greater measure than in the United Kingdom. These results suggest that the plan of the work as outlined in the Preface to the First Edition was fundamentally sound, and even, it may be said, anticipatory of the developments which have taken place in the teaching and practice of medicine. Apart from this original validity of conception, I attribute the success of the book to the high abilities and devoted efforts of my colleagues, the contributors, with whom from the beginning my relationship has been of the most intimate and happy character. No words of mine can adequately express my admiration and grateful appreciation of their help. All I can do is to tender them my cordial and abiding thanks. I desire to add that it has been an immense privilege to have been Editor of the first six editions of this Work.

I earnestly hope and venture to believe that this new edition will be, to an extent not less than its forerunners, of service alike to Teachers of Medicine, Consulting Physicians, and Senior Students, and that it may continue to be regarded as not unworthily representing British Medicine.

FREDERICK W. PRICE.

73 HARLEY STREET, LONDON, W.,

PREFACE TO FIRST EDITION

It is generally recognised that within recent years there has been a great advance in knowledge throughout the domain of Medicine. As an example of this might be cited the branch of cardiology. As the result of the introduction of the clinical polygraph and of the electro-cardiograph we are now able to analyse the cardiac action in a manner which was never possible before, and many of the problems in the study of diseases of the heart which have baffled clinicians for generations have been practically solved, while others are in process of solution. In the department of neurology the progress made has been scarcely less notable. It seemed to me, therefore, that now, more than ever, it has to be acknowledged that it is beyond the scope of any authority, however varied his range of knowledge, to do full justice to the ever-widening field of Medicine, and that a useful purpose might be served by the publication of a work of moderate compass and in one volume, in which the different branches of Medicine were dealt with by authors who have made a special study of them. It has also been thought advisable to include sections on Diseases of the Skin and Psychological Medicine. Tropical Diseases are also included.

In order to secure greater uniformity of method and style, I have generally adopted the principle of allotting a whole section to one author, or to two writing in collaboration, instead of enlisting the services of a large number of writers. I confidently anticipate that it will be recognised that I have been most fortunate in the selection of the various contributors to the volume, and I wish to offer to each of them my warmest thanks. I also desire to express my gratitude to Dr. A. P. Beddard, for the time he has very generously placed at my disposal, and for much valuable advice. It is a pleasant duty gratefully to acknowledge my indebtedness to Dr. Claude B. Ker for the use of blocks of figures taken from his *Manual of Fevers*, and to Dr. James Collier and Sir James Purves Stewart for a block of figure 96.

It is my earnest hope that the book may be considered a credit to the London School of Medicine.

FREDERICK W. PRICE.

133 Harley Street, London, W.,
January 1922.

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A TEXTBOOK OF THE PRACTICE OF MEDICINE

SECTION I

INFECTION

Effects of Bacterial Activity

When a bacterial invasion of the body tissues occurs the result is disease; the process is spoken of as an infection, and the bacterium is said to be pathogenic. The terms "pathogenic" and "non-pathogenic" are by no means rigid. No organism is pathogenic to all animals, and even organisms generally pathogenic to a given species may be introduced into an individual of that species, even in considerable quantity, without producing disease. On the other hand, organisms usually saprophytic, when introduced in sufficient quantity into an animal of a species usually immune, may cause disease.

Organisms pathogenic for one species of animal are frequently non-pathogenic for other species, and not a few organisms are pathogenic for man alone, except under certain exceptional experimental conditions.

Certain organisms which habitually exist under normal conditions as saprophytes in one part of an animal's body, may at the same time be the cause of an active infection in another part. For example, a member of the coliform group of intestinal bacilli, usually a harmless saprophyte in the intestine, may be simultaneously the cause of an active infection in the bladder. Bacteria which usually function as harmless saprophytes, but under certain conditions become pathogenic, are termed "commensals." Again, micro-organisms that are potentially infective may and do exist under saprophytic conditions; that is to say, apart from the animal body, and under different conditions as regards temperature, etc. Saprophytic bacteria that are incapable of invading living animal tissues may yet invade the animal body when any part thereof is so injured as to be dead, or is in process of dying. Certain varieties of bacteria, usually infective, may become saprophytic. The hosts are then termed "carriers." The best known examples thereof are the typhoid bacillus, the diphtheria bacillus and the meningococcus. The two former examples generally, if not always, occur after an infection, whereas the meningococcus is more often found existing in a saprophytic than in a pathogenic state. In these cases the bacteria do not exert any apparent harmful effect, but they are, of course, of great potential danger to the surrounding community.

A similar condition exists in connection with the paratyphoid bacilli and those of the food-poisoning group generally. This condition differs to some slight extent from that of the carriers noted above, in that there is some evidence, continuous or recurrent, of constitutional disturbance, though in the periods between recurrence, which may be prolonged, the condition closely resembles that of a carrier.

Infective bacteria are generally aerobic, or facultatively aerobic. True anaerobes have very little power of spreading through uninjured animal tissues unless they are accompanied by aerobes, though they may cause localised infections in tissues in which the oxygen supply is limited. Hence the bacteria usually associated with infections are aerobic organisms that flourish at body temperature.

A microbe may belong to a highly infective variety and yet its infectivity vary greatly. This property is known as *virulence*, and depends on various factors.

The *path of infection* also has a determining influence. Thus, staphylococci injected subcutaneously in a rabbit produce a local abscess, while if the injection be intravenous, pyæmic abscesses may lead to death. Typhoid bacilli must be swallowed to be infective, while it has been demonstrated that plague may be caused by rubbing *B. pestis* into the skin.

Subject of infection.—Healthy individuals differ greatly in their reaction to infective microbes, because of individual, racial or environmental characteristics, or because of age.

A *local susceptibility* may be brought about by trauma or interference with the circulation, conditions which may permit even anaerobic organisms to flourish.

An existing disease may modify the reaction of the host to an infection. Thus the subjects of diabetes are prone to staphylococcal and tuberculous infections.

Bacteria that are capable of spreading in the tissues usually have the power of causing *septicæmia*, that is, of flourishing in the blood stream, and, as a sequel, of producing *pyæmic* processes. Other bacteria causing acute infections appear in the blood stream during the earlier stages of the infection, but in the later stages tend to disappear therefrom, the *bacteriæmia* being incidental to, but not coextensive with, the infection. Streptococci and staphylococci are common examples of the former process, and the typhoid bacillus of the latter.

Results of Bacterial Infection

If the individual be in a healthy state, even a large quantity of virulent micro-organisms can gain admission to the body, and, owing to the local defences, may be destroyed before damage occurs; such a repelled invasion may cause no symptoms. When the local defences prove inadequate to ensure the complete destruction of the invading bacteria, the result is a local, or general, infection, or both.

A local infection may result in cellulitis or abscess formation, associated with more or less absorption of poisonous products; such a local infection may become generalised, leading to septicæmia or pyæmia. But whether the infection be local or general, or both, a greater or less degree of general

poisoning may occur, by reason of soluble poisons elaborated by the bacteria. These poisons are termed " toxins." *Toxins* are of two varieties—exotoxins and endotoxins.

Exotoxins are soluble poisons elaborated by certain classes of bacteria—notably diphtheria and tetanus. These exotoxins are destroyed by comparatively low temperatures; for instance, diphtheria toxin is destroyed by a temperature of 65° C. When an exotoxin is introduced into an animal's body, the specific effects thereof appear after an incubation period. *Endotoxins* can only be recovered by autolysis or trituration of the micro-organisms whch produce them. This means that those bacteria which only elaborate endotoxins can only poison an animal by proliferating within the tissues of that animal, while the poisoning produced by exotoxin may occur without invasion of the body by the organism concerned. Endotoxins will withstand a temperature of 100° C.

The difference between exotoxin and endotoxin is a fundamental one in specific therapy, as in a toxæmia from exotoxin a suitable antitoxin in appropriate amount constitutes an adequate defence, while in the case of toxæmia from an endotoxin the bacterium itself has to be proceeded against. The mode of action of toxins is very variable and depends upon the variety of bacterium. The toxins of diphtheria and tetanus tend to produce profound poisoning effects on the nerve tissues. Those consequent upon other infections produce other effects, prominently fever and degenerative changes in the tissues.

IMMUNITY

Definition.—Immunity is that function of the animal organism by virtue of which the effects of bacterial activity are resisted. Immunity is either natural or acquired.

Natural Immunity

Factors determining immunity are not well understood; but environment, habits, age and race partly account for them. The natives of countries where certain diseases are endemic may be far more resistant to those diseases than inhabitants of countries where the diseases are not endemic, as shown by the resistance of the negro to yellow fever. Conversely, diseases that have existed in mild forms for years endemically among one race may cause a veritable plague when introduced to a fresh race. Thus tuberculosis ravaged the North American Indians, and syphilis when introduced to Europe from America, where it was probably endemic, followed the course of an epidemic of a highly contagious disease.

There is also individual immunity, as shown by the fact that in any epidemic some individuals entirely escape infection, while in those infected all degrees of resistance are noted. In contradistinction to individual natural immunity, which condition does not lend itself to analysis, there is the condition of individual susceptibility—a condition to which considerable study has been devoted, chiefly in the direction of non-bacterial toxæmias, such as hay fever and the various toxic idiopathies.

Acquired Immunity

(i) *As the result of recovery from infection*

When an individual has recovered from certain infections such as typhoid fever, scarlet fever, measles and the other exanthemata, he commonly experiences immunity from those diseases in future. The duration of this form of acquired immunity varies greatly with different infections: that following influenza and pneumonia may be quite short. This acquired immunity was recognised centuries ago, and history shows that attempts at protection were made by inoculating infective material; it was on account of this knowledge that Pasteur began the study of protective inoculation which forms the basis of our knowledge of immunity.

(ii) *Artificial Immunity; Active and Passive*

Pasteur, in 1880, showed that injections of attenuated cultures of the organism of chicken cholera would protect the inoculated fowl against lethal doses of the virulent bacilli. From this observation resulted artificial immunity, and because the protection is elaborated solely by the action of the tissues of the infected animal, the term Active Immunisation was introduced by Ehrlich.

Von Behring, in 1890, discovered that the serum of actively immunised animals when transferred to other animals conferred immunity on the latter, and this process is termed Passive Immunity. It differs broadly from active immunity in that the protection afforded is comparatively transient, depending as it does on the actual amount of immune substance introduced.

Antitoxins

As already stated, toxins are of two kinds—exotoxins and endotoxins. The former exert their effects independently of the bacteria that produce them, while the latter only become effective when their parent microbes become dissolved. The injection of suitable doses of exotoxin calls forth the response of antitoxin; whereas the injection of suitable doses of endotoxin, *i.e.* vaccine, calls forth the response of bacterial antibodies. It is now known that other bacteria than those of diphtheria, tetanus and Shiga's dysentery produce appreciable quantities of antitoxin, namely *Streptococcus scarlatinæ*, *B. botulinus* and *Staphylococcus pyogenes*.

Since von Behring and Kitasato demonstrated the antitoxic properties of the blood of animals immunised against diphtheria toxin in 1890, an immense amount of work has been published, and improvements in the preparation of antitoxin have constantly accrued.

A unit of toxin is that quantity sufficient to kill a 250 g. guinea-pig in 4 days. The original Ehrlich unit of antitoxin was that amount that would save the life of a 250 g. guinea-pig injected with 100 units of toxin, but owing to variations in the strength and keeping qualities of different batches of toxin, the present unit of antitoxin is the amount of antitoxin

in a known weight of dried antitoxic serum preserved in England, the United States of America and Germany.

The preparation of diphtheria and tetanus antitoxins is comparatively simple, as is also the preparation of scarlatina antitoxin, but the preparation of powerful staphylococcal antitoxin is proving difficult.

Other anti-sera of therapeutic value are those prepared against infection by meningococcus, pneumococcus, streptococcus, anthrax, clostridium welchii, *B. dysenteriæ* and leptospira icterohæmorrhagiæ. The use of several of these sera has been considerably restricted since the recent expansion of chemotherapy.

The Properties of Immune Sera

Von Behring's discovery that the sera of immune animals could passively confer immunity shows that such immune sera contain substances either different from those, or in excess of those, present in normal sera; and, in 1894, Pfeiffer showed that if cholera spirilla were injected into the peritoneal cavity of a highly immunised guinea-pig, the bacilli lost motility, became granular and swollen, and finally disappeared. This phenomenon became known as Pfeiffer's phenomenon, or Bacteriolysis. It was then shown by Metchnikoff and Bordet that a similar result occurred *in vitro* in a mixture of heated immune serum and cholera vibrios if, and only if, normal serum be added. As a result of these and subsequent researches it was recognised that two substances are present in immune sera, one of which is peculiar to immune and the other common to immune and normal sera. The former, originally called " substance sensibilitrice " (Bordet), is now generally known as *amboceptor* (Ehrlich); while the latter, formerly called alexin by French writers, is now usually known as *complement* (Ehrlich).

It will also be recognised that the specific change that has occurred in an immune serum is the presence of amboceptor, which can only act in the presence of complement. Amboceptor is specific in that it only acts in connection with the bacterium or inoculating substance which calls it forth (antigen), while complement acts independently and in connection with amboceptor of any kind.

Bacteriolysis also occurs in connection with typhoid immune sera, but many other varieties of bacteria are not subject to it; it can, however, be demonstrated that those organisms, immunity against which is unaccompanied by bacteriolysis, are susceptible to other properties of immune sera. In connection, however, with bacteriolysis must be mentioned hæmolysis. Bordet, in 1898, showed that if an animal be immunised with the corpuscles of another species the serum of the immune animal acquires the property of destroying the red corpuscles of that species. This phenomenon of hæmolysis has become of great importance, as it forms the indicating phenomenon in the complement deviation test of Bordet and Gengou, and of its modification the Wassermann reaction. Similarly many other cytotoxic sera can be elaborated by injecting emulsions of appropriate cells.

Agglutinins.—The agglutination of bacteria in the presence of the serum of an immune animal was first observed by Charrin and Roger in 1889, and as a specific reaction was described by Gruber and Durham in 1896, when

Grünbaum and Widal simultaneously recognised the great importance of this reaction from a diagnostic point of view in the case of typhoid fever.

If bacterial substance be introduced into the tissues of an animal, either by infection or injection, agglutinin is formed, and will cause agglutination of the agglutinable substance in an emulsion of the homologous bacteria. The bacterial substance is an antigen, and inasmuch as it appears to be identical with the agglutinable substance, the latter is also frequently alluded to as antigen.

Agglutination occurs in two stages. In the first, sensitisation of the bacteria by a specific substance in the immune serum, agglutinin, occurs: and in the second, the bacteria adhere together, in clumps, and gradually settle by gravity. Such clumping only occurs in the presence of low dilutions of salts, acting as electrolytes.

Agglutination does not affect the vitality of bacteria, and it occurs with living or dead bacteria. Agglutinins are relatively thermostable, though an agglutinating serum which has been heated to between 62° to 70° C., or which has been kept for a long time, may show "zones" of agglutination, *i.e.* that with low and high dilutions of serum agglutination occurs, but with intermediate dilutions there may be no agglutination.

Among motile bacteria two types of antigen occur, the flagellar termed H, and the somatic termed O, and the agglutinins resulting from each have different characteristics. H agglutination results in large loose flakes, and H antigen is usually labile at temperatures of from 80° to 100° C., while the O agglutination results in small compact flakes, and the antigen resists a temperature of 100°. The H agglutinins tend to persist in an animal serum for a long time, and also tend to reappear in a patient's blood during a non-specific fever, so care must be exercised in reading a moderately high agglutination as diagnostic of the existence of infections of the enterica group. These considerations do not hold in connection with diseases such as undulant fever, or dysentery, as the O agglutinins do not tend to persist, or to be regenerated by non-specific fevers. In general, H agglutinations are rapid and may be read after 2 hours. O agglutinations are less rapid, and are seen at their best after 12 hours. The H antigens are generally more specific than the O antigens. For example, the O antigens of *B. typhosus* and *enteritidis* are very similar, if not identical, but their H antigens are quite specific. In the case of the Proteus group, however, the O antigens are far more specific than the H antigens within the limits of the group.

Felix and Pitt have shown that in the case of the typhoid bacillus, and possibly also in Salmonella infections, there is a marked difference in smooth strains, in that some are far more virulent than others. They have shown that strains recently isolated tend to be virulent because they possess a "Vi" antigen in addition to the H and O antigens of the smooth type of typhoid bacillus. The virulence of any smooth type being examined is tested by the intraperitoneal injection of mice, the test dose being 100×10^6 bacilli.

Vi antigen is heat labile, and agglutinative tests to demonstrate its presence must be carefully carried out with living suspensions at body temperature.

In practice the patient's serum, in a series of graded dilutions, is mixed with suspensions of fresh or preserved bacteria, and the mixtures incubated at 55° C. The highest dilution of serum containing specific agglutinins varies within wide limits according to the nature and state of the infection.

With regard to the enterica group, the following are usually considered as diagnostic:

B. typhosus . . .	1 in 64 or higher.
B. paratyphosus A . .	1 in 32 or higher.
B. paratyphosus B . .	1 in 128 or higher.

For classifying bacteria recovered from patients, specific immune sera are employed, the titre of which will be known, and the limits of agglutination denoting pathogenicity indicated.

Precipitins.—To a filtrate of cholera vibrios Kraus added anti-cholera serum, and incubated the mixture at 37°. After some time flocculi appeared. The same phenomenon occurred with typhoid filtrates and anti-typhoid serum, and in the course of time precipitating sera were prepared against a great variety of antigens, animal, bacterial and vegetable. It was found by Danysz, subsequently elaborated by Dean, that optimal proportions of antibody and antigen played an important part in the successful performance of the test, and it appears that a relative excess of either hinders the reaction. The strength of sodium chloride solution used has some effect also on the reaction, and Dean has shown that 0·2 per cent. is the most favourable. Originally it was thought that precipitin so acted on antigen—precipitinogen—as to precipitate the protein thereof, but it has been shown by many workers that the bulk of the precipitate is derived from the proteins of the antiserum. This is in obvious contrast to the agglutination reaction, in which the agglutinated bacteria are clearly derived from the agglutinogen.

The reaction is turned to account in Forensic Medicine, in the recognition of human blood in blood stains, in the recognition of the meat of different species of animals, and even in the detection of cereal adulterants. Methods of estimation of the strengths of toxins and antitoxins are also based on the precipitin reaction.

Anaphylaxis.—When a foreign protein is introduced into an animal, hyper-susceptibility may be produced, which hyper-susceptibility can be demonstrated by injecting after the lapse of ten days a further—in itself non-lethal—dose of the protein, when there occurs a condition varying from slight signs of illness ranging through various stages of respiratory distress up to sudden death. A second injection of antitoxin after a sufficient interval may produce anaphylaxis. In consequence of this the question of desensitisation becomes of great importance. If at some period more than 10 days after an injection of antitoxin it is desired to give a further dose the presence of the anaphylactic state should be negatived. This is done by a skin reaction. A small quantity, say 0·05 c.c., of normal horse serum (or antitoxin) is injected intradermally, or rubbed into a scarified surface. There occurs, if anaphylaxis—or a toxic idiopathy to horse substance—exists, an urticarial patch sometimes progressing to a vesicular eruption with a surrounding area of erythema. This usually occurs within half an hour, but is occasionally delayed. If anaphylaxis be demonstrated, the patient should be desensitised. If time be not of paramount importance, 0·025 c.c. of antitoxin is administered subcutaneously, and the amount is doubled every half hour. After 1 c.c. has been given, subsequent doses are given intravenously until 25 c.c. in all have been administered. When serum is being given to a patient whose idiosyncrasy is unknown, 1 c.c. of 1 in 1000 adrenaline

in a syringe should be at hand lest symptoms of anaphylaxis should appear.

Serum sickness.—The use of horse serum, whether normal or immunised, and especially when given by the subcutaneous route, often leads to certain symptoms of a non-specific character on or about the eighth day after the first dose has been administered. These symptoms consist of an urticarial rash, with pruritus which may be very troublesome, mild pyrexia, pain in and swelling of the joints and some malaise. The urticaria may be concentrated about the site of injection of the serum, or it may be generalised. There may be local or general œdema, but the latter is uncommon; so, too, are albuminuria and swelling of the lymph glands. In some cases the local urticaria appears much earlier than the eighth day; it may appear within a few hours of the initial puncture, the more general symptoms showing themselves towards the end of the week. "Serum sickness" is rarely serious. Treatment is by anti-pruritic lotions, such as saturated bicarbonate of soda solution, or dilute carbolic acid (1 : 100) or lotio calaminæ co, and by aspirin internally. It may be added that if the joint symptoms precede the rash—a rare event—some difficulty may arise in diagnosis.

THE FILTRABLE VIRUSES

A number of human diseases, examples of which are small-pox, rabies, yellow fever, chicken-pox, measles and epidemic poliomyelitis, are now known to be caused by ultra-microscopic viruses, and, arguing from analogy, encephalitis lethargica is thought to belong to the group, though proof is still lacking.

As a rule, these viruses measure less than 250 $\mu\mu$, and some of them measure much less. Particles less than 250 $\mu\mu$ cannot be resolved by ordinary microscopes, though Barnard, by the use of a short-wave ultra-violet light and lens systems of quartz has resolved objects as minute as 75 $\mu\mu$. Great diversity of size occurs amongst the viruses. For instance, that of foot-and-mouth disease of cattle measures about 12 $\mu\mu$, while that of pleuro-pneumonia of cattle, which occurs in two forms, measures from 150 $\mu\mu$ to 250 $\mu\mu$. With few exceptions, however, the viruses are ultra-microscopic, and will pass through filters that fail to pass the ordinary bacteria. The properties of the porcelain filters used vary considerably, and other factors besides the actual diameter of the pores have to be taken into account. Thus, the substance of the filter may adsorb the virus, even though the pores of the filter may be sufficiently large for its passage. The flexibility of the virus, and the pressure of filtration may also introduce variable factors. It follows, therefore, that the failure of a virus to pass through a filter does not necessarily mean that its particles are too large.

Though differing much in size and effects, most of the viruses have characteristics in common. Many of the diseases caused by filtrable viruses in man and animals are highly infectious, very minute doses of virus causing infection—an infection that spreads with great rapidity. Many of the virus diseases produce special intracellular bodies, termed inclusion bodies. These may be restricted to one particular tissue, or may be found in various tissues. They may occur in the cytoplasm or nuclei of cells, or in both, and vary

greatly in size. In some diseases the diagnosis can be made histologically by the recognition of these bodies, *e.g.* the Negri bodies in rabies. The fact that the inclusion bodies have been seen to develop *in vitro* in tissue-cultures suggests that the filtrable viruses are intracellular parasites, in which respect they differ from the majority of bacteria.

Some of the virus diseases, such as yellow fever, dengue and papataci fever, are insect-borne.

With the exception of pleuro-pneumonia of cattle, no virus has been cultivated *in vitro* in the absence of growing cells, though many can be propagated in tissue cultures, and on account of this exception, many, if not the majority of workers, hold the opinion that pleuro-pneumonia is not a virus disease. Generally speaking, therefore, viruses can only be propagated by animal passage.

Most of the viruses produce an active immunity which is very lasting, and in some of the diseases immune serum confers passive immunity. In measles the injection of immune serum will produce such a degree of passive immunity as to prevent an attack of measles in a contact, but such immunity is not lasting. If given about 6 days after contact, a modified attack of measles of very attenuated type will occur, subsequent to which permanent immunity ensues. Valuable clinical results have been claimed by many workers from the use of immune serum in the pre-paralytic stage of poliomyelitis, but the exact value of the method is difficult to assess. With few exceptions all agree that immune serum has no effect when once paralysis has supervened. Recent work published by the Rockefeller Institute shows that fully inactivated yellow fever virus will not confer immunity. Inactivated distemper virus will, however, immunise, and is indeed used as a preliminary measure in the prophylaxis of distemper, and inactivated virus also confers immunity in cattle plague, fowl plague, rabies, influenza (in mice), herpes and some other animal diseases.

Most of the filtrable viruses are resistant to glycerine, especially at low temperature, and remain unaltered for long periods in 50 per cent. thereof at 4° C., whereas the lethal effect of glycerine on bacteria generally is well known.

Complement fixation reactions between virus and antibody have been shown in many virus infections, and flocculation has been shown in the case of variola virus. Ledingham has shown that homogeneous suspensions of the elementary corpuscles from vaccinia and fowl-pox are agglutinated by the sera of convalescent animals, while normal serum has not this effect.

The following list comprises some of the human virus diseases under three headings:

1. *Certain*

Small-pox.
Chicken-pox.
Mumps.
Yellow Fever.
Dengue Fever.
Phlebotomus Fever.
Rift Valley Fever.
Lymphopathia Venereum.
Herpes Febrilis.
Herpes Zoster.
Infectious Warts.
Acute Anterior Poliomyelitis.
Psittacosis.
Rabies.
Encephalitis (St. Louis Type).
Influenza.

2. *Almost Certain*

Measles.
Encephalitis Lethargica.
Molluscum Contagiosum.
Rubella.

3. *Possible*

Common Cold.

BACTERIOPHAGE

In cultures of bacteria certain areas of transparence, increasing at the expense of the growth, have been recognised for years by bacteriologists, but had not attracted much attention, being dismissed as due to autolysis, until, in 1915, Twort found that the process could be transferred to fresh cultures indefinitely. He also showed that the lytic principle could be transferred in filtrates free of bacteria. He discussed the possibility of an ultra-microscopic virus being responsible.

D'Herelle, in 1917, carried out an important research on the phenomenon, and maintained that the lysis was due to an ultra-microscopic virus, to which he gave the name "Bacteriophage."

Much controversy has arisen as to the true nature of bacteriophage, two main opinions emerging—(1) that it is a living ultra-microscopic virus, and (2) that it is a ferment supplied by the bacteria themselves. All authorities appear to agree that the actual lytic agent is an enzyme, but disagree as to the origin of the enzyme.

Bacteriophage is very resistant to many influences deleterious to bacteria. Many specimens require 75° C. for half an hour to ensure destruction. Fæces sealed up in tubes for more than a year may still show bacteriophage. D'Herelle found it withstood 1 in 200 perchloride of mercury and 1 in 100 carbolic for 3 days.

Usually a bacteriophage to one organism has no effect upon a different variety, though a certain amount of overlapping with allied strains occurs.

Bacteriophage can act as an antigen, and when injected into an animal produces an antiserum which inhibits the lytic action.

JOHN MATTHEWS.
HORDER.
A. E. GOW.

SECTION II

INFECTIOUS DISEASES

A. BACTERIAL DISEASES

The main results of the invasion and infection of the body by micro-organisms are discussed in the section upon infection and immunity. It is important to distinguish clearly between "invasion," "infection" and "intoxication," and the reader is referred to the section mentioned for the consideration of these several processes.

TOXÆMIA

This term is applied to the condition of a patient who is absorbing into the tissues and circulation toxins elaborated at some local site of microbic infection. The diseases caused by the specific microbes of diphtheria and tetanus are examples of toxæmia, the sites of infection being in the former disease the fauces or larynx, and in the latter disease the damaged tissue about a wound or abrasion. The symptoms of toxæmia are variable, and depend upon the special affinity that the toxins concerned have for certain tissues or organs. There are, therefore, general symptoms common to many microbic infections: fever, rigors, malaise, vomiting, pains in the back and limbs, headache, sweating, etc.; and special symptoms, such as are manifested by an affinity of the toxin for nerve structures (paralyses, spasms, delirium, etc.), or for the heart (arryhthmia, tachycardia, cardiac asthenia, etc.), and others.

One form of toxæmia of great importance is that known as *Focal Sepsis*. In this condition there may be few or no symptoms referable to the primary local site of infection, yet the resulting toxæmia may manifest itself as fibrositis, arthritis, anæmia, rarefaction of bone, loss of weight, pyrexia, or a combination of these. In focal sepsis, pyrexia is not a marked feature except in some cases of coliform infection of the urinary tract and in a minority of dental apical infections. The likely sites for focal sepsis are the nasal sinuses, the teeth, the tonsils, the bronchi, the gall-bladder, the appendix, the intestinal tract and the genito-urinary tract in both sexes. Chronic infection may lurk in certain of these situations even in the absence of gross macroscopic lesions. The tonsils, for example, though not enlarged, may contain pus or inspissated secretion in their crypts: a scarred and ragged tonsil, or one which has venules on its surface is always suspect, especially when the lymph node behind the angle of the jaw is palpable. The search for focal sepsis must be thorough and systematic, and may necessitate certain

instrumental investigations, *e.g.* X-ray examination of the cranial sinuses, of the apices of the teeth and the periodontal membranes; a cholecystogram; a catheter for a specimen of urine; a speculum for a view of the cervix uteri. Bacteriological examination of a post-nasal swab, or of the apex of a tooth at the time of extraction, or of a catheter specimen of urine, of any uterine discharge, of material obtained after prostatic massage, or of the stools, etc., may be required. The correct interpretation of the findings from such investigations is often difficult.

SEPTICÆMIA

Septicæmia is a condition in which the infecting microbe transgresses the tissue barrier at the site of local infection and invades the blood stream, multiplying therein, and thus continuing the infection in a general manner. The mere existence of the microbe in the blood stream is not to be considered as necessarily constituting a true septicæmia. Thus we know that during the first few days of an attack of typhoid fever, of pneumonia, and of certain other diseases, the specific microbe can very often be isolated from the circulation by blood culture. The more thoroughly the investigation of microbic infections by blood culture is undertaken, the more patent it becomes that at some stage or other the infecting organism exists in the circulation. *Bacteriæmia* is a convenient term by which to express the (temporary) existence of micro-organisms in the blood stream in other states than true septicæmia.

There are two main conditions of septicæmia in so far as this is related to the local infection. (1) The local infection may be obvious, the septicæmia clearly resulting from this; or (2) no local infection may be discoverable, or the local infection may be, at best, merely surmised. Even at a careful post-mortem examination the source of local infection may not be manifest in some of the cases illustrating this type of septicæmia.

The *microbes chiefly concerned in septicæmia* are *Staphylococcus aureus*, *Streptococcus pyogenes* (vel *hæmolyticus*) and the pneumococcus. Much less commonly the gonococcus, Pfeiffer's bacillus, the meningococcus, and *B. pyocyaneus* perform this rôle.

The *local infections tending to lead to septicæmia* are chiefly concerned with the throat (streptococcus), the uterus ("puerperal fevers"), the subcutaneous tissues of the hand and foot (infections during operations and post-mortem examinations, septic wounds, etc.), and the site of surgical operations (post-operative septicæmia).

Symptoms.—The symptoms in septicæmia vary much; there is also great variation in the intensity and course of the disease. Some of the worst cases from the point of view of prognosis are those in which physical signs are conspicuous by their absence, whether as regards the site of the local infection or as regards the development of secondary lesions (thromboses, visceral inflammations, etc.). Thus, in a case of puerperal septicæmia, if a careful examination of the pelvic organs reveals no defect in the uterus or its adnexa, and if no signs of local concentration of the infecting agent be found elsewhere, the case is likely to be one of great anxiety.

The symptoms include pyrexia, usually considerable in degree, and most often intermittent in character. Rigors are not uncommon, though by

no means constant. The patient is generally free from pain and local discomforts, but feels exhausted and very ill. The mental state is usually normal; in some cases the outlook is disproportionately optimistic. Sweats are common, especially if the pyrexia is markedly intermittent. Diarrhœa may occur. Some degree of general abdominal distension is common. The spleen may be palpable. The pulse is quickened, the pulse tension lowered, and there may be subjective cardiac disturbances related to the toxic myocarditis which is an invariable result of the main pathological process. A progressive hæmolytic anæmia is one of the most striking features in most septicæmias, both clinically and upon examination of the blood. The leucocytes vary a good deal, and their number constitutes a helpful point in prognosis: the smaller the count the worse the outlook. Loss of weight is not a noticeable symptom, except in cases which become "chronic," nor must the absence of this feature lead, of itself, to a favourable view as to the outlook. Erythemata are often seen, both diffuse and discrete, especially in cases due to streptococcus infection; they are prone to be evanescent. Purpura is not uncommon. Joint pains and swellings are also common, and these not seldom disappear without any metastatic abscess formation. Pleurisy and pericarditis are not infrequent in staphylococcus infection.

Prognosis.—The prognosis is serious in all cases of septicæmia, though less so now than formerly. This is partly because, as the result of the earlier and more extensive use of blood cultures, more cases are recognised, and partly because the exploitation of chemotherapy has added useful treatment in many instances of the disease. Of serious import are the following: rigors; the absence of signs of the local infection, the absence of a leucocytosis, rapid progression in the associated anæmia, early dilatation of the heart, vomiting, pleurisy, insomnia, and delirium or stupor.

Treatment (see pp. 16–19).

PYÆMIA

When septicæmia is complicated by the formation of multiple abscesses, or of multiple foci of tissue necrosis, the clinical condition is conveniently spoken of as pyæmia.

All pyæmic patients are septicæmic, but not all septicæmic patients are pyæmic. Some septicæmias tend to be pyæmias from the first, in other cases there is a late development of the pyæmia after a period of simple septicæmia lasting for days or, it may be, weeks. In the great majority of cases of pyæmia the primary infection is obvious.

There are three types of pyæmia according to the anatomical distribution of the primary infection in relation to the circulation.

1. *Systemic venous pyæmia.*—This is the form which is seen in osteomyelitis due to *Staphylococcus aureus*, in suppurating wounds (staphylococcus, streptococcus, *B. coli*, etc.), in suppurations of the urinary and bronchial tracts and in suppurating dermatitis and cellulitis. The metastatic abscesses form in the lungs, kidneys, perirenal tissues, joints, bones, and, less often, in the heart wall and in the brain. The symptoms are those of a severe septicæmia together with those of the disease-processes set up by the focal events just referred to. Some of the cases are of long duration, and when this is so the patient is apt to become very emaciated.

2. *Portal pyæmia* (suppurating pylephlebitis).—This is the form of pyæmia resulting from certain pyogenic infections in the alimentary tract—rectum, colon, appendix, gall-bladder and elsewhere. The infection follows in ascending fashion the radicles of the portal vein, setting up a septic thrombosis and ultimately causing multiple abscesses in the liver. The symptoms are those of a severe febrile illness with acute or subacute abdominal signs, moderate jaundice, and an enlarging liver. The diagnosis is sometimes difficult, but when indubitable the prognosis is extremely grave. The micro-organisms concerned are generally of the coliform group, or streptococcus; mixed infection is not uncommon.

3. *Arterial pyæmia.*—This form of pyæmia is seen in septic endocarditis, with which disease it is, for the most part, identical. The focus of primary infection, so far as the pyæmic process is concerned, is the endocardium, and especially of the valves, where colonisation of microbes takes place, and whence innumerable septic emboli proceed into the arterial system. Seeing that in the great majority of the cases this focus occurs on the left side of the heart the emboli, if they set up metastatic areas of infection, do so in organs and tissues supplied by the systemic vessels: spleen, brain, kidneys, limbs, etc. In the less common instances, where the endocarditic focus is on the right side of the heart, the infection being grafted upon a congenital lesion, the emboli lodge in the pulmonary vessels, producing multiple infarcts in the lung, usually with associated pleurisy.

The microbes most often causing septic endocarditis are organisms of feeble virulence (streptococci of the salivary and fæcal groups, or *H. influenza*); this fact accounts for the infrequency of suppuration in the infarcted areas occurring in this disease. When, however, the endocarditis is due to such virulent microbes as *Staphylococcus aureus* and *Streptococcus pyogenes*, abscess formation does occur in the infarcts.

Treatment. (see pp. 16–19).

TERMINAL INFECTION

Micro-organisms which are found in the tissues in the course of a post-mortem examination are related to them in four different ways: (i) They may be the primary infection leading to the disease-process which causes death. (ii) They may be present as secondary infection, in association with the primary infection, and they may or may not be largely responsible for the death of the patient. (iii) They may be present as a "terminal infection," the disease-process from which the patient suffered being not itself manifestly of microbic origin, but one tending to lower the tissue resistance to infection. The terminal infection in these cases generally, as the name implies, precipitates the lethal event, or actually causes it. (iv) They may be present merely as an agonal or sub-mortem invasion, or even as a post-mortem invasion. It is necessary carefully to distinguish between the last two of these relations. The mere isolation of organisms from certain tissues (*e.g.* the mucoid material of the middle ear) in the post-mortem room does not prove that they were present in these situations during life, still less that they were operative by way of actual infection. It is even doubtful if the cultivation of organisms from the blood of the heart, or from the cerebro-spinal fluid, after death, give evidence of infection during life,

though some authorities consider that it does. Much depends, of course, upon the conditions at the time of the investigation.

Terminal infection does certainly occur, however, in well-recognised form, and quite distinct from sub-mortem invasion. The organisms most often responsible for the condition are the less virulent strains of streptococci (*S. salivarius* and *S. fæcalis*), the coliform group, staphylococci and the tubercle bacillus. *B. proteus* and *B. aerogenes capsulatus* are also found to operate in this manner at times.

The disease-processes in which terminal infection frequently occurs are cirrhosis of the liver, granular kidney, diabetes, leukæmia and morbus cordis. There is a latent form of septic endocarditis (most often streptococcal in origin) which is also of the nature of a terminal infection. Serous membrane tuberculosis, and especially peritonitis, is quite common in cirrhosis of the liver. Many of the patients in whom this terminal infection occurs are so ill at the time the event arrives that it frequently goes undiscovered, partly because their responses to infection are feeble and partly because clinical examination is difficult.

STREPTOCOCCUS INFECTION

The streptococci form a group of micro-organisms in which the different members vary greatly in virulence. They also vary in their morphological and cultural features and in their biochemical reactions. There is, therefore, no little difficulty experienced in any effort at successful classification. Broadly speaking, there are two main groups of the microbe. (1) There is the highly virulent group called *Streptococcus pyogenes* to which the alternative name *Streptococcus hæmolyticus* is applied, on account of its property of hæmolysing when cultivated on blood-agar. (2) And there is the more feebly virulent group *S. viridans* including the variants *S. salivarius* and *S. fæcalis* of some authorities. The first type is usually seen in long and curling chains when recently isolated, and the second is usually seen in short chains of two, four, or some number of relatively few members.

S. pyogenes (vel *S. erysipelatosus*; *S. hæmolyticus*) is the causative microbe in erysipelas, in acute abscess formation, in acute cellulitis and lymphangitis, in severe operation and post-mortem infections when these are of streptococcus origin, and in the more virulent streptococcus infections complicating the puerperium, influenza, scarlet fever, and some other specific fevers.

S. viridans (*S. salivarius* and *S. fæcalis*) is found in association with pyorrhœa alveolaris, with secondary streptococcus infection in rheumatic fever, with arthritis occurring in connection with focal infections, and with most chronic and subchronic infections of streptococcal origin. The streptococci found in the heart valves, and in the blood stream in cases of subacute septic endocarditis, are for the most part of this nature.

The clinical results of streptococcus infection vary according as the infection is by the first or by the second of these types of the microbe. In infection by *S. hæmolyticus* the disease-process is usually acute and often fulminant. Septicæmia results not infrequently, and pyæmia is not uncommon. If endocarditis results from the infection and embolism occurs, the infarcts

suppurate. In infection by *S. viridans* the disease-process is prone to be chronic, or at most subacute. Septicæmia is uncommon, except in association with endocarditis, in which condition embolic infarcts proceed to coagulative necrosis, but not to abscess formation.

Treatment (see below.)

TREATMENT OF THE FOREGOING INFECTIVE PROCESSES

A. General Measures.—These include rest, ample nutritious diet, abundant fresh air, the control of fever by hydrotherapeutic means, and the maintenance of a cheerful outlook in the patient and in his medical attendant. The nursing of these "septic" patients is of great importance, and experience of similar cases is a great asset.

B. Drugs.—Formerly very intractable, many of these diseases have recently come largely under control by the use of the sulphonamide group of bacteriostatic drugs. Sulphanilamide; sulfanilamide, U.S.P.; (colsulanyde; prontosil album; streptocide; sulphonamide P.) is the more efficient drug in combating infection due to streptococcus hæmolyticus. Sulphapyridine (Degenan; M. & B. 693) is especially useful against the pneumococcus and the gonococcus. Meningococcus and coliform infections, other than the typhoid group, respond well to either. Streptococcus viridans and staphylococci, so far, have proved much more resistant to chemotherapy. Whatever preparation is chosen it should be given intensively and the oral route is to be preferred whenever possible. Foods and drugs containing sulphur (therefore eggs and salines) and strong purgatives are to be avoided during their administration. In most cases the following scheme applies for an adult: grm. 2 of the drug are given as an initial dose, followed by grm. 1 every 2 hours until grm. 20 have been administered. When rapid absorption of the drug is essential it may be dissolved in lemon juice or citric acid; if more slowly, the tablet is given uncrushed. Subsequent dosage depends upon the degree of cyanosis produced and the general state of the patient.

Cyanosis consequent on the administration of sulphanilamide may be due either to methæmoglobinæmia or to sulphæmoglobinæmia, the latter being more frequent; when following sulphapyridine (Dagenan; M. and B. 693) it is usually the result of methæmoglobinæmia (Campbell and Morgan). Methylene blue, 0·5 grm. in cachet twice daily by mouth, will diminish cyanosis due to methæmoglobin but is without effect on sulphæmoglobin, which may persist for several weeks after the drug has been discontinued. Phenacetin, and other similar drugs, which may produce methæmoglobin should not be prescribed at the same time as a member of this group; aspirin may be employed to relieve pain. Vomiting is often troublesome; it may be relieved by draughts of sodium bicarbonate solution. Occasionally it is so severe that administration of the drug by mouth must be (temporarily) abandoned in favour of the intramuscular injection of the soluble sodium salt in 10 per cent. solution. Urticaria and morbilliform eruptions may occur. Tachypnœa and hæmaturia are seldom serious complications, but the development of acute hæmolytic anæmia or of agranulocytosis calls for immediate suspension of the drug. It has been noted that a mild grade pyrexia may persist after an acute febrile illness has seemingly responded successfully to this form of

chemotherapy—a "sulphonamide fever" which settles when the drug is stopped.

To control the progressive anæmia, over and above the general measures, arsenic is perhaps the most useful remedy; it may be given conveniently as sodium cacodylate, gr. 1, once or twice daily, in the form of intramuscular injection. The writers often combine it with nucleic acid, a useful stimulant to leucocytosis, in the following formula:

℞ Sod. cacodylatis, gr. 1.
Ac. nucleici (sat.) ad min. 15.

When the leucocytosis in pyogenic infection is small, intramuscular injection of 10 c.c. of pentnucleotide may serve to increase it; the injection must be made very slowly and may be given twice in the 24 hours.

C. Surgery.—All abscesses developing in the course of a pyæmia must be drained forthwith, either by aspiration or by free incision, the former for preference and, if practicable, especially in patients who are very ill. When dental extractions are indicated in the treatment of focal sepsis, not more than two or three teeth should be extracted at one sitting; a local anæsthetic should not be employed save when regional injection (nerve block) is possible. In such a case the site of injection must be at some distance from the site of sepsis, as there is grave danger of spreading sepsis by injecting into a septic tissue. Experience proves it to be most unwise to remove teeth at the same time that the patient is undergoing any other surgical operation.

D. Transfusion of Blood.—This measure may be helpful in particular cases, especially to combat severe anæmia, or so to improve the patient's general condition that he may be in a better state to derive benefit from other remedies.

E. Specific Therapy.—Measures which may be used to combat the infection by way of immune therapy are, it goes without saying, of much greater theoretical importance than those which act non-specifically. Unfortunately our knowledge of efficient specific remedies grows very slowly, and there are many gaps and guesses in it. All the same, careful consideration should be given in every case to the nature of the infection, and to the question if some form of specific treatment, whether by immune serum or by vaccine, or by both, may not be of service.

1. *Streptococcus Infection.*

(*a*) *Hæmolytic streptococcus infections.*—These include acute septicæmia, puerperal fever, certain complications of scarlet fever, erysipelas and acute cellulitis, in which "scarlet fever" antitoxin serum and sensitised *Streptococcus pyogenes* vaccine are the agents now chiefly used in immuno-therapy. Scarlet fever antitoxin has largely replaced the original *Streptococcus pyogenes* antiserum, but if no benefit is observed after the use of the former remedy recourse should be had to the latter. Concentrated serum should be given as early as possible: 10 or 20 c.c. intramuscularly, repeating 10 c.c. eight hourly as need be. Sensitised vaccine is made from strains of *S. pyogenes* recently isolated from several sources, and may be given in doses of 100, 250 and 500 millions subcutaneously on three successive days.

(*b*) *Streptococcus viridans infections.*—These are not amenable to serum

treatment. These organisms are frequently concerned in the ætiology of focal sepsis. When pyorrhœa alveolaris is the cause of focal infection, the material from which the vaccine is prepared is to be taken from the apex of an infected tooth immediately after extraction, and not from pus lying about the neck of the tooth which is always the nidus of secondary infections, erroneously thought to be causative of the condition. The initial dose may well be 5 million cocci, followed at intervals of 7 to 10 days by gradually increasing doses—10, 25, 50 and 100 million cocci. Even larger doses may be profitably given should no " reactions " occur.

Fibrositis, arthritis and allied conditions.—In embarking on the treatment by vaccine therapy it has to be realised that such treatment will be brief or long according to the time the lesions have existed. In this connection, moreover, it should be borne in mind that even if the lesions are not of long standing, the toxæmia leading to those lesions may be of much longer standing than at first suspected.

Recent cases of infective arthritis only rarely present themselves for treatment, but there should be an increasing tendency in this direction.

2. *Staphylococcus Infections.*

Chronic local infections.—These consist of boils, carbuncles, pustular acne, onychia, sycosis, otitis media (sometimes), eczema (sometimes), ciliary blepharitis, suppurating Meibomian cyst and certain discharging sinuses. Furunculosis and certain other staphylococcal infections were the first to be treated systematically by Wright's method of specific inoculation, and, as a class, these infections yield, with care, fairly satisfactory results.

A guarded prognosis must, however, be given in connection with each of the other forms of staphylococcus infection. And in all the cases care must be exercised to see that the general points in treatment are receiving attention. If these be omitted, failures will frequently be met with in those cases in which the infective factor is not very dominant. In acne, for example, it is unlikely that vaccines alone will affect a cure if local measures be omitted. Here, as always, the inoculations must be regarded as adjuncts to the general programme of treatment, not as a substitute for it.

In the case of suppurating wounds or sinuses, vaccine treatment should never be expected to take the place of efficient drainage, which must in all cases be secured in the first instance.

In the matter of *dosage* most workers agree in using a dose of 100 million in beginning the treatment of a straightforward case. If improvement follows, this is succeeded by doses of 250 to 300 million with intervals of 8 to 10 days. Relapses are quite common, and require a good deal of careful management. Either the doses are not sufficiently large, or the inoculations are repeated too frequently. Each case must be considered on its merits. In the experience of the writers there is often a tendency to stop the treatment too early. It is often of value to " space " the doses more widely as the treatment proceeds.

In the treatment of acne, a similar plan may be followed, or a mixed vaccine of staphylococcus and the " acne bacillus " employed. In sycosis the response to these doses is only satisfactory if the case is treated early. If it is of some standing, and much induration is present, the vaccine should be tentatively increased to 2000, 5000 and even to 8000 million cocci. The same rule applies to many cases of chronic acne. Once more, let it be urged

that it is courting disappointment to neglect necessary methods of treatment when dealing with these chronic skin infections.

It has become customary to employ stock vaccines in the treatment of furunculosis and other staphylococcus infections, and, as staphylococci appear to differ little in the matter of strains, the success of this convention justifies the practice. If, however, success is not attending the treatment, an autogenous vaccine should in all cases be obtained. This is perhaps more important if the infection is due to *S. aureus* than if to *S. albus*.

Acute local infections.—A single dose of vaccine certainly tends to cause an acute boil or carbuncle to abort, but it should be administered early to secure this effect. The dose chosen is usually 1000 million of mixed staphylococci. Care must, of course, be taken to give no dose of this size in the presence of any constitutional symptoms which may indicate a general infection. But a general infection may quite probably be avoided by the above-mentioned prompt treatment. In the case of boils of the external auditory meatus and other very painful situations, the more rapid development and consequent resolution of the lesion following administration of a vaccine are of considerable advantage.

Poisoned fingers and acute abscesses due to staphylococcus infection require much smaller doses. They are best treated by (say) 50 to 100 million cocci, with 3 or 4 days' interval.

ERYSIPELAS

Definition.—An acute specific disease, due to infection of the skin by *Streptococcus pyogenes*, leading to local dermatitis and constitutional symptoms, of which fever and toxæmia are the most prominent.

Ætiological Factors.—Infection by *S. pyogenes* is certainly the essential factor. The more carefully the cases are examined and the patients questioned the more certain it becomes that in the great majority of them some abrasion, it may be very slight, is present in the skin at the site of infection. This abrasion may be an actual wound, whether of a surgical operation or not. More often it is less apparent—a scratch, an insect bite, the chafing of a foot by a badly fitting shoe, etc. Contact by the human hand during the infliction of these slight injuries is not uncommonly a feature in the case.

Bad hygienic conditions seem to contribute to the incidence of the disease, such as defective sanitation and ventilation in public institutions. Formerly the disease was rife, almost epidemic, in hospitals, and chiefly amongst the surgical patients. During the puerperium a woman is prone to erysipelatous infection.

The disease is said to have a seasonal incidence (January to May), and Newsholme showed that the curves of its prevalence conformed somewhat to those of scarlet fever and acute rheumatism. We do not know, however, the reasons for this.

The disease is more common in women than in men, perhaps because of the puerperal cases. Alcoholism is a great predisposing factor. Gout is another factor rather commonly present.

Symptoms.—There is an incubation period of some 2 to 5 days. The onset is usually abrupt, often with a rigor (or a convulsion in little children)

certainly the most important, feature of gonococcus infection is its obstinate persistence. This organism is, relatively to many others, responsible for few deaths as the direct result of acute infection, but this low mortality ratio is compensated by a high degree of morbidity incidence. Once the invasion of gonococci has led to definite tissue infection, this is prone to become very intractable, resisting the most persevering and thorough efforts at defeating it. Gonococcus infection is too often measured by years rather than months, though there are oft-times intervals of comparative freedom from toxic effects upon the infected organs. Such a lesion as acute iritis, for example, may appear in the subject of old gonococcus infection, several years after the primary invasion, and the evidence that the inflammation is due to this source may be unimpeachable. The writer has known this to happen fourteen years after the primary urethritis. But it is sometimes very difficult to exclude a recurrence of the initial infection.

Once the inflammatory response to infection has passed the urethral stage, it is often very difficult to obtain direct bacteriological evidence of the nature of a suspected gonococcus infection. The number of organisms concerned may be small, they are often deeply embedded in the tissue spaces and cells, and they may not be shed into any effusions or secretions that chance to be available for clinico-pathological investigation. As yet, the indirect diagnostic methods (agglutination, complement fixation, etc.) are scarcely of sufficient trustworthiness to supply the data left lacking by the negative direct bacteriological results referred to.

Secondary infection, especially by staphylococci, streptococci and diphtheroid organisms is very common.

Clinical Results of Gonococcus Infection.—These may be considered under three headings: the results of the primary infection, the results of the zone of immediate spread, and the results of general dissemination.

(i) *The results of the primary infection.*—These are acute and chronic urethritis (with gleet); cervicitis; and conjunctivitis. These lesions do not come under consideration in a text-book of medicine.

(ii) *The results in the zone of immediate spread.*—These include peri-urethritis (and abscess), prostatitis, epididymitis and vesiculitis in the male; salpingitis with salpingo-ovaritis in the female; and cystitis in both sexes. In both sexes, again, the peritoneum may become infected locally, a much more common and important event in females than in males, as might be expected for anatomical reasons. Indeed, in women, varying grades of pelvic peritonitis, with plastic inflammatory changes, constitute perhaps the greatest bane of gonococcus infection, both from the physician's and the surgeon's point of view. Chronic ill-health, adhesions that permanently handicap the functions of the pelvic viscera, and acquired sterility are amongst the disabilities accruing therefrom. In the male, late results of infection are scarcely less serious by way of nemesis: urethral stricture, chronic prostatitis, "ascending" pyelitis and secondary colifo~m infection of the urinary tract.

(iii) *The results of general blood infection.*—These may be subdivided into a true septicæmia and pyæmic manifestations.

(*a*) *Septicæmia*, though rare, has been definitely established clinically and clinico-pathologically, both in America (Thayer, Blumer, Ahmann) and in England (Horder). Endocarditis, of a progressive and "ulcerating"

form, is present in most of the cases, and, though recovery has taken place in one or two known instances, the disease is generally lethal. Diagnosis turns upon the isolation of the organism from the blood stream in a case presenting the clinical features of septicæmia.

(*b*) ***Pyæmic manifestations.***—Of these the most important is ***gonorrhœal rheumatism,*** with associated arthritis, fibrositis, teno-synovitis and allied lesions (see p. 1335). Gonorrhœal rheumatism must be considered to be a form of gonococcus pyæmia, at least when seen in its acute and sub-acute types. The organism has been recovered from the affected joints in a large number of the cases, and in a few from the blood stream as well as from the joints. ***Spondylitis deformans*** has been traced to (old) gonococcus infection in a considerable proportion of cases.

Pericarditis and ***pleurisy*** have both been described as remote results of gonococcus infection.

Iritis, already referred to, is prone to be of the recurrent type. It is often ascribed to syphilis when it is much more probably of gonorrhœal origin.

Treatment.—In acute infections the use of sulphapyridine has proved very successful. In chronic infections the same remedy should be given a thorough trial, but the results are much less favourable. Antigen therapy may be cautiously attempted.

COLIFORM BACILLUS INFECTIONS

Continued and extended observations, made possible by the introduction of newer differential bacteriological methods, have resulted in the recognition of a large and important group of bacilli, called the coliform group, including members which differ as widely in pathogenicity as these two originally described bacteria, but also including the organisms of bacillary dysentery, the paratyphoid organisms, the various bacilli causing "food-poisoning," such as the Aertrycke bacillus, *B. enteritidis* of Gaertner, *B. suipestifer* and others.

Modes of Infection.—In health, coliform bacilli are confined to the intestine. The modes of infection of parts of the body other than the bowel are at times very apparent, at others obscure. Of any particular tissue there are three possible routes of infection: (1) The *direct* route, that is, by the immediate transference from the bowel to the infected area; (2) by the *lymphatics*; and (3) by the *blood stream.* In some infections, *e.g.* of the gall-bladder, pericolic tissues, pelvic cellular tissue, etc., the direct route is no doubt the one generally followed. Of the two indirect routes, however, some doubt exists as to the more likely one in certain cases, such as infection of the urinary tract especially; in some instances of this latter important condition it is clear that invasion takes place again, directly, through the urethra. The cystitis which still occasionally follows the use of the Catheter illustrates this; and the greater frequency of coliform bacillus cystitis in little girls than in little boys has been adduced in favour of this route. In the acute pyelitis complicating or following typhoid fever, it is highly probable, though not certain, that infection proceeds via the blood stream to the kidney, and thus to the pelvis. But in those acute primary infections of the urinary

tract, which are so common in both sexes, the mode of entry of the bacillus to the kidney pelvis is problematical.

Sites of Infection.—The sites of infection by coliform bacilli are very numerous. Mention will only be made here of those which form the basis of important disease-processes which demand recognition and treatment in practice.

1. The *bowel* itself may be the site of infection. This may take place (*a*) because the infecting strain of coliform bacillus has absolute pathogenic qualities; or (*b*) because the virulence of one or more of the usually saprophytic strains is increased; or (*c*) because the resistance of the mucosa is lowered by chemical or physical changes or by infection by another pathogenic microbe. From one or more of these factors acute or chronic *enteritis*, *entero-colitis*, or *colitis* may ensue. Gaertner bacillus poisoning, the result of eating contaminated food, is an important instance of (*a*), and perhaps also of (*a*) combined with (*c*). Some cases of *cholera nostras* appear to be due to coliform bacillus infection, and probably most sporadic cases of acute colitis. There is no great obscurity attaching to these infective processes. In a consideration of many cases of *chronic colitis*, however, the exact rôle of coliform bacilli is very obscure indeed; and this, even when we exclude a large number of cases of bowel defect to which the name *colitis* should never be applied at all. It is probable that many of the patients said to be suffering from *intestinal intoxication* are in reality the subjects of subinfection by coliform bacilli. But at present our criteria for judging accurately of such a condition are lacking. Mere qualitative bacteriological investigations of the fæces in such cases yield at most presumptive evidence, and quantitative investigations take us very little farther. We await some method of estimating tissue infection by the coliform group more constant than agglutination, which is rarely present in chronic cases, and is, therefore, of little use as a guide.

2. *Gall-bladder sepsis* is closely associated with coliform bacillus infection It is commonly held that subinfection of the gall-bladder by this microbe is one of the important factors in the evolution of cholelithiasis. However this may be, it is certain that coliform bacilli are frequent infecting agents in *cholecystitis*, both acute and chronic. The fact harmonises with the known frequency of gall-bladder infection during typhoid fever. The association of coliform infection of the urinary tract and of the gall-bladder is of common occurrence, and the removal of a gall-bladder which is the seat of chronic inflammation may react favourably upon the coincident urinary infection,

3. *Appendix inflammations*, *diverticulitis*, *pericolic suppuration* and local peritonitis complicating intestinal conditions, are all of them associated with coliform bacillus infection, and in many instances with this alone.

4. The *urinary tract* is infected with great frequency, with how great frequency we are only now realising, as the result of systematic cultivation of the urine in doubtful cases of the condition, and in obscure cases of illness in which no such condition is at first suspected. It is important to note, however, that the mere presence of coliform bacilli in the urine—it is assumed that catheter specimens only are being dealt with, or that, when this is not the case, there is good evidence that the bacilli actually come from the

bladder—does not establish an actual urinary tract infection. *Coliform bacilli* in the urine may signify one of either of the following conditions: (*a*) The elimination of the bacilli from the body through the kidney, without infection either of this organ or of the urinary tract; this process is usually of brief duration, and may be intermittent. (*b*) The excretion of bacilli (with pus) from an infected kidney or from some focus of infection adjacent to the urinary tract (prostate, urethra, pericolic tissues). (*c*) True infection of the urinary tract (pyelitis, pyelonephritis, cystitis, pyelo-cystitis). (*d*) Bacilluria.

Concerning (*a*) and (*b*) no more need be said in this place, but (*c*) demands more consideration.

Coliform Bacillus Infection of the Urinary Tract.—The cases met with may be conveniently described as falling into three groups.

(i) *Acute cases.*—In the majority of these cases the infection appears to arise in the pelvis of the kidney; some are undoubtedly vesical in origin; in not a few it is uncertain where the infection begins. The disease is at times quite fulminating in its acuteness, being ushered in by rigors, high fever (103° to 105°), delirium and great drowsiness. More often the symptoms are abrupt and severe, but not alarming. There may be pain and tenderness in the loin, and one or other kidney may be tender under bimanual examination. But in more cases than not there is a striking absence of both physical signs and focal symptoms, so that, unless the existence of the disease is borne in mind, and the urine is examined carefully, the patient is thought to be suffering from "influenza."

In those cases in which the bladder is, from the first, markedly affected, symptoms of *dysuria* are present—frequency, pain and strangury. Such symptoms draw attention, of course, to the nature of the process.

The *urine* shows a great range of variations in its features. There may be a fairly frank *hæmaturia*, a fact which is not so widely known as it should be: coliform bacillus infection is the explanation of a large number of obscure cases of hæmaturia. The amount of pus is very variable—it may be very considerable, or it may be represented only by leucocytes seen on microscopic examination. In very severe cases portions of the bladder mucosa may be shed in the form of sloughs, but this is uncommon. Like the pus, the bacilli vary greatly in the degree to which they are present in the urine; in some cases they are so abundant as to constitute by far the greater part of the total sediment. The colour and amount of the urine depend upon the degree of pyrexia and the amount of fluid ingested. Constipation is the rule, the tongue is generally covered by a creamy fur, and anorexia is common. As in so many acute coliform bacillus infections, the mental state tends to depression.

The disease is often a strikingly dramatic one in children; it is one of the few conditions which may be associated with a rigor, and there is a maximum of febrile reaction with lassitude and even stupor, and a minimum of serious effect upon the vital organs. It is not very uncommon to see a temperature of 105° or 106°, with big intermissions; the child is very ill during the pyrexial stage and comparatively well when the temperature falls. Marked drowsiness, even stupor, may occur; such a condition, indeed, should raise a suspicion of this infection in the absence of signs of meningitis. The disease is not very uncommon even in babies.

The course of the disease varies much. Prompt recognition of its nature, leading to appropriate treatment, usually results in defervescence and the disappearance of pus and bacilli from the urine in 7 to 14 days. But some of the cases last many weeks; it is fair to say that this is not seldom due to failure to diagnose the condition, or to employ efficient measures of treatment.

Relapses are very common even when, with chemotherapy, the urine is rendered sterile and the symptoms are relieved. Of *complications*, *prostatitis* is perhaps the one most often seen; *epididymitis* occurs less often, but is a very definite condition; *urethritis* may occur; *pyelonephritis*, especially in young children, may be the precursor of renal failure in later life. It is interesting to record that epididymitis may be the first symptom of the disease. This has, in the past, been frequently mistaken for tuberculosis.

(ii) *Recurrent cases.*—A not uncommon type of case is that in which symptoms of acute or of subacute infection occur at intervals over a number of years, the condition of the patient and of the urine being natural between the attacks. Recurring hæmaturia, thought to be due to acute nephritis, to tuberculosis or to calculus, is sometimes due to this condition. The probable source of these re-infections in any individual case is the colon.

(iii) *Chronic cases.*—These are either (*a*) the sequelæ to acute attacks that have never completely resolved; or (*b*) they arise insidiously; or (*c*) they follow instrumental procedures or operations upon the urinary tract; or (*d*) they complicate mechanical defects, such as stricture (acquired or congenital), enlarged prostate, and hydronephrosis; or (*e*) they occur as secondary infections in cases of renal or vesical calculus or of tuberculosis.

The symptoms in these chronic cases vary greatly. In one group it is the general toxic state that is the main feature—a sallow complexion, loss of tone, a low blood pressure, colon dyspepsia, headache and backache. In another group the local symptoms predominate—increased frequency of micturition, which may be extremely trying, pain during or after the act, and referred pain and discomfort in the vesical zone. In a third group there is little or no interference with health, general or local; but a vivid realisation of the existence of the condition troubles the patient's mind, leading sometimes to a state of bladder neurasthenia.

The urine in chronic infections shows as much variety as do the symptoms. The characteristic "fishy" odour is rarely absent; the reaction is generally acid, but infection by *B. proteus* renders the urine strongly alkaline; the amount of pus present may be very little or may be considerable, but the degree to which the patient is troubled by no means corresponds to the degree of pyuria; mucus is in excess; bacilli are constant and, like the pus, are very variable in quantity. Hæmaturia is uncommon in chronic infections, but it is easily induced by instrumental investigation, as are also "flares-up," of the chronic state, with the production of rigors, high fever, severe malaise and relative anuria. For this reason, methods of differential diagnosis which do not involve instrumentation should be employed before the patient is subjected to cystoscopy or ureteric catheterisation.

Bacilluria.—This term is properly applied to a urine which is loaded with bacilli, but in which there is no pus, or, at most, a few leucocytes seen on microscopic examination. It is a state of kidney elimination of bacilli rather than a condition of bacillary infection. It is usually of short duration. The appearance of the urine is characteristic: shimmering when agitated

and viewed by transmitted light. The smell already referred to as so typical of colon bacillus urinary infections is usually present here also.

OTHER SITES OF COLIFORM BACILLUS INFECTION.

(i) *The uterus and Fallopian tubes* are sometimes the site of infection, as in puerperal sepsis; but the infection is then usually a mixed one, with streptococci.

(ii) Some situations quite remote from the bowel are now and again infected by coliform bacilli—the *middle ear*, the *pleura*, the *bronchial tract*, *bones* and *joints*. Infection of the middle ear occurs as the result of impure water in swimming-baths.

B. COLI SEPTICÆMIA, unless it occurs as a terminal event, in which form it is not at all uncommon, is rare. When it does occur, however, it is by no means always fatal. Septic endocarditis, due to coliform bacilli, is rarer still; the only cases coming under the writers' notice have been of the nature of a terminal infection.

Treatment.—The treatment of cases of coliform bacillus infection may be considered under three heads—general, local and specific measures.

1. GENERAL MEASURES.—In all acute cases the patient is kept in bed, so as to ensure rest and warmth. Both of these are essential, and even in chronic cases it is of great importance to avoid cold and fatigue. As the *bowel* is the source of nearly all the infections, attention to it is paramount. It is quite impossible to say in how many seemingly unlikely cases the intestine, and especially the colon, will be found to give the clue to treatment, provided the possibility be borne in mind. Especially is this the case in acute and subacute cases. To correct constipation is not enough—constipation may not even be present—efforts must be made to change the bowel contents in such a way that they are no longer so good a nidus for growth of the bacillus. This is best attained by a *diet* which is low in total protein content; meat, eggs and raw milk are excluded entirely; junket, whey, buttermilk and cream being allowed. The following articles of food are also allowed: macaroni, boiled rice, raw and cooked fruit, salads, and lightly cooked green vegetables, jams, marmalade, honey, cold fat bacon and ham, and chicken and white game occasionally. Wholemeal bread and oatmeal porridge are recommended. On such a diet the consistency of the stools soon improves, and they lose their ill-digested appearance; as also mucus and sandy deposit, if these were present. They also become much less offensive to the smell. Plain drinks are encouraged—preferably between meals. If the case be acute, with considerable pyrexia, the practitioner generally considers milk the staple food indicated; but even in these cases it is often possible to demonstrate rapid progress so soon as milk is disallowed.

The choice of aperients is of great importance. In acute cases, calomel is very useful combined with salines, provided the patient is not taking sulphanilamide. In chronic cases, the most helpful form of laxative is of the paraffin and agar-agar type (emuls. paraff. liq. cum agar., B.P.C.), supplemented if necessary by a compound aloin pill.

A course of *high colonic irrigations*, following the Plombières method, is indicated if mucus persists in the stools despite the above measures.

In acute cases of infection of the urinary tract with high fever and dysuria, full doses of *alkalis* (sod. bicarb. and pot. cit.) combined with tincture of hyoscyamus are helpful for the first 3 or 4 days. Bicarbonate of soda may be

added to barley water and citrate of potash to lemonade; the patient is encouraged to drink freely of these fluids, at least 3000 c.c. (4 pints) in the 24 hours. By the time the urine has been strongly alkaline for 3 days the temperature will most likely have fallen: indeed, if the pyrexia persists unabated in such circumstances search should be made for some cause other than a coliform infection of the urinary tract to explain it. Now is the time to limit the fluid intake for an adult to 1000 c.c. (1½ pints) in 24 hours, and to give full doses of *sulphanilamide*. An initial dose of 2 gm., followed by 1 gm., two-hourly by day and four-hourly by night (*i.e.* ten doses totalling 11 gm. in 24 hours). This dosage is maintained for 48–72 hours and then halved for the next 3 days, by which time the urine will probably be sterile. In elderly patients with chronic cystitis the infection may be kept in check with the aid of 0·5 gm. three times a day on four days a week. (For other details of sulphonamide therapy, see pp. 16–17.)

If for any reason it is judged unwise to administer sulphanilamide (sulfanilamide U.S.P.), or if on trial the patient proves intolerant thereof, *mandelic acid* should be tried; with this drug also the fluid intake must be restricted. Salts of mandelic acid, such as ammonium mandelate, gm. 3 (grs. 45), given by mouth every 6 hours, diminish the growth of coliform organisms, provided the urine is kept highly acid, that is the *p*H between 5·0 and 5·5. Acid sodium phosphate, in doses of gm. 2 (grs. 30), should render the urine sufficiently acid; to determine that this is so, to half an inch of urine in a test tube add a few drops of methyl-red solution: the resulting colour should be pink. Each specimen of urine is so tested, and the dose of acid sodium phosphate adjusted accordingly. The treatment may have to be maintained for 7–10 days; recrudescence or recurrence of infection is not infrequent and demands a further course. Mandelic acid therapy is contra-indicated in all cases of renal failure, as the accompanying acidosis may cause a rapid rise in blood urea.

If these measures fail the *hexamine group* will do good in proportion as the infection is focused in the urinary tract and in the renal pelvis rather than in the bladder. To get the greatest service from hexamine in urinary tract infections it is best to keep the urine acid, and for this purpose acid sodium phosphate is serviceable. It is well to change the hexamine (gm. 0·3 to 1·6 or grs. 5 to 25 well diluted) for one or other of its derivatives now and again, reverting to the hexamine again later: hexamine sodium acetate (cystopurin), hexamine with citrate (helmitol), hexyl-resorcinol (caprokol). In chronic cholecystitis much larger amounts of hexamine have been employed, up to gm. 14 (grs. 200), given in ten equal doses in the 24 hours; it is essential that the reaction of the urine should be maintained alkaline lest hæmaturia and strangury ensue.

2. Local Measures.—Local suppurations are, of course, dealt with surgically. Reference has already been made to associated disabilities in some cases of urinary infection which also require surgical treatment. In bowel infections a useful adjunct in treatment is to endeavour by means of posture, massage and efficient supports to improve matters if enteroptosis be present.

3. Specific Measures.—There remains to be discussed the use of bacillary vaccines. These should always be regarded as supplemental to, rather than substitutions for, the scheme of therapeusis outlined in (1) and (2). In acute

cases vaccines are not indicated. In chronic cases, if vaccines are employed they should be given a good trial; it may be that a streptococcus is associated with *B. coli*, in which case an autogenous vaccine of this organism should also be given. Sometimes the good effects are striking, at others little or nothing is achieved. *The vaccine should invariably be autogenous in nature.*

TUBERCULOSIS

Definition.—Infection of the body by *Bacillus tuberculosis*, leading to lesions which are characterised by tubercles, microscopic or macroscopic, themselves undergoing changes leading to caseation, necrosis, ulceration and calcification, and having in close association with them varying degrees of fibrosis. The lesions of tuberculosis form the histological and anatomical basis of a large number of diseases which differ according to the organs affected, the extent of the lesions and the degree of resistance to infection shown by the tissues.

Ætiology.—The Bacillus Tuberculosis (Koch, 1882).—This is regarded by many bacteriologists as a member of the Streptothrix group of micro-organisms; that is to say, the bacillus found in tubercular lesions is considered to be the bacillary form of an organism allied to the Streptothricæ. The other phases in the life-history of the micro-organism are not met with in the actual disease-process, but may be demonstrated in old cultures and in certain experimental lesions. This view of the essential nature of the tubercle bacillus harmonises with our knowledge of its great power of resistance to various destructive agents; it also explains many of the tissue changes occurring in the disease, the latency seen in many cases of infection and the chronicity of many others. The bacillus measures 1·5 to 4 μ in length as an average, is slender, and when isolated from secretions or tissues is usually bent or curved, and tends to lie in small groups. It is "acid-fast" in its staining reactions, allowing of easy recognition; but it grows very slowly outside the body, requiring special media for the purpose of culture. The bacillus is capable of living for several months in dried sputum, and may be cultivated, or may be made to cause disease in susceptible animals, when obtained from the dust of ordinary living-rooms. The gastric juice does not destroy the bacilli, nor does the process of decomposition going on in dead tissues over a period of many weeks. The clinical importance of these facts is obvious. In contrast with these examples of resistance may be mentioned the fact that direct sunlight has a rapid lethal effect upon the micro-organism; so also has a solution of carbolic acid, of strength 1 : 20.

Known differences exist between the bacillus causing tuberculosis in man, in cattle, and in birds respectively. The *avian* form appears to be of little importance. The *bovine* type would appear to cause about 10 per cent. of all cases of tuberculosis in man. In children, the bovine type is found relatively more often. The *human* type of bacillus is less virulent to cattle than is the bovine type, but—though this cannot be made the subject of experiment—the bovine type is probably as virulent to man as is the human type. Of young children dying with primary abdominal tuberculosis, the fatal lesions, in nearly half of all cases, have been referred to the bovine bacillus. Again, in both children and adolescents suffering from tuberculous

adenitis, a large proportion of the cases examined could be referred to the bovine bacillus. Lastly, in lupus, about half of all cases appear to be referable to the bovine type of *B. tuberculosis* (Royal Commission on Tuberculosis).

Sources of Infection. —There are two great *sources of infection* of tuberculosis—phthisical sputa and tuberculous milk. Sources of minor importance are urine and fæces containing the bacilli as the result of active lesions in the urinary and intestinal tracts, and the flesh of tuberculous cattle eaten as meat. But the main source of the infecting bacilli of the human type is undoubtedly dried human sputa. Nuttall found that from 2 to 4 billion bacilli were expectorated in 24 hours by a patient whose phthisis was only moderately advanced. These bacilli are scattered freely in dust when the sputa become dried, and they lie about the surface of the patient's body, or they are projected directly into the air along with particles of moisture when patients cough or sneeze or even speak loudly.

Of the *bovine* type of bacillus it is probably not an exaggerated estimate to say that some 25 per cent. of all dairy cows in this country are tuberculous. In New York, Hess found tubercle bacilli in 16 per cent. of the 107 specimens which he examined.

Modes of Entrance of the Bacillus into the Body.—Although there are some other *channels and modes of entry* that have theoretical interest, the two chief ways by which the body is infected are undoubtedly ingestion of the bacilli by the alimentary canal and inhalation of them by the respiratory organs. Compared with these two, all other avenues of infection are trivial.

1. *Ingestion.*—Infection through the *intestinal mucosa* is considered to be the most common mode of production of tuberculosis in children, the main source of the bacilli being contaminated milk. This conclusion has the confirmation of clinical and post-mortem observations, as well as the support of experimental work by Behring, Calmette and others. Ghon has adduced facts which suggest that, even in little children, infection may be much more often brought about by inhalation than was formerly thought. Ghon's observations have been confirmed by Eastwood and Griffith, and by Canti.

Another channel of entry by ingestion is the *tonsils*; tubercle bacilli have been demonstrated by Hugh Walsham and others to pass through the tonsillar tissue to the cervical lymph glands. The tonsils are themselves rarely affected.

2. *Inhalation.*—Primary infection by the route of the air passages is difficult of proof and, indeed, some authorities regard it as negligible compared with (1). The great frequency of respiratory tuberculous lesions, however, and the incidence and mortality-ratio of pulmonary tuberculosis in ill-ventilated districts and buildings, are points difficult to explain satisfactorily without the assumption that in the majority of these cases infection takes place by inhalation. The sequence of events is considered to be somewhat as follows. Finely divided droplets carrying the bacillus are inspired during childhood. The bacilli are conveyed by the lymphatics to the glands which become inflamed but, later, heal. A few bacilli escape the gland filter and are redistributed by the blood stream in diffuse fashion in the lungs. Foci so produced mostly heal, but those near the apex do so less readily, and come to constitute the lesions of chronic pulmonary tuberculosis.

The statistics relative to contagiousness in tuberculosis institutions are conflicting.

3. *Inheritance.*—Inheritance of tissue-susceptibility to infection by tuberculosis is a definite fact. But inheritance of tuberculosis is problematical, if by this is meant the transmission of tubercle bacilli in the spermatozoön or in the ovum. In the few cases of "congenital tuberculosis" that have been authentically described, the transmission has probably been from a diseased placenta to the blood of the fœtus.

4. *Skin inoculation.*—This is of little more than theoretical interest. Post-mortem warts (*Verruca necrogenica*) are occasionally of tuberculous origin. Czerny, the surgeon, reported a couple of cases of inoculation during skin transplantation.

Among *other ætiological factors* the chief is undoubtedly the *inherited tissue-susceptibility* to infection already referred to. The exact nature of this susceptibility is not known, but its existence is one of the cardinal facts of clinical medicine. *Sex* seems not to be a factor. *Racial differences* in susceptibility are noticeable, though the distinction between morbidity-incidence and mortality-incidence must be made here—the former is high in the Irish, the latter in negroes. In the Jews, though the disease is common, the mortality-incidence is low. *Trauma* is definitely known to induce pulmonary infection, or, perhaps it should be said, pulmonary spread of the disease. All *occupations* tending to inhalation of dusty particles, and those which keep the workers in ill-ventilated and badly-lighted rooms and places, increase the liability to tuberculosis, especially of the pulmonary kind. If *bad economic conditions* concur with either of these the liability is increased. *Debility,* whether the result of acute illnesses, or caused by pregnancy, parturition, prolonged lactation, or exhausting modes of life generally, increases a natural susceptibility, and gives an acquired susceptibility when no hereditary weakness is present. Tuberculosis is not infrequently a *terminal infection* in such diseases as diabetes, cirrhosis of the liver, leukæmia and chronic nerve affections such as tabes dorsalis, etc. *Recurring and chronic respiratory catarrhs* seem at times to lower the local resistance to tuberculosis, though it is often matter for comment that so many patients with emphysema, asthma and chronic bronchial catarrh live for many years without developing pulmonary tuberculosis, provided they inherit no special tissue tendency to infection by the bacillus.

Incidence and Mortality.—The healthy human body is considered to be relatively immune to infection by the bacillus of tuberculosis. Against this statement, however, it must be said that, whether from the ubiquity of the causative germ, or from one or more of several factors enumerated in the preceding paragraph, some 70 to 80 per cent. of all adult cadavers carefully examined in Western countries show lesions due to the bacillus. It is said, too, that one-seventh of the whole race dies as the direct result of tuberculosis. The disease is one of "low resistance," this being the result either of inherited predisposition or of acquired loss of resistance, or of both of these.

The results of infection are of great variety and of all grades of intensity. The variety depends upon the tissues affected, and the route of spread of the infection. The intensity depends upon the degree of relative virulence shown by the bacillus, and the amount of resistance shown by

the patient. Tuberculosis may exist without appreciable disturbance to health, and the lesions produced may be commensurate almost with the whole length of a patient's life. On the other hand, the infection may cause an illness of the most severe character, killing the patient in a few weeks. The results of infection are described elsewhere in this book under appropriate headings, but *general infection* leading to the condition termed general tuberculosis is included in this article.

Diagnosis.—The Isolation and Recognition of the Bacillus.—In all doubtful cases of tuberculosis this is a point of vital importance. Clinical evidence of the existence of the disease, however complete it may seem to be, must never lack the confirmation of bacteriological proof, whenever this is possible. ("Physical signs are the signs of conditions, not of diseases.") Seeing that the only radical proof of the existence of the disease is the demonstration of the bacillus in material derived from the patient, attention must first of all be directed to this investigation. By comparison with this demonstration, even the most definite "reaction" to one or other of the tuberculin tests, or the most strikingly positive result with the complement-fixation method, is untrustworthy. It behoves the practitioner, therefore, to watch jealously for any material that may be available for bacteriological use, and to be quite certain that such material is not obtainable before falling back upon indirect clinico-pathological evidence (see below) to support the diagnosis.

In cases of suspected phthisis, every effort must be made to secure sputa, and it may be necessary to check a habit of swallowing expectorated material. The single, isolated plug of mucus, which is often expectorated in the early morning, should not escape attention. In little children, sputa, as such, are usually absent, but if vomiting occurs in association with lung disease the vomit should be searched for fragments of sputa. In suspected disease of the kidney or urinary tract, the urine must be collected carefully and submitted to examination. Cases of *albuminuria* or of *hæmaturia*, in which there is not clear evidence of diffuse nephritis, should raise the question of tuberculous disease of the kidney. The fæces should be scrutinised in doubtful tuberculosis of the lung, peritoneum or bowel. If any *puncture-fluid* is obtainable—as from the pleura, the spinal theca, or a joint—this is valuable for investigation in any patient suspected of tuberculosis.

The methods of dealing with these materials are not difficult, though they require thoroughness and patience when the bacilli are present in scanty numbers. The very different significance to be attached to a positive as against a negative result must never be lost sight of; the former affords proof of the existence of a tuberculous lesion, the latter gives at most a presumptive evidence against it.

In dealing with *sputa*, the original carbol-fuchsin method of Ziehl-Neelsen should first be tried. If the results, after carefully searching 3 or 4 films for half an hour, are negative, the sputa should be shaken up thoroughly with ten times its bulk of carbolic acid, of strength 1 : 20, allowed to sediment, the supernatant fluid run off, and films made of the residue. If the sputa are seen to be thin and watery, this method is likely to give a negative result. If so, one of the digestion methods may be used—either pepsin and hydrochloric acid, or "anti-formin." The use of the last-named substance, consisting of a mixture of equal parts of bleaching powder solution and a 15 per

cent. solution of caustic soda, is found by some workers to give excellent results. An amount of this fluid, equivalent to about one-fifth of the bulk of the sputum, is mixed with it, allowed to act for 3 to 4 hours, the mixture centrifugalised, and the deposit dealt with by one of the staining methods in ordinary use. The bacilli are, by the disintegrating action of the "anti-formin," isolated from the albuminous vehicle and concentrated in the deposit.

Urine is best dealt with by the carbolic acid method (*v.s.*), subsequent centrifugalisation, and staining of the deposit. The smegma bacillus (also acid-fast), which may be present if the specimen has not been obtained by catheter, is differentiated by allowing the stained films to remain in alcohol for ten minutes; the tubercle bacillus is not decolorised. In *pus*, the search is much facilitated by the use of "anti-formin," and this is a useful adjunct in the examination of fæces also. A patient suspected of tuberculosis of the bowel often suffers from diarrhœa; when this is the case, Emery's suggestion of giving sufficient opium to cause a solid stool is useful. The superficial parts of the motion are most likely to yield the bacillus, and are dealt with accordingly.

Puncture-fluids very frequently give negative results to ordinary microscopic examination, on account of the scantiness of the bacilli in them. However, the clot (if such occur), or the centrifugalised deposit, should always be searched thoroughly, as the demonstration of even a few bacilli of undoubted morphological characters is decisive. Cerebro-spinal fluid should be incubated, without shaking, for 24 hours, and the "spider-web" clot stained for bacilli. Failing this demonstration, the fluid must be used for inoculation purposes, a guinea-pig receiving a liberal amount (not less than 10 c.c. if possible). The inoculation method of diagnosis is, of course, available for the above materials also, as a final test.

The demonstration of tubercle bacilli in the *blood* has received attention of late years, but with widely different results in different hands. Reputable authorities state that bacilli can be seen in stained films in a very high percentage of all cases of tuberculosis, wherever the lesion may be. Others fail to confirm these results.

Indirect Methods of Diagnosis.—These depend upon the presence in the tissues of certain sensitising and immunising substances. They are indicated in doubtful cases of tuberculosis in which no material is available for investigation by direct methods (see above). The relative values of these methods are still under assessment; at present their values are probably in the order of their description here.

1. The Tuberculin Test.—The test depends upon the fact that infection by the tubercle bacillus renders the tissues supersensitive to the toxins of the bacillus, if these be introduced into it artificially. This supersensitiveness is shown by the production of certain "reactions" which are recognisable and are regarded as more or less "specific" in their nature. The test is performed in three ways.

(*a*) *The subcutaneous test.*—The use of "old tuberculin" by this route (Koch's test) is not without danger, and has been superseded in human practice by other methods.

(*b*) *The skin test* (Pirquet's test).—This is best employed quantitatively. Three or more strengths (*e.g.* 25, 50 and 100 per cent.) of a solution of old tuberculin are rubbed lightly into the skin of the arm, which has been

previously scarified. The appearance of papules and erythema at the site of vaccination constitutes a positive reaction.

(*c*) *The eye test* (Calmette's test).—This test is now seldom used.

(*d*) *The intradermal test* (Mantoux).—0·1 c.c. of 1 in 1000 and of 1 in 10,000 old tuberculin are injected into the cutis. Redness and œdema, appearing within a few fours and reaching a maximum on the following day, constitute a positive reaction. The test is an extremely delicate one and this fact restricts its clinical value.

(*e*) The erythrocyte-sedimentation rate is increased in all cases of active tuberculosis, but not only in this disease.

2. The Complement-Fixation Test.—This test is analogous to the Wassermann test for syphilis. It is claimed by some workers that it is positive in over 90 per cent. of cases of tuberculosis. The difficulty seems to be that it cannot be relied upon to distinguish an active lesion from one that is not active. Seeing that old and caseous tuberculous lesions exist in such a large proportion of all persons likely to be tested, and that these old lesions still suffice to give the complement-fixation test, its value is quite doubtful unless undertaken in a quantitative manner.

3. The Tuberculo-Opsonic Index.—This is now only of historical interest.

4. Cytological Evidence of Tuberculosis. — Another, and very useful, evidence of tuberculous infection is to be obtained in cases of pleural, peritoneal and meningeal exudates, by estimating the relative numbers of polymorphonuclear cells and of lymphocytes. It is found that, in pure tuberculous infections, the cell exudate is largely, and often almost entirely, lymphocytic in character. In pyogenic infections it is very largely polymorphonuclear; in mixed infections (tubercle with pyogenic infection) the cell-exudate is also of a mixed character (Widal and Ravaut).

Treatment.—This is prophylactic and curative.

1. Prophylactic.—The widest possible view should be taken of the preventive measures which are necessary in order to stamp out the disease. If, as seems certain, the three dominant factors in the persistence of the disease are—(i) the inherited tissue-susceptibility; (ii) the bacillus; and (iii) bad hygienic and economic conditions of life, it is clear that the problem is not a simple one.

(i) Families having an inherited tendency to tuberculosis should recognise the fact earlier and more thoroughly than is usually the case. The upbringing of the children needs special care, and occupations should be chosen for them when they reach puberty which keep them in the open air. Climatic considerations are also of importance in the case of these families.

(ii) As already stated, the two great sources of the tubercle bacillus are the sputa from infected pulmonary cases and tuberculous milk. The former of these is both a public and a private concern—the latter is almost entirely public. Pasteurisation is an effective safeguard.

(iii) This resolves itself into a series of sociological questions.

2. Curative.—*Non-specific measures.*—These consist in efforts at improving the patient's nutrition so as to increase the tissue-resistance to the infection—ample fresh air, plenty of good food, bodily and mental rest and exercise undertaken in graduated fashion under expert supervision. De-

tails of all these measures are given in the article dealing with pulmonary tuberculosis (p. 1208).

Specific measures.—With two exceptions tubercular sera and vaccines are of historical interest only. These exceptions are (*a*) Koch's Tuberculin; (*b*) Bacille Calmette-Guérin (B.C.-G.).

(*a*) *Tuberculin.*—This is used most for urogenital tuberculosis. (Doses as in text.)

(*b*) *B.C.-G.* (*Bacille Calmette-Guérin*).—This is a "live" vaccine prepared from a strain of tubercle bacillus which has been so attenuated that it has lost much of its capacity for producing disease.

It has been widely used in France for prophylaxis. Three doses of living bacilli are given by mouth to infants during the first 10 days after birth, before natural infection has occurred.

About 100,000 infants in France, mainly those born of tuberculous parents, have been treated. It is too early to assess the results, but there is one great objection to the method, *i.e.* the possibility that the organism itself may be capable of regaining virulence in the human body.

Chemo-therapy.—A number of substances have been used from time to time. The most recent, and perhaps the most successful, is Sanocrysin. (See p. 1210.)

General Tuberculosis

Synonym.—Acute Miliary Tuberculosis.

Definition.—A disseminate form of tuberculosis, giving rise to a very severe and fatal disease analogous to the septicæmias in pyogenic infection.

There are three clinical forms of the disease, according as the symptoms are chiefly referable to the lungs (the *pulmonary form*), or to the brain (the *meningitic form*), or are those of a general infection without focal signs. This latter form is often termed the *typhoid form*. The pulmonary form is described in the section dealing with pulmonary tuberculosis. The meningitic form is described in the section on meningitis.

Symptoms.—The *general* or *typhoid form* resembles typhoid fever very closely. There is usually a period of vague ill-health—as there is in typhoid fever—preceding the more severe illness. When the latter develops there is headache, insomnia, a soft but frequent pulse, rapid respirations, a dry tongue, slight cyanotic flush and pyrexia, which is usually less continued in character than in typhoid fever. Not infrequently the temperature curve is that of a quotidian intermittent fever. In a few cases the rise of temperature takes place in the morning instead of in the evening, a feature not infrequently seen in other pyrexias of tuberculous origin, though not confined to these. Progressive loss of flesh takes place, and also anæmia, but this latter condition may only be found by blood examination, the dusky flush of the face often masking the blood state on mere clinical examination. Towards the end of the illness, suspicious signs of one or other of the more focal manifestations of the infection often arise: copious fine râles over the lungs, tumidity of the abdomen with palpable enlargement of the spleen and liver, or cerebral symptoms suggestive of meningitic involvement. In a suspected case the chest should be examined radiologically, since the suggestive "snow-storm" appearance may be present if general tuberculosis has existed for more than ten days or so.

Diagnosis.—As the term "typhoid form" suggests, the disease resembling general tuberculosis most closely is typhoid fever. During the first week, or even during the first two weeks, diagnosis may be very difficult. In favour of typhoid fever are the persistence of headache, the presence of epistaxis, relative infrequency of the pulse-rate, diarrhœa and early tumidity of the abdomen. In favour of tuberculosis are a frequent pulse-rate, early cyanosis and intermission in the temperature curve. There is leucopenia in both diseases. A positive blood culture occurs during the first week in most typhoid cases, and agglutination with the patient's serum may reasonably be expected after the end of the first week.

Course and Prognosis.—The disease is invariably fatal, and usually within a period of 6 weeks from the onset of fever and symptoms directly referable to the disseminate infection. A few cases last as long as the eighth week, and one of the writers (H.) has seen a well-authenticated case in which the patient lived until the middle of the tenth week.

Treatment.—This is entirely palliative, there being no specific measures at present known to check the progressive nature of the infection, or to avert its lethal issue.

CEREBRO-SPINAL FEVER

Synonyms.—The name here chosen seems least open to objection. "Cerebro-spinal meningitis" is the best alternative, but cerebro-spinal meningitis may be caused by other micro-organisms than the meningococcus, and meningitis may not be present at all, or may not constitute the chief lesion, in some cases of meningococcus infection. "Epidemic cerebro-spinal meningitis" is much less desirable, because it suggests that there is an essential difference between the epidemic and the sporadic cases of meningococcus infection, which difference does not in fact exist. "Meningococcus infection" brings the various pathogenic possibilities of the micro-organism into line with those of the pneumococcus, with which it has close analogies, but the term does not connote a disease.

Definition.—A specific disease, due to infection of the body by the meningococcus, occurring both in epidemic and in sporadic form, and most often manifesting itself as an acute meningitis tending to involve the whole cerebro-spinal axis.

Epidemics of cerebro-spinal fever are marked by several features peculiar to the disease, offering a striking contrast with other epidemic diseases. For a long time these features were very difficult of explanation, until the existence of "carriers" became recognised, and supplied the solution to much of the epidemiological problem. Amongst these curious features may be mentioned the erratic nature of the outbreaks, the inability to trace the connection between one epidemic and another, the relative or even total escape of certain localities close to others in which the disease was rife, and the small proportion of persons affected in any one district. In closed communities, such as camps, and especially in times of war, the disease finds a fertile soil. When the "carrier rate" rises above 20 per cent. an epidemic is likely to ensue.

On clinical, bacteriological and epidemiological grounds there is no distinction to be drawn between sporadic and epidemic cases of cerebro-

spinal fever. But it is not entirely by means of the sporadic cases that the infecting agent persists, but by " carriers " also. There is little doubt, however, that from the sporadic cases, as from a smouldering infection, new epidemics light up. The present conception of the disease, from an epidemiological point of view, is that of a very widespread infection, with a total morbidity that is very low, but with foci of more intense virulence here and there. These foci of more intense virulence appear and disappear, being preceded and followed by a somewhat higher level of permanent incidence in the districts concerned.

Ætiology.—The geographical distribution of the disease is very wide—world-wide, in fact. A certain affinity is shown for the north temperate zone.

Epidemic cerebro-spinal meningitis is a disease of winter and spring. This seasonal incidence is borne out by all observers, and is a very important feature of the disease. It compares markedly with the seasonal incidence of poliomyelitis epidemics, which are at their height in the summer months.

The question whether cerebro-spinal fever is contagious or not has been a matter of much dispute. The facts would appear to indicate that the disease is contagious, but that the degree to which it is so is very slight. The proofs of the contagiousness of the disease are, briefly, these—(1) the occasional transmission of the disease to doctors and nurses ; (2) the occurrence of a succession of cases in one family and in the same house ; (3) the importation of the disease into a new country or locality ; (4) the mode of spread in any locality ; (5) the immunity enjoyed by collections of persons living under the same conditions as those affected by the disease, but unable for some reason to come into contact with them (Netter and Debré). Although direct contagion is uncommon, plenty of authentic instances of its occurrence have been reported.

THE MENINGOCOCCUS.—The meningococcus (*Diplococcus meningitidis intracellularis* of Weichselbaum) is rather smaller than the *M. catarrhalis* and larger than the gonococcus—the other two pathogenic diplococci which are Gram-negative in staining reaction. It is a strict aerobe, and requires the addition of some animal protein or of legumin to ordinary culture media to ensure growth. After cultivation for three or four generations it will grow on ordinary agar, but sub-cultures die rather suddenly. Optimum growth takes place at 36° to 37° C., and growth ceases at 42° C. and at 25° C. Vitality is low, especially to drying ; sunlight kills in less than 12 hours.

Types of the Meningococcus.—By employing the agglutination test, controlled by the absorption test, M. H. Gordon has differentiated four separate types of meningococci occurring in the cerebro-spinal fluid of actual cases.

IMMUNE SERA.—These were proved by Jochmann and by Flexner to possess potent immune substances when prepared from the horse by the usual technique. Standardisation is still, as in the case of nearly all bactericidal sera, almost impracticable. The great advance of past years has been the preparation of type-sera, following Gordon's researches. By the use of these the results of serum treatment, previously somewhat disappointing in this country, proved to be more successful.

The primary habit of the meningococcus, both in actual cases of the disease and in " carriers," is the upper part of the naso-pharynx and the posterior nares.

Symptoms and Course.—Cerebro-spinal fever is protean in its features and especially in its modes of onset. Out of the large number of different manifestations that occur, certain cases repeat themselves with sufficient constancy to constitute clinical "types," capable of description and of recognition.

1. The Ordinary or Acute Type.—The incubation period is difficult to estimate with accuracy; there are reasons for considering it to be 4 or 5 days. The illness begins with the usual symptoms of an acute specific fever, and for the first day or two, or for longer than this if the possibility of the disease under consideration is not borne in mind so as to lead to a special examination, there may be nothing to distinguish the illness from one or other of several acute febrile infections.

The onset is usually sudden, with fever, headache, general malaise and vomiting. The temperature usually rises rapidly and attains a fairly high degree on the first day (102° to 104°).

The headache is usually very intense, is often referred to the occiput, and shows little or no response to the customary palliative drugs given to relieve it.

There is frequently a rigor in the adult, or a convulsion in the infant or child. Vomiting is more often met with in children than in infants, and is quite common in young adults.

In addition to the three cardinal symptoms at the onset—headache, fever and vomiting—the following are quite common, but are not nearly so constant: delirium, pains in the neck and limbs, and some degree of catarrh either of the nose, naso-pharynx, conjunctiva, or ear. In some cases there is considerable bronchial catarrh and in others definite enteritis. In addition to the pains referred to the limbs there may be pain and swelling of the joints.

After some 2 to 4 days of these initial symptoms evidence of meningeal irritation begins to show itself in more or fewer of the following developments. The vomiting is repeated, despite the fact that the invasion symptoms are past. The pulse is irregular in rhythm, and in older children and in adults it is often relatively infrequent when compared with the height of the temperature. The respirations are irregular. The vasomotor system is unstable, leading to periodic flushing of the face and to the presence of *tâches cérébrales*. The patient lies on his side with legs drawn up and prefers the shelter of the bed-clothes. The pupils are dilated and the light reflex is sluggish. There is photophobia, with intolerance of noise and of all kinds of interference. Examination of the neck reveals a stiffness of the muscles, which cannot be overcome without pain. The hamstrings are found to be taut, so that the knees cannot readily be extended if the hips are flexed (Kernig's sign). The abdomen is retracted and the superficial reflexes are abolished. The mental state is one of restlessness and mild delirium with troublesome insomnia. The headache may become quite intolerable and may require morphine for its reduction. In a considerable number of cases a rash appears during the first week—either a number of large rose spots about the trunk and limbs, or a macular eruption like that of measles or a few small petechiæ scattered over the trunk, neck and extremities. Herpes is common, and is generally situated at the usual places—the angle of the mouth, the chin and the nose. There is a leucocytosis of considerable degree (20,000 to 40,000).

Towards the end of the first week the mental state changes to a condition which may perhaps best be described as one of resistant stupor: the patient can be roused by an effort at examination, or by a change of position; but either proceeding is resented, and he quickly resumes his huddled posture. The headache is less constantly severe, but shows sudden and marked exacerbations, often nocturnal, with complete insomnia. The neck rigidity increases, and the head is retracted. The back also becomes stiff. Flesh is lost rapidly. Polyuria is common, with polydipsia. The temperature generally remains fairly high, and, although this is by no means invariable, the fever approximates to the continued type.

Assuming that the course of the disease is not interrupted by lumbar puncture or by specific therapy, the condition of the patient remains much the same during the second, and perhaps during the third, week of the illness. But the wasting continues. The temperature often becomes intermittent in type. One of the three modes of termination will be followed.

(*a*) *Recovery.*—This is gradual when it occurs, and is often interrupted by sudden recrudescences, throwing the patient back into a state which leads to renewed anxiety. The temperature chart is often interrupted in its defervescence by sudden rises, with or without a corresponding recrudescence of the meningitic symptoms. Ultimately the fever completely subsides, the patient ceases losing flesh, the headache and stupor pass off, and the rigidities slowly disappear. The pulse-rate remains high for some time in a good number of cases, and some authors regard this as a sign that the patient is not yet free from the possibility of relapse, and therefore as an indication for caution in treatment. The actual stage of convalescence, once it is established, is rarely interrupted. If the temperature and pulse-rate have remained normal for fourteen days, the risk of relapse may be considered to be passed. It may be some weeks, however, before the patient is free from stiffness.

(*b*) *Death.*—The ordinary type of the disease is not often fatal during the first 2 weeks. When it is, the stupor passes into true coma, the pulse and respiration rise in frequency, and the temperature often shows a sudden ante-mortem rise.

(*c*) *Becoming chronic.*—More often, if the ordinary type terminates fatally, it is by passing into a subacute or chronic stage. If the "crises" already referred to continue, or if, despite the fall of temperature, there is no corresponding improvement in the general condition, a state of progressive emaciation supervenes, with a tendency to chronic hydrocephalus. The wasting is sometimes extreme, so that bedsores are unavoidable. The rigidity becomes marked, and approaches, even in adults, that degree termed cervical opisthotonos in infants. Feeding becomes difficult, and this adds to the wasting due to trophic disturbances. The sphincters usually relax, leading to incontinence. Papillœdema develops. The patient may continue in this unsatisfactory state for several weeks, or even months, and yet may eventually recover, and without any residual defects. More often, however, he gradually succumbs to the disease, or, if he eventually survives its ravages, it is to be left with mental defect, deafness, blindness, hemiplegia, or diplegia.

Opinions differ as to the frequency of true relapses in cerebro-spinal fever. This is probably due to the fact that what some authorities term relapses

others consider to be merely recrudescences. It is certain that the latter are very common; indeed, they are a characteristic feature of the disease.

2. The Superacute Type.—This form of the disease is common at the height of an epidemic. The invasion symptoms are abrupt, and the patient is from the first very ill. Delirium is marked, with most tiresome insomnia, and the headache may drive the patient to a state of acute mania. The temperature is usually very high (104° to 106°), and intermits. Skin eruptions are more constantly present than in the ordinary type; but are by no means necessarily petechial in character. Discharges are apt to occur from the nose and conjunctival sac. The tongue is dry and tremulous. The meningococcus can generally be grown from the blood by culture, and has even been demonstrated in cover-slip preparations made from the blood direct. The leucocytosis is high (30,000 to 40,000). After 3 or 4 days the active mental state changes to stupor; if the cerebral pressure is not now relieved by lumbar puncture this stupor passes into coma. Even if the pressure is relieved by this procedure there is a great tendency for the patient to slip back into a comatose state; then, with pulse, respirations and temperature all rising, with insensitive pupils and absence of corneal reflex, the surface of the body becomes livid, the lungs congested, and death occurs.

3. The Fulminating or Malignant Type.—This form is prone to occur during the evolution of an epidemic. But it is by no means rare as a sporadic manifestation of the disease. It is more often seen in older children, adolescents, and adults than in infants and younger children. The abrupt appearance of fever, headache and active delirium, rapidly passing into coma, and the whole course of the disease may not exceed 12 hours.

In all fulminating cases of cerebro-spinal fever there is a rapid development of septicæmia. In some of them the septicæmia covers the whole of the disease, symptoms of meningitis being absent, and the meninges being free from gross lesions on examination post mortem. Even more constantly than in the superacute type is a blood culture positive: but the course of the disease is too rapid to admit of a diagnosis by this method during life.

4. Mild Types.—These cases are said to be common during the decline of an epidemic. It is at present quite impossible to say with what frequency they occur, because it is certain that many of them are overlooked. They are often treated as cases of "influenza," owing to the resemblance they bear to that disease. Many cases of acute fever with headache and pains in the back and limbs are regarded as "influenza" from a diagnosis by exclusion. They are not subjected to a lumbar puncture because the condition does not seem sufficiently grave. And if they recover from an illness of a few days' duration this is thought to be confirmatory of the diagnosis. In the presence of an epidemic of cerebro-spinal fever, however, a very close scrutiny of these cases should be made, and if there is even doubtful neck-rigidity or Kernig's sign, the cerebro-spinal fluid should be examined. Even when lumbar puncture is not at first decided upon a swab from the naso-pharynx should be investigated for the meningococcus.

During an epidemic a patient who presents the symptom-complex of headache, malaise, pains in the back and limbs, slight fever, and some stiffness of the neck is probably suffering from a mild grade of meningococcus infection, and should be treated as such, by a lumbar puncture and the administra-

tion of sulphonamide. Subsequent measures will be determined by (*a*) the course of the disease; (*b*) the result of the examination of the cerebro-spinal fluid; and (*c*) the result of the examination of the naso-pharyngeal swab. The value of these cautionary measures is sometimes made apparent by the patient becoming rather suddenly worse after a few days, when it may be quite obvious that the nature of the disease is what was originally suspected.

5. Post-basic Meningitis of Infants (Cervical Opisthotonos of Infants).—These cases were first described (1878) by Gee and Barlow. These observers recognised that they were dealing with a specific disease which had no causative association with tuberculosis, syphilis, or rickets. At the time of these authors' observations no epidemic of this type of meningitis had been described, and the cases were thought, even by later writers, to be met with in sporadic fashion only. It has, however, been recognised that this clinical manifestation of meningococcus infection may occur in epidemics. The post-basic type has been less frequent in this country in recent years.

The characters of the micro-organisms present in these cases were originally thought by some workers to differ from those of the micro-organisms found in the acuter cases occurring in epidemics. This distinction has disappeared of late, and there is more or less consensus of opinion that, although the strain may vary, the causative diplococcus is essentially the same in the acute as in the chronic, and in the epidemic as in the sporadic cases.

Seeing that the clinical features, again, do not differ materially in this type of meningitis from those often seen in cases occurring in older children, and occasionally even in adults, nor from those often seen in infants at times of an epidemic, it follows from these considerations that the inclusion of cases of post-basic meningitis in a general account of cerebro-spinal fever is amply justified.

Post-basic meningitis occurs chiefly in infants between the ages of 6 months and 2½ years. The same type of the disease may, however, be seen in children up to the age of 4 or 5 years. The onset is usually sudden, with a convulsion in many cases, and very frequently vomiting. The temperature rises abruptly, but does not, as a rule, remain high. In most cases the fever has become slight, or is absent, by the end of the first week of the illness. A large number of the patients suffering from the disease are therefore without fever when they come under observation.

The main and characteristic sign of the disease, the retraction of the head, becomes marked about the third or fourth day. It usually persists, with increasing severity, throughout the whole course of the disease. With it the back becomes arched, so that in extreme instances the occiput and the sacrum may meet. The extremities are usually in a condition resembling tetany, the stiffness being persistent rather than paroxysmal. Progressive wasting is another constant feature, and the degree of emaciation is often very considerable and very rapid. Of the other symptoms vomiting is one of the most common, and may be very troublesome. The pulse and respirations are usually frequent, and may be irregular.

The disease in most cases quickly enters upon a chronic course. The infant lies motionless in its characteristic attitude for hours at a time, but is not usually comatose. Feeding is not as a rule difficult. The pupils are fully dilated. Blindness is present sooner or later in 30 per cent. of the cases

(Langmead), the origin of the condition being central, since papillœdema of any magnitude is quite uncommon. Blindness is rare in the cerebro-spinal meningitis of older children and adults.

Lumbar puncture yields similar results to those found in the ordinary type of the disease; but, as the condition progresses, it is found that the meningococcus fails to appear in the fluid, and the polymorphonuclear cell-content changes to lymphocytosis, indicating the chronic stage of the infection. Dry punctures are not uncommon, indicating the probable closure of the foramen of Magendie by the plastic exudate at the region of the bulb and fourth ventricle. Fluid removed from the ventricles during life, or the examination of fluid found in the ventricles post mortem at this stage, often reveals the meningococcus, showing that the disease is still, in its chronic phase, to be regarded as a persisting infection. Indeed, *the post-basic meningitis of infants is probably to be considered as a meningococcus infection of the pia-arachnoid system with a special tendency to involve the cerebral ventricles by ependymitis.* The peculiar symptoms and course of the disease are thus explained.

Owing to the early development of hydrocephalus in this type of the disease, and the elastic nature of the infant's skull, the head enlarges in all directions, with bulging of the fontanelles and opening of the sutures between the bones. The shape of the skull thus approximates to that of congenital hydrocephalus. The eyes are turned downwards, and the sclerotics above the cornea are exposed by retraction of the upper lid. If this condition of acquired hydrocephalus has lasted for some weeks, there may be enlargement of the superficial veins about the nose and orbits, and running over the temporal regions to the vertex.

The mortality in this type of the disease is very high, probably over 80 per cent. Some of the cases linger for many weeks, and a few very gradually recover, with, all too often, residual blindness and also perhaps deafness. But the majority succumb to the intracranial pressure effects produced by the distended ventricles, in from 4 to 6 weeks from the onset of the disease.

Complications.—1. *Hydrocephalus* may arise soon after the onset of the disease, or it may develop, and often rather suddenly, during its course, or it may be the final anatomical expression of the infective process, the counterpart of the symptom-complex seen in the chronic state of the disease. Certain symptoms are specially suggestive of the condition: pallor, cyanosis, increased frequency of the pulse with diminution in its tension and volume, shallow respirations, and stupor or coma supervening rather suddenly upon a previous state of consciousness.

If hydrocephalus arise at a later period of the disease than the end of the first week it may show itself with surprising suddenness, and sometimes in patients who seem to have been improving satisfactorily. In addition, to the symptoms just enumerated, there is a recrudescence of the headache, vomiting and fever, which may have to a large extent subsided. More often it appears gradually and concomitantly with the progressive cachexia of the chronic type of infection. A valuable sign of its presence in children and adults is the presence of a resonant note to percussion over the anterior horn of the lateral ventricle (Macewen). This sign is best obtained by placing the head in an upright position and inclining it to one side. The sign is not present in infants in whom the fontanelles are still open.

Hydrocephalus of the chronic stage of the disease is seen very constantly in infants suffering from the post-basic type of infection. Emaciation is a constant feature. The child lies for hours without stirring. There may be reiterated automatic acts, such as the biting of nails or the loosening and pulling out of teeth. The patients are rarely comatose. Vomiting and convulsions may occur.

2. *Psychic Disturbances.*—These are not very common, if the delirium and stupor are excluded. But the delirium may develop into mania, urged thereto by the violence of the headache. During convalescence it is not very uncommon to observe temperamental changes, such as puerility or emotionalism, which rarely persist for very long. Secondary dementia is, however, not unknown.

3. *Motor Defects.*—Cranial nerve palsies are very uncommon. There are three groups of paralytic complications, but none of them is common.

(*a*) *Hemiplegia* and, less often, *monoplegia* of cortical type. This usually appears at the height of the disease, and is generally of temporary duration.

(*b*) *Flaccid paralysis* localised to one extremity or to a part of one extremity. The tendon-jerks are lost. Muscular atrophy may ensue, and R.D. may develop. The prognosis for the limb is by no means bad, and complete, or almost complete, recovery is probable.

(*c*) *Spastic ataxia.*—It is not uncommon to find convalescent patients very unsteady on their legs when they first begin to walk. Little children often refuse to walk at all for a time, even if they had learnt to do so before the illness began. Older children sprawl about the floor. Adults tend to topple over in an indiscriminate manner. In the majority of these cases there are no signs of organic disease, and the return to a normal gait is usually only a matter of time. In a few of the cases, however, the ataxia is accompanied by exaggerated knee-jerks, true ankle-clonus and extensor plantar response: a state of spasticity. The sphincters are intact, and there is no anæsthesia or analgesia. According to Sophian, who drew attention to these cases, the pupils often remain dilated, with a sluggish light reflex. Recovery, though slow, is the rule.

4. *Special Senses.*—Complications involving the eye are very variable, and yet, in relation to the essentially nervous character if the main lesions of the disease, they are not very common. Fortunately, with the single exception of that form of blindness so often seen in the recovered cases of the post-basic type of the disease, very few if the eye complications are permanent. Inflammatory lesions include conjunctivitis, keratitis, iridocyclitis and (rarely) cellulitis of the orbit. Nervous lesions include extrinsic ocular defects which are not uncommon, but are generally transitory (*i.e.* spasmodic). Amaurosis is relatively common in the post-basic infection of infants; it is fortunately unusual in the more acute infection of children and adults. It is in most cases unaccompanied by any changes in the optic disc, and is therefore to be attributed to cortical changes associated with hydrocephalus. In some cases, however, a state of secondary optic atrophy is present. Optic neuritis is not a common complication; but papillitis, or a lesser degree of change even than this, is said by French authors to be extremely common.

The chief complication affecting the ear is meningitic deafness. This is a common and very serious complication, serious because when it occurs it is

apt to be permanent. The auditory defect generally begins early in the course of the disease, and usually before the end of the first week. It is usually bilateral, which adds to the seriousness of the trouble in the event of its becoming permanent.

5. *Arthropathies.*—A certain degree of painful stiffness, and even swelling of the joints, is not at all uncommon as a transitory symptom in cerebro-spinal fever. Occasionally, however, one joint shows evidence of much more intense infection, becoming red, swollen and very painful with the slightest movement. It may suppurate, and secondary infection may occur.

6. *Other complications* are the broncho-pneumonia already referred to in little children; occasionally pneumonia in adults; and enteritis.

Lumbar Puncture.—In any suspected case of meningitis a lumbar puncture is as clearly indicated as is puncture of the chest in a suspected case of pleuritic effusion, or a blood-count in a suspected case of leukæmia.

The Cerebro-spinal Fluid in Meningococcus Meningitis.—1. *Pressure and the amount.*—The pressure is generally more than 200 mm. of cerebro-spinal fluid as measured by a manometer fitted to the lumbar puncture needle. The amount of fluid which flows away before the normal pressure is re-established depends upon the pressure and the consistency of the fluid; it averages about 30 c.c.

2. *Naked-eye appearance.*—Various grades of turbidity are met with, from very slight opalescence to a highly purulent exudate. The degree of turbidity varies with the stage of the disease at which the lumbar puncture is undertaken. In the invasion stage the fluid may be almost clear; in the acute meningitic stage the fluid shows marked turbidity; later, again, as the inflammatory phase passes, the fluid becomes clearer. The presence of blood probably always means that a vessel has been punctured by the needle. Some degree of clotting takes place when the fluid is allowed to stand, flakes of fibrin appearing at the bottom of the tube.

3. *Chemistry.*—The protein is increased in amount: instead of the faint opalescence which appears on boiling the normal fluid, a definite coagulum is produced, and an opaque ring appears when the fluid is poured gently on to the surface of strong cold nitric acid. A quantitative estimation of the protein shows that it may be present to the extent of 0·2 to 0·3 per cent. The globulin moiety of the protein is also increased. Sugar is greatly diminished and often absent. The chloride content also is lowered as in other forms of meningitis: it is seldom less than 700 mg. per cent., whereas in tuberculous meningitis a reading below 680 is the rule.

4. *Cytology.*—In the early or invasion stage of the disease there is a quantitative increase in the lymphocytic content, a fact which often escapes observation if the lumbar puncture be delayed. With the arrival of the acute meningitic inflammation the chief cell present is the polymorphonuclear, usually in large numbers. At the stage, therefore, at which most lumbar punctures are undertaken, the cell content is chiefly polymorphous (70 per cent. to 80 per cent.). Later, when the stage of chronic hydrocephalus ensues, the lymphocyte again becomes the dominant cell, and in much greater numbers than in healthy fluid. Most observers, however, describe cases of undoubted meningococcus meningitis in which the cell content is chiefly lymphocytic throughout. In the post-basic type of the disease the cells are most often lymphocytes for the greater part, and the same may be said

of cases which are in a chronic stage whilst under investigation, whether the chief seat of the effusion be at the root of the bulb or elsewhere.

5. *Bacteriology.*—Films made direct from the cerebro-spinal fluid, or, better still, from the centrifugalised deposit, show intra- and extracellular meningococci in the great majority of cases at some time or other in their course. If a careful search be made and no cocci are discovered, it must not be assumed that none are present until the device of incubating the fluid as a whole before it has been allowed to cool is undertaken, and until cultures made upon suitable media are found to be sterile. The number of cocci seen, and their disposition with regard to the cells of the exudate, are matters of great variability. These things depend in the main upon (*a*) the stage of the disease, (*b*) the intensity of the infection and (*c*) the influence of treatment.

Diagnosis.—*The chief difficulty lies in not suspecting the presence of the disease.* It is, of course, much more easy to bear in mind the possibility of cerebro-spinal fever during the presence of an epidemic than at other times. Cases which go undiagnosed, at least during the first part of their course, are those sporadic cases which generally happen to be atypical.

The reason why it may not be possible to decide on clinical grounds whether meningitis is present or not is because several infective processes, other than that due to the meningococcus, are apt to produce symptoms highly suggestive of meningeal irritation. This state of meningeal irritation, when due to toxæmia and not due to actual meningitis, has been termed *meningism* or *meningismus*. The question whether such a state is entirely toxic, or whether it is due to definite though slight changes in the meningeal tissues which just stop short of an inflammatory exudate, is problematical.

The diagnosis of cerebro-spinal fever may be conveniently considered under three heads—(1) from various acute infective processes with toxæmia, leading to "cerebral" symptoms; (2) from certain acute cerebral diseases of primary origin; (3) from other forms of meningitis.

1. The Diagnosis of Meningitis from Toxæmia merely.—The question is settled partly by the clinical data and partly by an examination of the cerebro-spinal fluid. In a case of fever with "head symptoms," the following differential points should be borne in mind:

(1) *If headache and delirium synchronise, meningitis is probably present, and not merely toxæmia.*—Contrast an ordinary case of typhoid fever (toxæmia), in which headache and delirium alternate, the patient being free from pain when he is delirious, with cerebro-spinal fever (meningitis), in which the patient's headache and delirium are both present at the same moment.

(2) *Vomiting.*—If this occurs not merely at the onset of the fever, but on subsequent days also, at a time when the invasion period of the infection may be said to be passed, it is evidence of meningitis.

(3) *Pulse and respirations.*—Irregularities in rhythm are in favour of meningitis, and so is a relatively low pulse-rate in comparison with the height of the temperature, provided typhoid fever can be eliminated.

(4) *Papillœdema*, though its presence is much in favour of meningitis as against toxæmia merely, is not of much value in this connection, because it is usually absent at the early stage of the disease when the diagnostic problem requires urgent solution.

bacillus is isolated from the lumbar puncture fluid, with the exudate of an acute meningitis, and definite symptoms, are not usually cases in which influenza has been suspected, still less diagnosed. Such cases are preferably termed "Pfeiffer bacillus meningitis."

(4) *Typhoid meningitis.*—A true infection of the meninges may occur in typhoid fever, but it must not be inferred that a patient necessarily has typhoid meningitis because the bacillus is grown from the lumbar puncture fluid. This may occur without clinical evidence of meningitis and without histological and chemical changes in the cerebro-spinal fluid characteristic of meningeal inflammation.

(5) *Tuberculous meningitis.*—This is by far the commonest form of acute meningitis and therefore deserves fuller mention. The most helpful points in a differential diagnosis from meningococcus meningitis are the following. Tuberculous meningitis is rarely so sudden in its onset, the meningitis symptoms being preceded by a longer period of malaise, which begins less abruptly than the invasion symptoms of cerebro-spinal fever. The temperature is seldom high, except as an ante-mortem event, the usual range being 99° to 101°. Retraction of the head is transient and ill-marked, or is absent. Photophobia is more common than it is in cerebro-spinal fever. In adults aphasia is often a common and an early symptom. True (paralytic) squint is common. The "peevish" condition in children is much more marked during the first week. In both children and adults the depth of the stupor after about the tenth day is much greater. The discovery of tubercles in the choroid is pathognomonic, but these lesions rarely appear before the third week of the disease, and are therefore not of much service for diagnosis. Some authors lay stress upon the presence of signs of tuberculous disease elsewhere in the body as assisting in the diagnosis, but this is, of course, not true. Except in the case of adults, and by no means always then, there are rarely any such signs. The leucocyte count affords no differential help as from cerebro-spinal fever, a leucocytosis of considerable size (15,000 to 30,000) being present in tuberculous meningitis. The abdominal reflexes are usually retained, whereas in meningococcal meningitis they are prone to be lost early.

However high a degree of probability that a patient is suffering from meningitis may result from a general examination, confirmation of this view rests entirely upon the results of lumbar puncture. For three reasons it should not be deferred: it establishes the diagnosis that meningitis is present; it decides the nature of the infection; it is a valuable aid to treatment in the event of a positive result.

Prognosis.—The mortality in cerebro-spinal fever is undoubtedly higher in the epidemic than in the sporadic cases, if the post-basic meningitis of infants, in which the mortality is very high, be excluded. There are, however, no good figures upon which to base an estimate of mortality in the sporadic cases. In epidemics the mortality prior to the introduction of serum treatment was about 70 to 80 per cent. After its introduction the mortality fell to half this figure. With sulphonamide treatment the figure has probably reached 10 per cent.

The influence of age is noteworthy. The disease is extraordinarily fatal in infants (patients under 2 years of age). This statement holds good both for the post-basic cases which are so often subacute or chronic in character, and

for the acute cases. The mortality is lowest between the ages of 5 and 10 years.

A fulminating form of onset is invariably bad, and the mortality in these cases is very high, if indeed it is not 100 per cent. In the cases with less vicious invasion symptoms, one or more of the following symptoms betoken a grave issue: early loss of consciousness, wild delirium, persistent insomnia, extensive hæmorrhagic eruption, cyanosis. Later in the course of the disease the worst sign is the appearance of hydrocephalus.

The degree of fever, the intensity of the headache, the amount of rigidity, the presence of marked emaciation, frequency and irregularity of the pulse, rhythmical respirations, the presence of herpes—none of these things yields any information of value in predicting the issue of the disease. *In few other diseases, if in any, is it possible for the patient to be so ill and yet to recover completely, as in cerebro-spinal fever.*

The most important fact bearing upon prognosis is the stage in the disease at which treatment is begun.

Treatment.—1. PROPHYLACTIC.—The principles governing prophylaxis are those applicable to infectious diseases in general. Although it would appear that the healthy carrier is more responsible for the spread of the disease than the patient himself, it is none the less important to isolate every case of the disease and to exercise all precautions against further contact with healthy persons. Whenever possible the patient should be transferred to a hospital, and preferably to an institution where the staff is accustomed to deal with infectious diseases.

All contacts who are found to be carriers should be placed under quarantine, and should be kept there until the naso-pharynx is free from meningococci. The carrier should live as far as possible in the open air. For lavage of the naso-pharynx, and for a gargle, a weak solution of izal may be used, or peroxide of hydrogen, or a 1 : 1000 solution of permanganate of potash, adding 1·5 per cent. of sodium sulphate to assist penetration (Gordon). For spraying the nose or fauces, a 1 per cent. solution of iodine with 2 per cent. of menthol in parolein may be used.

The use of a meningococcus vaccine for the purpose of clearing the throat has not proved to be successful.

2. CURATIVE.—(1) *Drug treatment.*—The introduction of sulphanilamide has revolutionised the treatment of this disease. It is of vital importance that the drug should be given at the earliest possible moment after the diagnosis has been made or is strongly suspected. In the majority of cases adequate doses are well tolerated and, whenever possible, the drug should be administered by the oral route; if the patient is too ill to swallow, it is given by a stomach tube. Only when vomiting is frequent is sulphanilamide to be administered by injection. For an adult the initial dose in the acute form is grm. 2, followed every two hours by grm. 1, so that a total of 12–13 grm. are given in the first 24 hours. During the second and third days grm. 1 should be administered every 2 hours by day and every 4 hours by night, that is, 10 doses in each 24 hours. If treatment on these lines has been started before the fourth day of the disease it is probable that the temperature will have fallen by the end of the third day of treatment. If so, the dose of the drug should be halved during the next 2 days, though the frequency of administration should be maintained.

The persistence of an ensuing temperature of 99°–100° does not necessarily imply that the infection is still active (see p. 39).

(2) *Serum treatment.*—The indications for the use of serum are (*a*) intense toxic symptoms, (*b*) unsatisfactory response to sulphonamides and (*c*) evidence of idiosyncrasy to these drugs (see p. 16). In (*a*) the serum is used as supplementary to sulphanilamide, not as a substitution for it. It is given intrathecally in doses of slightly less bulk than the amount of cerebro-spinal fluid removed. In highly toxic cases it may also be administered intravenously, in doses of 50–100 c.c. diluted to 250–500 c.c. with normal saline.

The serum may be allowed to flow by gravity into the *lumbar cisterna* following lumbar puncture, or it may be injected with a syringe which fits the lumbar puncture needle; the serum must be warmed to body heat and the injection made very slowly. The volume of serum injected must not exceed that of the cerebro-spinal fluid withdrawn. Serum may also be introduced into the *cisterna magna.* To reach this the needle must pass through the posterior atlanto-occipital ligament, which is not nearly so thick and resistant as are the interspinous ligaments between the spinous processes of the lumbar vertebræ, before entering through the foramen magnum. The posterior rim of the foramen magnum in the adult is just over 1 cm. from the posterior surface of the medulla oblongata, whereas a distance of only 0·5 cm. separates the lowest part of the medulla from the posterior arch of the atlas; the puncture therefore should be made as near to the upper border of the atlanto-occipital ligament as possible, and the needle inclined upwards. The patient lies on his left side, with the head erect; if head retraction be present, a general anæsthetic is essential in order that the requisite position may be assured. The uppermost bony point palpable in the mid-line of the back of the neck is the spine of the axis. The skin in this area is cleaned and, if general anæsthesia is not used, the tissues are infiltrated with sterile local anæsthetic. After this has had time to act, the skin is nicked with a sharp-pointed knife just above the level of the spine of the axis in the middle line. A fine lumbar puncture needle with a very short bevel is now inserted through the nick, and its direction so adjusted that it is continuous with a line passing through the level of the external auditory meatus to emerge on the forehead about 3 cm. above the bony prominence at the root of the nose, known as the glabella. The needle pushed steadily along this line will impinge on the occipital bone just posterior to the foramen magnum; the correct depth is thus determined and the needle withdrawn, almost to the skin, its direction altered slightly downwards and on reinsertion the point enters the cisterna just below the rim of the foramen; this is apparent to the operator by the sense of diminution in resistance to the passage of the needle. The cisterna magna is entered at a distance of 4·5 cms. from the skin in an adult of average build.

With regard to repetition of the serum, Flexner laid down an arbitrary rule for guidance on this matter, recommending the use of serum daily for 4 or 5 doses, and advising that after this the practitioner should be influenced by the subsequent clinical condition of the patient and by the state of the lumbar puncture fluid at successive operations. Some such custom as this remains the usual one in the ordinary type of the disease. It is desirable to vary this rule in individual cases.

If the case is of the superacute type, it is well to repeat the dose of serum in 8 to 12 hours and again after the same interval. In this way an effort is made, consistent with the precautions already referred to, to get as much serum as possible into the cerebro-spinal sac during the early stages of the disease. After these initial 3 doses an interval of 24 hours may be allowed to pass before the next dose is given.

No doubt the best indication for the repetition of the serum is the condition of the meningitic exudate as seen at successive punctures. The lumbar puncture fluid should always be examined by a competent observer whenever this is possible. The indication for further serum is proportionate to the number of meningococci still present. But it is not often practicable to prepare a stained film of the fluid straightway so as to be guided by the result. The decision whether to use serum or not must in most cases be determined by a consideration of the clinical condition together with the naked-eye characters of the fluid. In regard to the latter it may be said that if the fluid is still turbid (indicating the presence of polymorphous cells), it is well to give more serum.

(3) *General management.*—The diet is to be adjusted to the patient's condition. The disease is an exhausting one, and as full a dietary as is consistent with the state of the digestive secretions is to be allowed. If the fever is a conspicuous feature, and the patient is drowsy or delirious, the mouth is usually dry; the diet is then necessarily restricted to fluids, which should be given in the form of diluted milk, and freshly prepared meat essences, in small quantities at frequent intervals. Water should be given freely. If the patient is in a state of stupor the act of swallowing must not be relied upon; feeding must then be by the passage of a nasal tube three or four times in the 24 hours. According to the age of the patient, from 5 to 10 ounces of citrated milk and water (equal parts), or of peptonised milk, or of beef essence are allowed to run into the stomach from a funnel attached to the tube and held at the necessary height above the bed. If vomiting is troublesome, peptonised milk should only be used, or whey or albumin water. If this symptom is persistent, it may be advisable to put no food at all into the stomach for 24 to 48 hours, relying upon saline injections (5 to 20 ounces according to age) per rectum every 6 hours, supplementing these, if thought desirable, by the subcutaneous use of a 10 per cent. solution of dextrose in normal saline.

The bowels are usually constipated; it is therefore frequently necessary to use purgatives, avoiding salines if sulphonamide is being given. If the patient is comatose early in the disease, when treatment is beginning, it may be advisable to give 2 minims of croton oil in butter or moist sugar.

Urinary difficulties do not usually occur unless the patient is unconscious, in which case it is important to bear in mind the possibility of retention, which may lead to "overflow incontinence." This condition indicates the use of the catheter, with the customary care in the matter of asepsis.

(4) *The treatment of certain symptoms.*—Headache is usually the most distressing symptom calling for special treatment. Phenazone, caffeine, and acetylsalicylic acid may all be tried in full doses; morphine may be imperative in some cases, because nothing else may be of any service. Restlessness,

delirium and insomnia,—if these symptoms are troublesome a trial should be given to some such combination as the following:

R Ammon. bromid., grs. 10-30.
Tr. valerian. ammon., min. 10-30.
Syr. chloralis, min. 20-120.
Aquam ad fl. oz. 1.
S.—Secundis horis ad doses iv–vi.

The pains and the stiffness are best treated by warm baths at a temperature of 102° to 104° F.

If the delirium is exhausting or the condition verges upon mania, vapour of chloroform may be used, or morphine with atropine may be given. Hyoscine should be avoided.

In arthritis the affected joint is best treated by fixation, by the application of hot stupes, and by liquid. If the effusion becomes considerable, or does not quickly yield to these measures, the joint should be aspirated.

(5) *The repetition of the lumbar puncture.*—A lumbar puncture of necessity precedes the diagnosis. When sero-therapy is in force the puncture is, of necessity, repeated at each dose of serum. There remains the question of the therapeutic value of thecal drainage here as in the other forms of pyogenic meningitis undergoing sulphonamide treatment. There are reasons for thinking that drainage at certain intervals, especially in children, tends to prevent the development of the most serious of the complications of the disease, a state of hydrocephalus. The writers are of opinion that the process has beneficial effects upon the course of the disease in many cases. This, notwithstanding the fact that whole groups of cases have been successfully treated by chemotherapy with no further lumbar puncture than that made for diagnosis.

(6) *Treatment of hydrocephalus.*—If a condition of hydrocephalus has been diagnosed, it is advisable to tap the lateral ventricles and to inject serum. This procedure is not so difficult nor so dangerous as may be supposed.

(*a*) The patient is usually an infant with open fontanelles. The region of the anterior fontanelle is shaved and the skin is sterilised. A stout needle, to which a syringe can be attached, is inserted at the lateral angle of the fontanelle, and is gently pushed towards the mesial line for a distance of an inch or an inch and a half. In older patients a special drill may be necessary. The fluid is usually under considerable pressure, so that it becomes quickly known when the needle reaches it. It is not necessary or advisable to attempt to withdraw more fluid than comes into the syringe with very gentle aspiration. With great care, an amount of serum less in bulk than the fluid withdrawn is now introduced into the ventricle.

(*b*) In older children and adults the operation of decompression becomes necessary; and here again, though a much more serious procedure, the practitioner should not hesitate to give the patient the benefit of the operation and of the use of serum by this special route.

HORDER.
A. E. GOW.

TETANUS

Synonym.—Lockjaw.

Definitions.—An infective disease, due to the toxins of the tetanus bacillus, and showing itself by tonic spasm of the masseter and other muscles with paroxysmal exacerbations.

Ætiology.—The bacillus of tetanus is a slender rod 4 to 5 μ in length and from 0·3 to 0·8 μ broad. It is a spore-bearing anaerobe. The vegetative forms are slightly motile, and when stained by special methods show numerous fine flagella arranged all round the bacillus. In material from infected wounds, and usually in cultures after 24 hours' incubation at 37·5° C., spores occur. These are terminal, giving rise to the characteristic drumstick appearance. As cultures grow older the numerical proportion of spore-bearing forms increases, and in very old cultures only spore-bearing forms or spores are found.

Distribution.—In nature the tetanus bacillus is found in the soil of highly-manured districts, and in the dejecta of various animals, especially the herbivora, in the intestines of which it exists without causing pathogenic effects. By comparison with the widespread distribution of the bacillus and its spores the disease is rare. In infected wounds the bacillus occurs with other spore-bearing anaerobes associated with pyogenic cocci, and saprophytic organisms of various kinds. In consequence of its association, in nature and infected wounds, with other organisms, the bacillus is difficult of isolation, as a large proportion of the associated organisms grow with much greater rapidity. Use is made of the fact that the spores will resist a temperature of 80° C. for an hour. Suspected material is inoculated into agar or serum-agar slopes or deep tubes of glucose-agar, and incubated for 48 hours. The culture is then subjected to a temperature of 80° C. for three-quarters of an hour, and subcultures are made on agar plates which are incubated anaerobically. By this means all non-sporing bacteria, and the vegetative forms of the spore-bearers, are killed, and only spore-bearing organisms remain to be dealt with.

The disease follows *injury* to the tissues in most cases, and even when no injury is known to have occurred, it is highly probable that some slight abrasion has been present. The term "idiopathic tetanus" has been given to those cases in which no discoverable injury is present. Those wounds, usually of the hands, in which the tissues have been badly damaged rather than cleanly cut, are specially liable to be followed by tetanus infection. Cases have occurred from the use of contaminated gelatin used in subcutaneous injections, and from catgut sutures similarly infected.

Tetanus is more common in tropical than in temperate zones. A special form of the disease, *tetanus neonatorum*, is peculiar to the tropics, and results from sepsis in attending to the child's navel. This variety, which has occurred in epidemics, is "almost peculiar to infants of the filthy poor" (Hirsch, 1886).

Pathology.—In nature the disease is produced by the introduction of infected material through an abrasion or wound, which may be so minute as to escape detection. Probably there is no such thing as idiopathic tetanus, but infection is possible through the bronchial or even intestinal mucosa.

If the bacilli or spores, free from toxin or from pyogenic cocci, be intro-

duced into an animal, infection may fail to occur, the protection afforded being probably accounted for by phagocytosis, for if spores enclosed in a paper sac be introduced into a susceptible animal infection occurs, as the sac protects the spores from phagocytosis. The presence of pyogenic cocci, other micro-organisms, and the fragments of bone and foreign material incidental to compound fractures and gun-shot wounds, all conduce to the conditions favourable to growth of the tetanus bacillus.

The *period of incubation*, following infection with tetanus bacilli, varies with different animals. In man a period of from 2 to 14 days occurs, but the period may be longer, and as a rule a long incubation period means a more favourable prognosis.

Tetanus toxin.—The tetanus bacillus, like the diphtheria bacillus, produces its pathogenic effects by reason of the soluble toxin it elaborates. Bacterium-free filtrates of cultures, as shown by Kitasato, when injected subcutaneously or intravenously into mice, cause tetanic spasms, at first in the neighbouring muscles and later more generally, and death has resulted.

Tetanus toxin is one of the most powerful poisons known, the fatal dose of a probably impure toxalbumin for a mouse being found by Brieger to be 0·0005 mgm.

Different degrees of resistance to the toxin are shown by different animals. The horse and man are the most susceptible. On a basis of weight the horse is twelve times and the guinea-pig six times as susceptible as the mouse, while the hen is two hundred thousand times as resistant. The incubation period is shorter when toxin is intravenously injected than when introduced subcutaneously, and is shorter in smaller than in larger animals.

It has been proved that toxin is absorbed by the end-plates of motor nerves. This was shown by severing the sciatic nerve of an animal near the spinal cord. The corresponding hind limb was then injected with toxin. A portion of the divided nerve was then placed in another animal and tetanus resulted, while if the nerve were cut distally, and a proximal portion thereof were transplanted, no infection occurred, though in both cases the nerves were equally bathed in lymph containing toxin. And, again, if an excess of toxin be injected into a sound limb only that portion of a nerve distal to a section in another limb shows absorption of toxin. Introduction of a lethal dose of toxin into a nerve such as the infra-orbital, containing no motor filaments, is not followed by characteristic tetanus symptoms.

The toxin passes centripetally up the nerve and affects the motor nerve cells corresponding thereto, thus accounting for the longer incubation period in larger animals. If antitoxin be injected into a mixed nerve, such as the sciatic, toxin is prevented from passing up that nerve; but toxin injected into a similar nerve will act lethally even though a large excess of antitoxin had been previously injected intravenously. In one case, indeed, it was shown that a dose of toxin injected into the sciatic nerve of a highly immunised animal caused tetanus. Possibly these results are accounted for by the now well-known difficulty of bringing antibacterial and antitoxic bodies in the blood to bear on the cells of the central nervous system, a difficulty which has been met, to a certain extent, by the introduction of intrathecal medication.

Symptoms.—The incubation period has already been referred to. The

earliest symptom is, in the great majority of cases, the so-called *trismus* or tonic spasm of the masseter muscles. Beginning as a slight stiffness, this increases until the jaws are firmly clenched, the patient being unable to open the mouth. The stiffness may involve the muscles of the neck at the same time as the jaws, or a little later. The facial muscles are affected next, and the facies presents the *risus sardonicus* due to the tension in the frontalis and in the muscles at the angles of the mouth. The muscles of deglutition are another group early affected. There is, from these parts, a steady spread of the spasm to the trunk and then to the limbs. Rigidity tends to appear early in the rectus abdominis and in the adductors of the thighs. The tendon jerks are exaggerated and attempts to elicit them produce spasms, local or general. The tonic spasm in the muscles of the trunk usually show exacerbation in paroxysms, with resulting postures termed respectively opisthotonos, emprosthotonos and pleurothotonos, according as the muscles of the back, abdomen or one side of the body are in a state of spasm. These paroxysms may be induced by divers irritants, and are agonisingly painful. Retention of urine is common.

Less common manifestations include a local contracture of muscles in the neighbourhood of the wound, which may precede trismus or more general spasm by several days. Thus, in a wound of the forehead there may be a facial palsy or an ophthalmoplegia on the same side or, with a wound of the hand or foot, painful spasm of the muscles of the limb may develop before spasm appears elsewhere. In some of these local forms general spasms may be absent throughout or, if trismus is present, this may be transient. In "*local tetanus*" the incubation period is sometimes as long as 30 days.

The disease is often apyrexial, but in some cases the temperature rises with the development of the general symptoms, which include headache, pains in the back, anorexia, constipation, insomnia, yawning, sweating and a facies of great anxiety. Consciousness remains clear. The cerebrospinal fluid is unaffected.

Course.—The course of the disease is variable. Sometimes it is as short as 4 or 5 days, the patient dying of spasm of the glottis, asphyxiation, bronchopneumonia, heart failure or exhaustion. Other cases, less fulminant, last from 7 to 14 days. A few seem to deserve the term "chronic."

Diagnosis.—A relatively trivial disease which may, however, cause some anxiety from its resemblance to the trismus of tetanus, is the fixation of the jaw seen in certain cases of *septic throat* and *septic*, especially impacted, *teeth*, with phlegmonous involvement of the floor of the mouth, periosteum, etc. Careful examination of the mouth nearly always suffices to determine the real nature of these cases, and the presence of enlarged and tender cervical glands assists the diagnosis.

Strychnine poisoning presents features resembling tetanus in that the spasms are very similar in both diseases. But between the spasms in strychnine poisoning the muscles are relaxed, a condition never seen in tetanus. Another point of distinction is the fact that trismus and cervical rigidity never exist alone in strychnine poisoning, whereas they frequently do in tetanus.

In any doubtful case of injury, in which there are damaged tissues, bacteriological investigation of the exudate and of material from the depths of the wound should at once be made.

Prognosis.—This is always grave. The mortality in a large series of cases appears to be nearly 60 per cent. (Hill). Infants and children rarely recover. The absence of fever, a more or less normal pulse-rate, a long incubation period, and a slow development of the symptoms are favourable points. If the patient reaches the tenth day of the disease, his chance of recovery is considerably increased.

Treatment.—1. PROPHYLACTIC.—All wounds of a suspicious character should be well curetted under a general anæsthetic, the raw surface should be thoroughly treated with antiseptic and antitoxin administered.

Antitoxin has for some time been used in connection with wounds infected with road-sweepings, or garden soil, and in America chiefly in cases of wounds connected with Independence Day celebrations, in consequence of which injections a very definite fall in the death-rate resulted.

During the War of 1914–1918 antitoxin was used on an extensive scale. During the early period, with no special arrangements for prophylaxis, the incidence was about 8 per 1000. Later, with the use of 500, and then 1500, units of antitoxin, the incidence fell to 1 in 1000.

In 1924 it was shown that tetanus toxin might be so treated as to lose its toxicity and still retain its antigenic power. The material, called "toxoid," has been proved of great service as a preventive agent. At the R.A.M. College it has been shown that two doses of 1 c.c. each of toxoid, given at intervals of 6 weeks, confer immunity lasting at least 2 years. In the French Army the regulations make inoculation with toxoid compulsory; 2 c.c. of mixed T.A.B. vaccine and tetanus toxoid are given on three occasions at 3 weeks' interval.

2. CURATIVE.—Keep the patient as quiet as possible in a dark and noiseless room. Feeding may be impossible by mouth, in which event nasal feeding may be attempted, and if this, too, is impossible because of spasm, recourse must be had to glucose enemata. The vapour of chloroform is the best remedy by which to control severe spasms, and a mixture of chloral and bromide in full doses should be given between the chloroform administrations. A more or less continuous use of morphine or hyoscine is the alternative measure.

It is profoundly important that no delay whatever should occur in the use of serum. Injections of serum may be made subcutaneously, intramuscularly, intravenously, or intrathecally. The latter method achieves much easier access to the affected nerve cells, and is certainly preferable, though it is usually, and rightly, combined with other methods, the more gradual action of the antitoxin when given by the subcutaneous or intramuscular methods tending to balance the rapid elimination of that given intrathecally. A lumbar puncture is made, and 20 c.c. of cerebro-spinal fluid are replaced by an equal, or even slightly greater, quantity of a high titre antitoxin. In an acute case from 50,000 to 100,000 international units may usefully be thus given in the first few days, and subsequently the intramuscular or subcutaneous methods may be resorted to. Paterson, in Australia, has suggested much larger doses, in a scheme as follows: On admission, 200,000 units are given intravenously and 80,000 intrathecally. The intravenous dose is repeated after 12 hours and thereafter at 24 hours' interval. The intrathecal dose is repeated every 4 hours at first and is gradually reduced. Concurrently with these large doses of antitoxin, tetanus toxoid is also indicated. An immediate

dose of 1 c.c. of toxoid should be given as soon as the disease is suspected, and repeated after 4 days.

Less success has attended the therapeutic use of tetanus antitoxin than is the case with diphtheria antitoxin. This result is largely, if not entirely, accounted for by the relative slowness in the onset of symptoms in tetanus as opposed to diphtheria. The argument for the prophylactic use of antitoxin in every case of a wound contaminated with road material or soil contaminated with animal excreta becomes correspondingly strengthened.

ANTHRAX

Synonyms.—Wool-sorter's Disease ; Splenic Fever of Animals.

Definition.—An acute infective disease caused by the *Bacillus anthracis*. There are three clinical forms of the disease, according as the lesion is in the skin (malignant pustule), in the lung (pulmonary anthrax), or in the intestine.

Ætiology.—*B. anthracis* is a large Gram-positive bacillus possessing a capsule. On artificial media it grows in long filaments which, owing to the fact that the filaments do not readily break up into individual bacilli, tend to bend upon themselves and thus cause the outlines of the colony to assume a whorled appearance that is characteristic. Spores always develop in cultures in the presence of free oxygen.

In the tissues, however, the bacilli occur in straight rods measuring from 5 to 10 μ by 1 to 1·5 μ, the longer forms generally being found in attenuated cultures, and the bacilli found in the gelatinous œdema are usually longer than those found in blood. Spores never develop within the infected animal since free oxygen is necessary. The micro-organism is non-motile.

In the herbivora, especially sheep and cattle, the disease occurs epidemically and the infection assumes a septicæmic type. The spleen may be two or three times its normal size, and on section may be diffluent. An impression preparation from the cut surface shows enormous numbers of bacilli together with blood cells and mononuclear leucocytes. The liver and kidneys are in similar condition, and the lymphatic system is extensively involved.

The bacilli in the blood are invariably in the vegetative form, and it is only after being voided from the body that they produce spores, these being extremely resistant to adverse influences. It is claimed that spores may remain on the ground in a state of latent activity for as long as 12 years. But it is suggested by M. Fadyear and others that soil infection counts for little in this country, most cases being traceable to imported food stuffs, hides and brushes.

The carnivora are relatively immune, especially the dog.

Man occupies an intermediate position, and the disease is always communicated to him directly or indirectly from animals. Two principal forms occur, malignant pustule, a local infection through a cut or abrasion of the skin or a hair follicle, and wool-sorter's disease, an infection starting in the trachea and bronchi from the inhalation of dust containing spores.

Infections of the intestinal tract may occur but are rare. Such infections must originate from spores, as the bacilli do not withstand the action of gastric juice.

Bacteriological Diagnosis.—In a case of suspected malignant pustule direct microscopic examination will usually show the bacilli in the fluid in the surrounding vesicles. Sometimes examination of the sections of the excised malignant pustule is necessary. Cultures on agar will show in 24 hours the characteristic wavy-outlined colonies. Blood cultures in man never show the bacilli until just before death. Putrefaction rapidly destroys anthrax bacilli, hence the recognition of the bacillus in putrefying tissues entails careful bacteriological examination and animal experiments.

A guinea-pig may be inoculated with suspected material, and if anthrax be present will usually die within 2 days, and the bacilli may be demonstrated in the spleen.

Immunity.—Pasteur, noting that one attack of anthrax immunised an animal, elaborated a method of artificial immunity. He attenuated cultures by growth at 42·5° C. Sheep survived when inoculated with such cultures, and proved immune to a subsequent injection of a highly virulent living culture. By carrying out this process of active immunity the mortality among animals was greatly lessened. Marchoux showed that the serum of such animals conferred a certain degree of passive immunity; and Sclavo, by using a mixture of such immune serum and progressively attenuated cultures and virulent cultures, obtained very high degrees of immunity in the ass. Sclavo's serum is stable, and if given in quantities of 40 to 100 c.c. at an early enough stage in the disease is almost always successful.

Formerly the local effects of infection were considered due to the mechanical damage to the tissues by the rapid multiplication of the bacilli. Later it was considered that the tissues were injured by simple deprivation of oxygen. Now the result is considered to be a toxic phenomenon. There are three clinical forms of the disease.

I. Malignant Pustule.—The site of infection is nearly always upon an exposed part of the body—face or hands or forearms. The incubation period appears to be very short, perhaps not longer than a few hours. A small red papule forms, which rapidly becomes vesicular and then incompletely pustular. By the time vesication occurs there is a surrounding zone of intensely red œdema, becoming a brawny induration by the end of the second day. By this time a ring of secondary vesicles often surrounds the initial lesion, which has now formed a dry and almost black scab, generally raised above the surface of the affected skin. A frequent associated lesion in the case of the arm is lymphangitis, spreading upwards to the lymph glands, which become enlarged and painful. There is rarely much pain at the site of the initial lesion, though there is usually a good deal of itching and tenderness. Fever is almost constant, and in severe cases may be quite high. The patient is then very ill, with intense toxic symptoms. Mild cases occur, however, and in them both the local and the general symptoms are much less marked.

The prognosis turns upon the severity of the symptoms, especially of the toxæmic state. Death is sometimes very rapid—it may occur within the first week.

In some cases the initial papule and vesicle are ill-marked, but the attendant œdema is excessive (*malignant œdema*). The mortality in this type of the disease is a good deal higher than in the type in which the pustule is well formed.

II. Pulmonary Anthrax.—In this variety of the infection the bacilli are inhaled with dust from infected hair or wool. The result is the rapid development of fever, generally ushered in by a rigor, with very intense toxic symptoms and the signs of bronchitis. Cerebral symptoms develop, with great weakness. The whole course of the disease may be very short, even as brief as 24 hours. Recovery probably never takes place, even if the diagnosis has been made at an early stage.

III. Intestinal Anthrax.—This is probably the least common form of the disease. The infection is due to eating meat or drinking milk from animals suffering from splenic fever. The symptoms are those of a severe gastro-enteritis—fever, vomiting, diarrhœa and intense weakness. The spleen is enlarged. This form of the disease has been found to occur in small epidemics. The mortality is high, though not so high as in II.

Treatment.—(i.) Prophylactic.—This consists in the specific immunisation of animals subject to the disease, the complete destruction of dead bodies, and in the careful disinfection of all skins, hair and wool, before these are handled in any industrial occupation.

(ii.) Curative.—General measures (rest, etc.) are taken towards the prevention of a general infection. The pustule is kept clean, but is neither cauterised nor incised. A large dose of Sclavo's anthrax anti-serum (40 c.c. at least) is given as soon as possible by the intravenous route. This is repeated intramuscularly at intervals of 12 to 24 hours, the dose being gradually reduced. If the serum is not available, 0·6 to 0·9 g. of neoarsphenamine or one of its equivalents may be injected intravenously and repeated in 48 hours. Some observers consider this treatment to be as good as by serum for malignant pustule, provided it be given within 4 days of the onset of the disease. Treatment by sulphapyridine, given intensively (see pp. 16–17), has also proved successful.

GLANDERS

Definition.—An infectious disease, occurring not infrequently in the horse and in the ass, occasionally transmitted to man, and characterised by the formation of granulomatous nodules in the nose (glanders), and in the subcutaneous tissues (farcy).

Ætiology.—The *bacillus of glanders*, or *Bacillus mallei*, is a short rod, straight or slightly bent, of 3 to 4 μ in length by 0·5 to 0·75 μ in thickness. It is non-motile, and possesses no flagella, nor does it form spores. It can be cultivated on ordinary media at 37° C., but gives a more characteristic growth on potato.

The bacillus stains somewhat faintly with the usual aniline dyes, so that a mordant, such as carbolic acid, is usually employed, but even when deeply stained there is a tendency to decolorise rapidly. The staining is markedly irregular, this irregularity being a diagnostically helpful point. It is Gram-negative.

Pathology.—The disease chiefly affects horses, mules and asses—the latter being the most susceptible. Horned cattle are immune, but goats and sheep are occasionally infected.

In the horse, infection may take place through any abrasion of the skin, but most frequently through abrasion of the nasal mucous membrane from

infected water-troughs or feeding-mangers. The infection may be acute or chronic. In the acute form (glanders proper) there is fever and prostration, and in two or three days there occurs ulceration of the nasal mucosa with a sero-purulent discharge, leading on to involvement of the lungs, and death within a few weeks. In the chronic form—farcy—there is involvement of the lymphatic system associated with the original site of entry. The lymph vessels become enlarged—farcy pipes—and irregular thickenings—farcy buds—occur, which may soften and suppurate.

The disease may be latent, and can then only be diagnosed by the "mallein" test. In the human being the infection is generally derived directly from the horse, and is therefore usually confined to those in close connection with horses; but the disease has been contracted in the laboratory.

The *toxin* of *B. mallei* or mallein is an endotoxin, being derived from the bacterial bodies, in which respect it differs markedly from the toxins of tetanus and diphtheria bacilli. One of its chief characteristics is its resistance, it being capable of withstanding temperatures of 120° C. and prolonged storage with but little loss of strength. It is prepared by growing cultures in glycerin broth for 3 or 4 weeks, and sterilising these by boiling or autoclaving at 115° C. The cultures are then allowed to stand, and the supernatant fluid being decanted off, this is then filtered through a Chamberland filter. The resultant filtrate, to which one-half of 1 per cent. of carbolic acid is added, constitutes *mallein*. It contains the soluble portions of the bacteria, and substances from the altered medium, and is a similar product to tuberculin. It is used in doses of 1 c.c. to detect a glanders infection in the horse. As the reaction in a "glandered" animal is severe, both locally and constitutionally, it is unsuitable for use in man.

Forms of the Disease.—Both glanders and farcy have been known to occur in man in acute and in chronic forms. All forms are rare.

Symptoms.—1. Acute Glanders.—The incubation period varies, but is in most cases 4 days. At the site of infection in the nose there occurs an inflammatory swelling surrounded by œdema and lymphangitis, with a papular eruption soon becoming pustular. In a few days other and similar swellings appear, which soften and ulcerate, so that the mucosa of the nose becomes generally infected, leading to profuse muco-purulent discharge. The whole nose swells; it may be very considerably. The ulceration extends deeply so as to involve the cartilage and bone. The cervical lymph glands are usually enlarged and may soften, forming abscesses. Constitutional symptoms are present by this time, and death, usually with pneumonia, occurs about the middle of the second week.

2. Chronic Glanders.—This form resembles closely the disease as seen in the horse. There is a chronic profuse coryza, associated with widely scattered muscular and subcutaneous nodules. Unless the nature of the disease is suspected, it may go undiagnosed for some time.

3. Acute Farcy.—This is the form of the disease resulting from accidental inoculation of the skin. A local lesion of a highly inflammatory kind leads quickly to a spreading zone of lymphangitis, subcutaneous nodules (farcy buds) appearing in the track of the infection, softening and forming abscesses. The patient becomes severely ill, with symptoms of a general infection, and the course of the disease is of much the same duration as in acute glanders.

4. CHRONIC FARCY.—This only differs from acute in that the "buds" are associated with much less inflammatory reaction, the constitutional symptoms are much less severe, and the course of the disease is much longer. A few of the cases have extended over 12 months.

Diagnosis.—Acute glanders has been mistaken for small-pox, owing to the likeness of the papulo-pustular eruption to the specific eruption of this disease. The chronic forms are at times mistaken for the other infective granulomata (syphilis, tuberculosis and actinomycosis). Exact diagnosis turns upon bacteriological methods, direct or indirect.

The *bacteriological diagnosis* in man may be simple if a superficial swelling exists which may be opened. Direct cultures may be made therefrom, preferably on potato, and a rapid diagnosis made. It may be, however, that weeks elapse before such an opportunity occurs, or before some deeply situated swelling calls for operative interference. In such cases serum reactions, such as the complement-fixation test and agglutination, are indicated, and in a case watched by one of the authors the diagnosis was made by the opsonic test several weeks before the bacilli were cultivated from the tissues.

If material containing *B. mallei* be injected intraperitoneally into a male guinea-pig, tumefaction and suppuration occur in two or three days in the tunica vaginalis, and the bacilli can be recovered therefrom after about six days.

Treatment.—PROPHYLACTIC.—The utmost care must be taken in nursing, destruction of old dressings, etc.

The site of inoculation, if obvious, should be excised, and the underlying tissues should be treated drastically by strong antiseptics. All abscesses should be opened promptly and efficiently drained. The general symptoms are met by treatment similar to that given in any septicæmia.

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TULARÆMIA

Synonym.—Deer-fly Fever; Pahvant Valley Fever; Ohara's Disease.

Definition.—A plague-like general infection of small rodents, hitherto confined to the United States, Japan and a district in Siberia; also recently in Norway, communicable to man. The disease has the peculiarity, in which it resembles Malta fever, of being extremely infective to laboratory workers handling the causative organism, *Bacterium tularense*, and attention to this aspect has been drawn by an important paper by Professor Sir John Ledingham and Dr. F. R. Fraser, in the *Quarterly Journal of Medicine*, vol. xvii., describing three cases occurring at the Lister Institute.

Ætiology.—In 1911 M'Coy, during plague work among ground squirrels in California, discovered a plague-like disease not due to *Bacillus pestis*, and in 1912 M'Coy and Chapin isolated the specific organism from the blood of infected animals, and it was named *Bacterium tularense*. Subsequently the organism was found in various rodents, and endemic centres of the infection have been recognised in various areas of North America. The first human case of infection appears to have been reported by Pearse in 1910, but bacterio-

logical proof connecting it with *B. tularense* was provided by Francis subsequently. Where the infection is endemic among rodents, human cases are not uncommon, and possibly some have recovered unrecognised. The infection is conveyed from animal to animal by various blood-sucking parasites. The fæces of infected bugs have been shown to be infective. Polluted water has recently been thought to be a source of infection in Norway and U.S.A. There is thus no difficulty in understanding how endemic centres of infection are kept up, and human infections in the field are readily understood. But it is difficult to explain the cases of infection in laboratory workers. It is suggested that a possibility is respiratory infection during the anæsthetising of experimental animals, when coughing is not uncommon, and the bacillus is certainly contained in bronchial secretions, as well as the excreta generally. The question appears to be parallel to the difficulty of explaining the great liability to laboratory infections with *Br. melitensis*.

B. tularense is a minute, Gram-negative cocco-bacillus, measuring, according to M'Coy and Chapin, 0·3, with a breadth of 0·2 μ. It is not easily stained by the ordinary dyes, unless a mordant, such as carbolic acid or aniline, is added. It is refractory to growth on ordinary media, the original cultures being obtained on a medium composed of egg-yolk. It will grow readily on serum glucose agar if a piece of rabbit spleen be added thereto.

Pathology.—In animals, nothing characteristic is found. At the site of inoculation some diffuse necrosis may be seen, and occasionally swelling of the corresponding lymph glands. The spleen, liver, lungs, and kidneys may show small necrosis areas. Human cases contracted in the field, probably from some blood-sucking fly, will show a local ulceration at the site of the bite, with swelling, and possibly suppuration, of the local lymph glands. Cases contracted in the laboratory provide no pathological data, for there is no evidence of the portal of infection, and the blood shows no characteristic changes.

Symptoms.—The infection expresses itself in two ways: (1) Dealers in rabbits may develop a necrotic papule, which is followed by acute lymphadenitis in the area affected. Suppuration may occur, with considerable pyrexia and toxæmia. (2) Laboratory workers studying the infecting agent have suddenly developed pyrexia, with marked malaise and no localising symptoms. The temperature subsided at the end of 3 weeks in the American series of cases, but it remained up for a longer period in the London series, and in one case there were irregular rises of temperature for a period of a year. The marked features of the majority of the cases were the malaise, the recurrent nature of the fever, and the prolonged inability to work.

Diagnosis.—In endemic areas, people handling rabbits and other rodents, who develop fever, with or without localising signs of insect bites, should be under suspicion. In this country, only laboratory workers are likely to be infected. In either case, the diagnosis depends upon specific agglutination of *B. tularense* antigen. Very definite agglutinations were noted towards the end of the second week after the commencement of the disease, and the titre rose rapidly and remained high during the long convalescence.

Prognosis.—This appears to be of about the same order as that in Malta fever. The disease is not fatal, but causes a long period of inability to work.

Treatment.—No account is given of any attempts to confer immunity,

either prophylactic or phylactic, and the treatment would appear to be one aiming at rest, with measures to counteract the anæmia that tends to supervene.

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SCARLET FEVER

Synonym.—Scarlatina.

Definition.—An acute specific fever of sudden onset characterised by faucial inflammation, a punctate erythema of the skin, and a tongue at first furred but later raw with prominent red papillæ. Desquamation follows, and inflammatory sequelæ may occur, involving especially the ears, cervical glands and kidneys.

Ætiology.—Scarlet fever is a disease of temperate climes and seldom gains a foothold in tropical or subtropical countries. It is endemic in large cities and populous centres, tending to flare up every few years in local epidemic form owing to the accumulation of susceptible material. Its general epidemic prevalence, however, is irregular, and no definite periodicity has been recognised. In the United Kingdom it is prevalent in the latter part of the summer and reaches its maximum at the end of the autumn; the period of least prevalence being the spring. Of late years, although the incidence has not appreciably declined, the mortality has fallen and the type of case become less severe. Severity, however, still varies greatly in different years and in different localities.

The case mortality of scarlet fever (proportion of deaths to attacks) is not more than 0·5 or 2 per cent. It is greatest in the first year of life and diminishes with age. Females are more liable to infection than males, but attacks in males are rather more likely to terminate fatally.

Of predisposing causes, childhood and the absence of acquired immunity are the most important. Infants under one year of age seldom contract the disease. The maximum incidence occurs during the fifth and sixth years of life, a period slightly later than is the case with such diseases as whooping-cough and measles. Adults are not exempt, but scarlet fever is rare in the aged. As a rule, one attack protects permanently, but second attacks do undoubtedly occur. Multiple recurrences should probably be referred to some other cause than scarlet fever.

Poverty, by entailing shortage of food, overcrowding, and defective isolation facilitates the spread of the disease and augments its death-rate.

The infective agent resides in the mucous secretions of the nose and throat and in the secondary suppurative lesions. The disease is infectious from its commencement, but the exact duration of infectivity cannot be determined for any given case. Six weeks' isolation is generally sufficient if by that time the mucous membranes are healthy and the skin free from sores. Many authorities reduce this period to 4 weeks for mild and uncomplicated attacks. Desquamation is not regarded as dangerous unless the scales are contaminated by the patient's discharges, and the infectivity of urine which remains albuminous has never been proved. The infectivity of scarlet fever is not nearly so great as that of measles, varicella or small-pox.

In most cases infection is by droplets derived directly from a person suffering with, or recently recovered from, the disease, but transmission by infected fomites or infected milk may also occur. Aerial infection by dust is possible. It is an important fact that discharges from the nose, throat, mouth and ear may remain infectious for many weeks, and pre-existing purulent discharges also become infectious when scarlet fever is contracted. The occurrence of catarrhal infection of the nose or throat in a scarlet fever convalescent may lead to a recrudescence of infectivity.

Intermediary carriers have on occasions spread the disease without themselves showing signs of infection. On rare occasions, too, convalescents, although apparently healthy, have for months remained capable of transmitting the fever. The infectivity of carriers appears to be intermittent, and the receptivity of those exposed is increased by close contact, debilitating circumstances or acute disease, of which diphtheria may be cited as an example. Attendants on scarlet fever cases, although long immune, may finally contract the disease.

Infected milk may be responsible for localised and, sometimes, for more widespread outbreaks of the fever. In most instances the milk has been infected from a human source, but possible derivation of infection from cows with ulcerated udders and teats is suggested by the well-known Hendon outbreak. Scarlet fever is not known to be transmitted by water or by sewage. Cases of wound infection are not numerous, but puerperal scarlet fever is well recognised.

Pathology.—Klein, in 1887, isolated a streptococcus from the teats and udders of cows at Hendon, and considered it the causal agent in a milk-borne epidemic of scarlet fever. It was customary, however, to regard the streptococci found in the throats and tissues of scarlatinal cases as secondary invaders, it being impossible to grow these organisms from the blood of patients suffering from the fever in its toxic, and presumably uncomplicated form.

Drs. George and Gladys Dick, of Chicago, however, produced evidence that scarlet fever is a *local* infection of the throat by a hæmolytic streptococcus, and attribute the general symptoms of the disease to toxins absorbed from the local focus. They have infected patients with scarlet fever by swabbing the fauces with a pure culture of their organism and have elaborated a test analogous to the Schick test in diphtheria. This is the *Dick test*. It is made by the intradermic injection of 0·1 c.c. of a 1 in 1000 dilution of toxic broth filtrate in saline solution. Boiled filtrate is used as a control. An erythema at the point of injection, maximal in 24 hours, indicates susceptibility to scarlet fever. The same types of reaction occur as in the Schick test (*q.v.*) but in the Dick reaction the erythema is not indurated. During the first few days of scarlet fever a positive result may be expected, but the test may prove negative for some days after the administration of anti-scarlatinal serum. A few convalescents remain positive to the test, the majority become negative. The new-born infant of a susceptible mother is usually Dick-positive.

Griffiths has shown that the hæmolytic streptococci of scarlet fever are members of a group comprising many different serological strains.

Susceptible persons can be immunised by subcutaneous injection of increasing doses of scarlatinal toxin at intervals of 7 days. For adults four

or five injections are required, commencing with 500 "skin test" units and ending with a dose of 50,000, 80,000, or even 120,000 units. The skin test unit of scarlet fever toxin is the smallest amount which gives a standard positive reaction in persons susceptible to scarlet fever, and a negative reaction in persons immune to the disease. The standard reaction is the appearance within 24 hours of an area of erythema not less than 1 c.m. in diameter. If too large an initial dose of immunising toxin is given, a transitory "miniature scarlet fever" may result, but this is rare. The simultaneous injection of 2 or 3 minims of 1 : 1000 adrenaline chloride solution prevents serious reactions. Immunity develops more slowly than in the case of diphtheria, and its duration is indefinite but prolonged. If the Dick test proves positive 6 months after, a further injection is recommended in the case of those nursing scarlet fever.

By immunising horses, an antitoxic serum is produced, which may bring about a rapid amelioration of the toxic symptoms of scarlet fever, but has little influence in preventing complications.

Schultz and Charlton pointed out that intradermic injection of 1 c.c. of the serum from a patient convalescent from scarlet fever will, in a few hours, cause a local blanching of the rash of the fever. This is known as the blanching test. W. Mair suggests that the test is due to antitoxic immunity in the donor, which will account for its occasional failure, and also the fact that the serum of some donors not known to have had scarlet fever, will give the reaction. The antitoxin prepared from the Dicks' scarlatinal streptococcus possesses the same blanching property, and now is used for the test.

The post-mortem appearances in scarlet fever are not distinctive. The rash, unless hæmorrhagic, disappears after death. Such gross changes as are found in the fauces, cervical glands, lungs, heart, kidneys and liver, together with moderate enlargement of the spleen and lymphoid structures, merely indicate an acute infective process. In severely toxic cases, early decomposition with much post-mortem staining of the tissues, fluidity of the blood and subserous ecchymoses, indicate the intensity but not the nature of the infection. In cases surviving longer, inflammations of the lungs, serous sacs, endocardium, pericardium and joints may possibly be present, and desquamation may be recognised. Scarlatinal nephritis is described as being essentially glomerular in type, but other parts of the kidney are also involved.

Symptoms.—The incubation period is short, the period which elapses between infection and the development of the first symptoms being from 2 to 4 days, with an average of 72 hours, or 4 days from exposure to rash.

Invasion is abrupt, the cardinal symptoms being vomiting, headache and sore throat. In some severe cases vomiting may be so urgent as to suggest irritant poisoning, especially if accompanied by diarrhœa; in mild cases vomiting may be absent. Rigor is uncommon, convulsions occasionally occur in children. Cough and catarrhal symptoms are decidedly rare, but a mild conjunctival injection is not unknown. The skin is hot and dry, the cheeks flushed, and the eyes bright. The limbs ache, the appetite is in abeyance, and the tongue rapidly becomes coated with white fur, through which the papillæ project as red points (*strawberry tongue*). Slight nocturnal delirium is common. The temperature rises rapidly, and even on

the first day may reach 103° or 104° F. An undue acceleration of the pulse is usually a marked characteristic, rates of 160 or more are common in young children, and rates of 120 to 140 in adults.

Very mild cases often occur, and in these the symptoms of invasion may be absent, the rash being the first indication of the disease.

Uniform injection of the tonsils, fauces, and uvula is present in the early stages of the disease. Later, the injection becomes more vivid, the tonsils are swollen, and a distinct follicular exudate often appears; inflammatory œdema of the fauces soon makes its appearance in severe cases, and may be accompanied by free mucous secretion. The tonsils may become covered by a thin necrotic film, or a more or less coherent exudate may form which may encroach on the faucial pillars and base of the uvula, and closely simulate the membranous exudate of diphtheria. In the more severe forms of scarlet fever, the tonsillar and faucial inflammation is very intense, and both ulceration and sloughing occasionally occur; thick muco-pus trickles down from the naso-pharynx, the nasal sinuses are invaded, and acrid discharge blocks the nostrils and excoriates the upper lip. The respiratory obstruction is especially severe if adenoids are present. In severe cases, inhalation broncho-pneumonia is a decided danger.

A punctate injection may often be seen on the soft palate and adjacent part of the roof of the mouth even before the appearance of rash on the skin, and is of diagnostic value. The eruption usually appears within 24 hours of the invasion, but may be delayed sometimes for several days. It appears first on the upper part of the chest, the root of the neck and the upper arms as a finely punctate erythema; sometimes it is first seen in the axillæ. It quickly spreads to the trunk and limbs, reaching the legs last. The cheeks are merely flushed, and the existence of an area of circum-oral pallor is a well-known and striking feature. The thick skin of the palms and soles is also in most instances free from the distinctive rash. The eruption often shows a symmetrical intensification in certain regions, such as the lower abdomen and groins, the inner aspects of the thighs, the axillæ, the back, and the points and flexures of the elbows and knees.

Of the two elements of the rash, one is minutely punctate, the other erythematous. It is the former which gives it its distinctive character. On coarse skin the puncta are particularly large. When the erythematous element is intense the skin may actually appear œdematous and the puncta be quite obscured. In such cases, on subsidence of the rash, yellow staining may be apparent. In addition to punctation and erythema, minute petechiæ or small linear hæmorrhages are sometimes seen in the flexures of the elbows (*Pastia's sign*), groins, wrists and knees. By application of a tourniquet to the upper arm, petechiæ may be rapidly produced at the flexure of the elbow. This is the *Rumpel-Leede phenomenon*. It may also be positive in measles, purpuric states and peliosis rheumatica. These hæmorrhages remain when the rash has faded, and together with coarse injected papules on the outer sides of the arms and legs afford valuable evidence. The rash on the buttocks and extremities may assume a slightly blotchy papular appearance, and so bear a distant resemblance to that of measles. Minute sudamina sometimes accompany the rash, giving rise to the variety known as *scarlatina miliaris*. Itching is not common, and urticaria is rare, but in some cases accompanies or precedes the outbreak of the rash.

The rash may be quite transitory or may last a week or even longer. Generally speaking, it is more pronounced in severe attacks, but sometimes attacks which are quite mild show rashes of considerable intensity and persistence. A dusky, blotchy, morbilliform eruption, generally limited to the convexity of the knees and elbows, but sometimes more widespread, may supervene in grave cases. It is known as the *septic rash.*

At the time of the initial faucial inflammation the glands at the angles of the lower jaw are swollen and tender. During the eruptive period a moderate enlargement of the axillary and inguinal glands, sometimes of the posterior cervical glands as well, is often to be detected. The spleen is rarely to be felt. At times the glandular swelling leads to confusion with rubella, but the glands do not attain the size or show the marked tenderness characteristic of the latter disease.

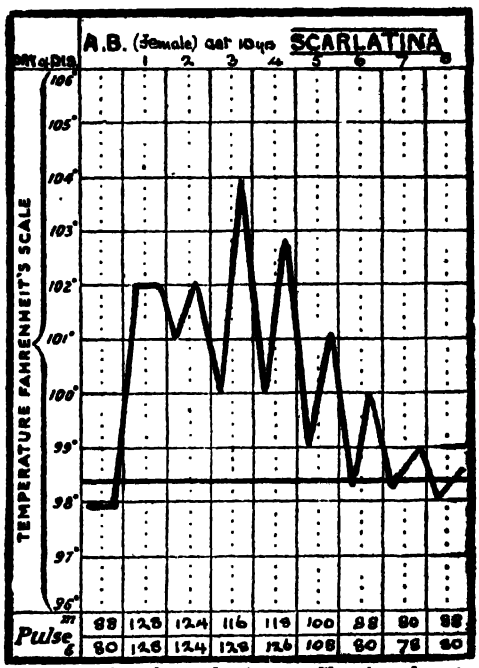


FIG. 1.—Simple scarlet fever. Showing abrupt onset and rapid lysis.

In an average case a rapid rise of temperature (Fig. 1) marks the invasion, but the maximum may not be attained until the full development of the rash on the third or fourth evening, when readings of 103°, 104° or even 105° F. may be registered. Slight morning remissions occur. The fall is by lysis, reaching the normal by the fifth or sixth day of the disease. Termination by crisis is unusual. In bad cases of a septic type, the fever is prolonged, with increasing daily oscillations as septicæmic symptoms become prominent. In the malignant or toxæmic type of the disease, the fever is higher from the first and shows less remission, but occasionally is subnormal throughout. A protracted remittent fever may occur in scarlet fever without local symptoms or complications to account for it; this variety is sometimes known as the "typhoid type."

Abrupt rises of temperature during the convalescent period may signalise the onset of such complications as adenitis, otitis, nephritis, endocarditis, empyema, or a metastatic abscess. Sometimes such pyrexial attacks occur without ascertainable cause, but a thorough examination of the patient is always necessary. Very mild cases of scarlet fever without obvious febrile disturbance certainly exist.

Desquamation is a well-known characteristic, but the degree to which it

occurs is very variable. The tongue peels in patches or strips, and by the fourth day is raw with prominent papillæ (*raspberry tongue*). The flushed cheeks begin to shed a fine powder during the febrile period. Fine peeling of the lobules of the ears, of the margins of the lips, and of the skin at the root of the neck, possibly also above the pubes, next makes its appearance. By the end of the first week, peeling is generally well marked on the neck, chest, inner sides of the arms, and possibly on the trunk. Within a fortnight it may be seen on the hands and possibly on the feet. It may not be complete on the latter until over 6 weeks from the onset of the fever. Partial re-desquamation often occurs on the soles and is not infectious. The characteristic of the desquamation is the pinhole or ringed form in which it commences, the horny layers of the skin being shed first over the summits of the papillæ, forming apertures which enlarge centrifugally and fuse with their neighbours. Where the skin is thick, as on the hands and feet, it tends to separate in larger flakes, or may even be thrown off in the form of incomplete casts. A rather characteristic form of peeling is sometimes seen on the finger-tips when separation begins, as a split parallel to the free edge of the nail.

In severe cases considerable loss of hair may accompany or follow desquamation, but is temporary only, at all events in the younger patients. Furrows may also appear across the nails and take several weeks to reach the free edge.

Although desquamation typically proceeds as described above, there are cases of true scarlet fever where it is insignificant. It is unsafe to pronounce definitely against scarlet fever until 3 weeks have elapsed. In doubtful cases the hands and feet should be watched with care. A change to negative in the Dick test is confirmatory. A dry powdery appearance of the palms and soles is sometimes the sole indication of peeling. During desquamation the skin may appear harsh, dry, cracked or even eczematous.

A polymorphonuclear leucocytosis makes its appearance shortly after infection and reaches a maximum with the full development of the rash. It persists a variable time. A unique feature in favourable cases is an increasing eosinophilia during convalescence. Fluidity and slow coagulation of the blood are indications of severity, but apart from this blood examination has little prognostic value. Döhle has described certain bodies seen in the polymorphonuclear leucocyte when stained by Leishman's method as being characteristic. They appear in the acute stage as more or less definite blue spots in the cytoplasm of the cells. They are, however, not exclusively found in scarlet fever.

VARIETIES.—These are: (*a*) Simple or Benign; (*b*) Septic or Anginous; and (*c*) Toxic or Malignant. Surgical or Wound Scarlet fever and scarlet fever occurring during pregnancy or the puerperium, also have special characteristics.

Simple scarlet fever is characterised by an onset of moderate severity in which the initial vomiting is not repeated and sometimes is absent. The faucial inflammation is slight, and the temperature, which may reach 102° F., has almost reached its acme in 24 hours; generally the climax is reached by the third day and amelioration of symptoms is then rapid. The urine may be normal throughout, or a trace of albumin may accompany the febrile disturbance. By the third or fourth day the tongue, at first slightly coated,

has peeled, and slight powdering may be evident on the cheeks. Convalescence is rapid.

The *septic or anginous* variety comprises most of the severe and fatal cases. It is characterised by intense faucial inflammation and a tendency to the development of septicæmic manifestations. Repeated vomiting, sharp diarrhœa and prostration may signalise the onset. The faucial inflammation is either severe from the first or unexpectedly becomes so after a lapse of 2 or 3 days. The tonsils are much swollen and a patchy or coherent membranous exudate may form. Rapid and destructive ulceration of the tonsils, soft palate and its pillars sometimes occurs. The mucous membrane of the mouth may be excoriated and bleed at the slightest touch. The pharynx, and even the upper aperture of the larynx, may become involved in the inflammation, although, as a rule, implication of the latter is more suggestive of diphtheria than of scarlet fever. The discharges from the throat excoriate the angles of the mouth and a purulent acrid rhinorrhœa irritates the nares and upper lip. Deglutition is painful, respiration is obstructed, and the patient often sleepless, restless and later delirious. The cervical lymph glands become swollen and tender, and peri-adenitis or extensive sloughy cellulitis of the neck may ensue. This sometimes gives rise to fatal hæmorrhage by eroding large veins or even an artery. Cyanosis and coldness of the extremities and cardiac dilatation are common. The rash is generally intense, dusky and blotchy. The temperature often reaches 104° or 105° F. in the early stages of the disease, and pyrexia may persist long beyond the ordinary period and, changing its type, assume a remittent or intermittent septicæmic form.

Death may occur in the first week; more often life is prolonged into the second week, by which time circulatory failure becomes pronounced; hypostatic congestion of the lungs or spreading broncho-pneumonia occurs. Otitis, arthritis, suppurations of the serous sacs, endocarditis, or nephritis may appear as complications, and a true scarlatinal pyæmia be evident.

Many patients show septic symptoms of a much milder type and make good recoveries. In grave cases which recover, improvement is very gradual and usually sets in towards the end of the second week, but may be later.

Toxic or malignant scarlet fever is characterised by a toxæmic condition out of all proportion to the degree of inflammatory reaction in the throat. Such cases are marked by high fever, cerebral disturbance, profound prostration and circulatory failure. The rash is often petechial, but in the most severe attacks the patient may die before it has time to appear, and the real nature of the disease may only be revealed by the supervention of scarlet fever in contacts. The throat may be intensely injected, but the œdema, ulceration and thick purulent secretion which characterise the septic variety may be absent altogether. Sometimes convulsions precede death, but mostly delirium merges into coma. Rarely, however, the patient dies of circulatory failure with vomiting, prostration and extreme pallor, but with clear intellect, suggestive of the type of death seen in some cases of diphtheria.

Sufferers from the malignant type of scarlet fever mostly succumb within a week of the onset, sometimes within 24 hours. But, as in the septic form, cases of the toxic or malignant type are not now so common or characterised by such extreme malignancy as was formerly the case.

Rarely scarlet fever assumes a purpuric form, with bleeding into the skin

and sometimes from the mucous membranes also. This complication makes its appearance towards the end of the second or during the third week, and often proves fatal. It is possible that some of the cases formerly described, where hæmorrhages occurred early in the eruptive stage of the disease, were really hæmorrhagic small-pox with prodromal rashes of scarlatiniform character.

Surgical scarlet fever may be a sequel of operations, wounds or burns and scalds. It is often seen after operations on the nose and throat. The incubation period is short, often less than 3 days, and the rash may make its first appearance round the wound. Faucial inflammation save in throat cases is often slight, and faucial swabs may be negative. The infected wounds show a great tendency to suppurate. If the infection starts from a wound or abrasion on a limb, injected lymphatic vessels are often evident which show a characteristic punctate rash. The corresponding lymph glands are enlarged and tender. When the fever follows burns or scalds the incubation period is also short and the accompanying angina may be slight. Cases of surgical and of burn scarlet fever where the throat is not especially involved are not highly infectious. They are often left in general wards with impunity, but there is no doubt that occasionally they spread the infection.

Scarlet fever may arise in the pregnant woman. In early pregnancy it is rare, and is said not to lead to abortion ; but occurring later it is very prone to produce abortion or premature delivery. When the infection occurs either immediately before or immediately after labour, it is apt to assume a grave form with a very high mortality from septicæmia ; but there is no doubt mild attacks may occur even at this period.

Anomalous forms of scarlet fever occur in which one or more of the cardinal symptoms are lacking. In some only sore throat is recognised (*Scarlatina sine eruptione*), and yet the patient may transmit the typical disease. The cases of infectious sore throat which often herald outbreaks of scarlet fever belong to this category. In others the rash is so ephemeral or atypical that its true nature escapes recognition ; in yet others, the rash is the most pronounced feature, both fever and sore throat being insignificant. In cases where the rash is very scanty or insignificant, desquamation may not be at all marked.

Complications.—These may be divided into two groups ; those which arise locally in connection with the faucial and pharyngeal inflammation, and those of a general or more remote character. To the first group, in order of frequency, belong otitis, cervical adenitis, rhinitis, secondary tonsillitis and stomatitis, and aspiration broncho-pneumonia. The second group includes rheumatism, albuminuria, nephritis, endocarditis, pericarditis, pleurisy and empyema.

In severe cases complications show a great tendency to occur in combination rather than singly.

Otitis.—This is met with in from 10 to 15 per cent. of the cases, and is an inflammation of the whole mucous tract of the middle ear. Its greatest frequency is in childhood, and its incidence is favoured by the presence of adenoids. It is more common in severe cases, and may show itself by the end of the first week of the fever or later. It is often bilateral. Earache with an injected and bulging tympanic membrane are the signs to be expected, but sometimes a free discharge of muco-pus or pus and blood from the ear is the

earliest indication. Unexplained pyrexia not due to fresh faucial or glandular extensions or to one of the distant complications should always lead to a careful examination of the ears. Perforation generally occurs in the upper part of the tympanic membrane. Deafness may occur, but fortunately is transient in most cases. Pain and tenderness with slight œdema of the mastoid appear in some instances, and may be accompanied by restlessness, vomiting and fluctuating temperature. The intensity of these mastoid symptoms may vary from day to day. In children the mastoid air cells are very superficial, and pus easily makes its way beneath the covering periosteum.

Sometimes the labyrinth becomes implicated. In such cases deafness, vomiting, vertigo and nystagmus may occur. Labyrinthine deafness may be permanent.

Such intracranial complications as meningitis, extradural abscess, lateral sinus thrombosis, cerebellar or temporo-sphenoidal abscess, belong to the more chronic forms of ear disease, but occasionally they arise during the acute stage. Persistence of mastoid tenderness with some local headache and slight fever may be the only signs of inflammatory mischief invading the dura in the vicinity of the lateral sinus.

In most instances scarlatinal otitis subsides in a few weeks and the perforation of the membrane closes.

Secondary Adenitis.—A rapid and considerable swelling of the upper cervical lymph glands may occur during the convalescent stage of the fever. The swollen glands are usually those behind the angle of the mandible or higher up under the insertion of the sterno-mastoid muscle. The adenitis generally supervenes during the second, third or fourth week of the disease. It is marked by local tenderness and a sharp accession of fever. In favourable cases the temperature becomes normal in a day or two and the glandular swelling rapidly subsides, but suppuration may ensue.

Secondary tonsillitis should suggest the possibility of diphtheritic infection. Peritonsillar abscess may also occur. Ulcerative stomatitis with much fetor of breath and sometimes even sloughing of soft tissues and necrosis of bone are also looked upon as secondary infections. Vincent's organism and diphtheria bacilli should be sought for in such cases.

Rhinitis.—Acrid or purulent rhinorrhœa is characteristic of septic attacks. The air sinuses may become infected. A rhinorrhœa which occurs in the later stages of the fever is often responsible for the transmission of infection. True diphtheria bacilli are more frequently found in the nasal than in the ear discharges of those suffering from scarlet fever.

Nephritis.—Slight albuminuria during the eruptive stage of scarlet fever is transitory and of no great importance, but about the third week nephritis may supervene. It is to be expected in a little over 3 per cent. of the cases, and is more common in severe than in mild attacks. Chill, damp and exposure favour its incidence. The onset may be insidious or fulminant. In the insidious cases albuminuria, at first slight, and even intermittent, is the first sign. In the fulminant cases, headache, vomiting, pyrexia and even rigor may mark the onset. The urine becomes heavily loaded with albumin, casts and blood, and there is more or less suppression. The temperature may rise gradually or suddenly and show marked daily remissions. Lumbar pain is uncommon, but abdominal pain and constipation are marked features of some attacks. The amount of dropsy is very variable; it may be con-

siderable in ambulant cases. Anæmia is of rapid onset and very pronounced. The pulse tension is raised and cardiac hypertrophy is soon established, sometimes dilatation ensues. In a favourable case some improvement occurs within a week, the secretion of urine increasing, but the hæmaturia and albuminuria take much longer to clear up. In some cases albuminuria persists and chronic interstitial nephritis may ensue. The duration of an average attack may be put at 7 weeks, but is subject to much variation. Broncho-pneumonia, pulmonary œdema, œdema of the glottis, and uræmic symptoms occur in severe cases. Convulsions may be recovered from, but coma is of bad augury.

In the septic type of scarlet fever sharp hæmaturia with casts and streptococci may accompany other pyæmic manifestations.

Rheumatism.—This is common, and usually makes its appearance towards the end of the first week. The arthritis is fleeting and mostly involves the hands and wrists. Joint effusions are not always present. The temperature is raised. Sometimes the endocardium and pericardium are implicated, as in ordinary rheumatism, but the profuse sweats and creamy tongue are absent. Scarlatinal rheumatism is more common in adolescents and adults than in children. A mono-articular or multiple suppurative arthritis with, it may be, other pyæmic manifestations is sometimes seen.

Cardiac complications.—There are three groups: those due to toxæmia; those secondary to rheumatic or pyæmic complications; and those accompanying nephritis. The toxæmic effects are cardiac dilatation and acceleration of the pulse, which are so characteristic of this fever.

Scarlatinal rheumatism is occasionally the precursor of simple or more rarely of malignant endocarditis. An unfortunate feature is the tendency to pick out the aortic valves. The influence of nephritis in producing rapid cardiac hypertrophy or inducing dilatation has already been mentioned. Pericarditis may occur quite early in some cases of the septic type. The effusion is generally purulent.

Pulmonary complications.—Neither bronchitis nor broncho-pneumonia is common, but aspiration broncho-pneumonia may complicate septic cases. Œdema of lungs may arise during the course of acute nephritis. Lateral sinus pyæmia may give rise to pyæmic infarction of the lungs, empyema and even pneumothorax. A primary empyema, often of insidious onset, occurs in some patients. Lobar pneumonia is rare; occurring early in the disease, it is streptococcal in nature and the prognosis is very grave.

Streptococcal peritonitis is a very rare event.

Nervous complications.—If the delirium of onset, the nervous manifestations of uræmia and the cerebral complications of otitis be excluded, it may be said that nervous disturbance during the course of scarlet fever is rare. In those predisposed, epileptic fits may signalise the invasion. Hemiplegia with convulsive onset, incomplete paraplegia and peripheral neuritis have all been described. Chorea develops occasionally, usually in association with arthritis and endocarditis. Tetany sometimes occurs. Mental disturbance of a maniacal or melancholic type is an infrequent sequel, or may show itself during the acute stages.

On rare occasions gangrene of the extremities has been encountered. It is sometimes embolic in origin and leads to mummification, but gangrene has also been described in association with purpura and in

congenital syphilis. Post-scarlatinal diphtheria was, in pre-antitoxin days, one of the gravest complications. Diphtheria may develop at the onset of the fever, but more often appears during early convalescence. It occurs more often in hospital-treated cases than in others. Every throat inflammation about the nature of which there is the slightest doubt should be subjected to bacteriological examination at once. This is a more rational procedure than the indiscriminate injection of all scarlatinal patients with diphtheria antitoxin. All nasal and ear discharges should also be bacteriologically examined.

Relapse and Reinfection.—A recurrence of the fever and rash before complete recovery from the initial attack occurs in from 0·5 to 7 per cent. of the cases. In hospital it is not uncommon for the original infection to be replaced and protracted by one of different serological type.

Diagnosis.—Bacteriological identification of the *Streptococcus scarlatinæ* is not sufficiently easy to afford much help in diagnosis. A positive Dick test before the third day of the attack is in favour of scarlet fever (it should become negative later) but a negative result does not exclude it. A positive Schultz-Charlton blanching test, made by the intradermic injection of 0·2 c.c. of a 1 in 10 dilution of immunised horse serum applied to the newly developed rash, preferably on the lower abdomen, is of more value. The reaction takes 8 hours to develop, and attains a diameter of 3 c.m. or more. The chief difficulty arises with mild attacks and with patients who come under observation after the initial stage. In the former the rash is evanescent, constitutional disturbance slight, and the tongue often atypical. A history of a previous attack is of great weight, but diagnosis can only be confirmed by the supervention of desquamation or of some characteristic complication. Sometimes the infection of a contact gives the clue. In days immediately following the rash significant signs are: slight staining of the trunk, faint striæ in the flexures of the elbows, knees and groins, or a triangular patch of punctate erythema over Scarpa's triangle. The submandibular glands may be enlarged, and coarse papules resembling goose-skin present on the outer aspects of the arms and legs. The tongue has usually peeled by the fourth day and remains raw and papillated for about a week. Slight albuminuria, in the absence of diphtheria, is significant.

Desquamation of the typical pinhole type rarely occurs in other conditions than scarlet fever; the character of the accompanying symptoms and the time of appearance of the peeling must be taken into consideration.

Simple tonsillitis is distinguished by the absence of punctate rash, a tongue which remains heavily coated, and absence of desquamation. But an erythema may be present, with fleeting muscular pains and sometimes otitis, and even endocarditis or nephritis may occur as complications.

Careful scrutiny of the body for a rash will usually prevent confusion with *diphtheria*. When faucial exudate is present in scarlet fever, it is usually softer and less coherent than in diphtheria, and any grey ulcerated areas are depressed below the general surface. In scarlet fever, too, the faucial pillars and soft palate may show the punctate rash, whilst pallor of the throat is more distinctive of diphtheria. In scarlet fever, febrile disturbance is more marked, initial vomiting is common, and delirium may occur. The fugitive erythema which sometimes appears on the chest in diphtheria is not

punctate. Bacteriological examination is decisive, but the two diseases may coexist.

When *influenza* is rife, cases of scarlet fever are apt to be overlooked; but in influenza rashes are exceptional, and careful observation of the progress of the disease will soon lead to a correct diagnosis.

Lobar pneumonia may, in children especially, by its abrupt onset, high fever, vomiting and faucial inflammation, give rise to suspicion of scarlet fever, a suspicion favoured by the flushed face and circumoral pallor which may be present. But the throat affection is trivial, the respirations are rapid and accompanied by action of the alæ nasi, and there is no punctate rash on the chest. Sooner or later consolidation of the lung may be detected, often in such obscure cases at the apex or high in the axilla.

Food, drug, serum and enema rashes often cause difficulty. Of drugs the most important rash-producers are copaiba and similar oleo-resins, quinine, phenazone, the salicylates, aspirin and belladonna. Arsphenamine compounds and sulphonamides may also do so. Anomalous distribution or polymorphic character of the rash should at once arouse suspicion, especially so the discovery of urticarial wheals. The history and accompanying symptoms are of importance.

Erythema scarlatiniforme is characterised by a punctate eruption which is sometimes patchy and confined to the trunk. The rash is remarkably persistent, and desquamation may ensue whilst it is still in the florid stage. The peeling is profuse and the subjacent skin often erythematous. The characteristic sequelæ of scarlet fever are wanting. The disease is not known to be infectious and is very apt to recur, which gives a clue to its recognition. *Acute exfoliative dermatitis* is by some regarded as identical with it.

German measles in the scarlatiniform stage closely resembles scarlet fever. The diagnosis turns on the trivial character of the accompanying symptoms, which are chiefly catarrhal, and the tender swelling of the posterior cervical mastoid, and occipital glands. Even when the rash is scarlatiniform on the trunk, distinct morbilliform elements may often be recognised about the wrists and on the lower extremities, and this, with the history of an initial spotty rash on the face and around the mouth, is of great significance. The eyes are suffused and subsequent desquamation is insignificant. Sequelæ are practically unknown.

Measles is more easily distinguished. The rash is different and invades the face. Catarrhal symptoms are pronounced and Koplik's spots are present. Difficulty is only likely to arise in those cases of scarlet fever where a blotchy rash is present, or where the appearance of a septic rash may simulate intercurrent measles.

Prodromal rashes of a scarlatiniform type may appear in small-pox, chicken-pox and measles. In small-pox, the punctate rash is usually confined to the bathing-drawers area and to the axillæ. Sore throat is in favour of scarlet fever, whilst rigor and severe lumbar pain suggest small-pox. The eruption of the latter disease appears on the third day, and a doubtful case should always be isolated over that period. The initial rashes of small-pox are said to be absent in children under 10 years of age.

The eruption of chicken-pox may be preceded by a rash which is scarlatiniform, but it is more likely to be erythematous. The diagnosis turns on the

condition of the fauces and tongue, the absence of the other signs of scarlet fever, and the speedy appearance of the characteristic vesicles.

As a prodromal rash in measles, a scarlatiniform eruption is decidedly rare. The marked catarrhal symptoms which accompany it will arouse suspicion, which is confirmed by the discovery of buccal inflammation and Koplik's spots.

Prognosis.—The mortality of scarlet fever varies with the type of the prevailing epidemic. Of late years, in Great Britain, a mortality of less than 1 per cent. has been the rule. Of other factors, age is the most important, the mortality being greatest in infancy, diminishing rapidly after the second year, and continuing to fall until puberty is reached, the least fatal period being from puberty to 36, after which age a slight rise occurs. The death-rate is slightly higher in males than in females. Tuberculous infections are likely to be lighted up by the infection, and puerperal patients run a grave risk of septicæmia. Chronic renal disease, if present, is likely to be adversely influenced.

Malignant attacks are very fatal, and the septic type of attack is also very serious, especially if broncho-pneumonia supervenes. In adults, marked sleeplessness and delirium are unfavourable signs, and in children, convulsions occurring after the initial stage. With regard to complications, nephritis in many instances clears up, especially if detected early and properly treated. Grave symptoms are uræmic convulsions, coma, repeated vomiting and suppression of urine. Œdema of lungs often precedes the fatal issue.

Of other complications, pericarditis is the worst. It is often purulent and may be associated with empyema. Hemiplegia, if of vascular origin, mostly becomes permanent. The danger of otitis media is remote rather than immediate.

Treatment. — PROPHYLACTIC. — Infectivity ceases mostly within a period of 6 weeks. A negative throat culture does not always indicate cessation of infectivity, and this test is not employed as a routine measure. Late desquamation of the hands and feet is not a source of infection, but discharges from the nose, throat or ear are dangerous. Convalescent carriers are responsible for something less than 3 per cent. of the cases treated in fever hospitals. The dangerous carrier is often characterised by unhealthy conditions of the nose, throat or ear, discharges from which may have reappeared owing to the supervention of catarrh. Patients with persistent tonsillitis, adenitis, rhinorrhœa or otitis should be isolated for at least 12 weeks from the commencement of the fever. The discharge of patients direct from wards containing others in the acute stage of the disease should be avoided ; isolation for a day or two in a separate apartment is advisable. It is safer to remove those who remain Dick-positive during convalescence from all contact with acute cases. In cold weather the practice of bathing on the very day of discharge is not recommended, as a catarrh may be thus induced. Patients should not pass straight from isolation into the company of children and other susceptible persons.

Individuals in close contact with scarlet fever have at times been found to convey the infection, but a greater source of danger is the convalescent carrier, whose infectivity persists beyond the usually recognised period. The infectivity of such carriers has been known to last for weeks and even months ; there is some evidence that it is intermittent.

The rules originally formulated by the Medical Officers of Schools may be taken as a safe guide in practice, *i.e.* isolation for not less than 6 weeks, provided convalescence is complete and there is no evidence of inflamed throat or of discharge from the nose or ear, no suppurating or recently enlarged glands, and no eczematous patches about the nostrils, mouth or elsewhere. For very mild attacks, 4 weeks in hospital followed by 2 weeks convalescence is sufficient. The quarantine period for contacts is 10 days, provided disinfection was efficiently carried out at the commencement of that period. In institutional and ward outbreaks the contacts should be Dick-tested for susceptibility and throat swabs examined for hæmolytic streptococci. Those who harbour streptococci should be isolated. The susceptibles in ward outbreaks usually receive 5 or 10 c.c. of antitoxin, which establishes a temporary passive immunity.

CURATIVE.—Doubtful cases should be isolated until a definite diagnosis is made. Their premature transfer to a scarlet-fever ward is unjustifiable. Isolation of scarlet fever at home is most successful when a whole floor can be set apart for the patient and attendants, and there are no children of susceptible age in the house. The sick room should be large, light, freely ventilated and adequately warmed, the temperature being maintained at 55° F. to 60° F. Overalls should be worn by attendants, and all articles used by the patient sterilised at once.

The action of the skin is promoted by a daily wash and a tepid sponge every evening during the pyrexial stage. This may be replaced by a daily warm bath when defervescence is complete. The bed coverings should be adequate, but not too heavy. During convalescence, flannel or wool is the proper clothing; chill is by all means to be avoided. During the febrile stage the diet should consist of milk, barley water, or plain water and weak tea. When the temperature falls, beaten-up eggs and farinaceous food may be added and the diet gradually increased, nitrogenous food being allowed early in small amount. Most patients are fit for full diet within a week of the subsidence of the fever. Children, at all events, should be confined to bed for 3 weeks from the onset; by this means chills are avoided, the usual period of onset of nephritis passed, and the throat healed before the patient gets up. When the weather is warm, outdoor exercise may be allowed with advantage in the third or fourth week.

Attention should be paid to the mouth, teeth and gums, since oral sepsis is believed to bring its own train of local complications. The bowels should be regulated with mild aperients.

In all but the mildest cases concentrated scarlatina antitoxin should be given early. The dosage varies from 3000 to 15,000 U.S.A. units according to severity. A unit is the amount which neutralises 50 "skin-test" doses of the standard scarlet fever toxin. Administration is repeated daily in severe cases if necessary. The serum is given intramuscularly. If the intravenous route is chosen, reactions may be very severe, the serum should be diluted, and to guard against anaphylaxis, a preliminary intravenous test injection of $\frac{1}{10}$ c.c. in normal saline is advisable. Preliminary desensitisation is essential in sensitised patients.

Sulphonamide preparations are valuable in the presence of streptococcal complications, but do not influence the toxæmia of the disease.

Osman states that the incidence of nephritis is diminished if sufficient alkali is administered to keep the morning urine alkaline.

Pyrexia, with restlessness, insomnia and delirium, may be controlled by tepid sponging and acetylsalicylic acid or paraldehyde. A cold pack at 60° or 70° F. for 15 or 20 minutes is beneficial when nervous symptoms are pronounced. After the middle of the second week, if albuminuria is present, cold sponging and cold packing should be avoided.

Persistent vomiting may be controlled by the use of diluted or citrated milk or temporary substitution of albumin water. Liquor iodi mitis in doses of 3 or 5 minims is often efficacious. When swallowing is painful the feeds should be small and often repeated. For the local treatment of the throat and nose, gargles are quite ineffective, and sprays have but little cleansing influence. Alkaline carbolic or boric lotions should be applied by gentle syringing or through a douche-can under low pressure. The syringe nozzle, which should be short, is passed into the mouth behind the back teeth, the patient lying on the side of with the head low. It may be necessary to envelop children in a large towel which secures the arms. For very septic and offensive throats a free chlorine lotion should be used every 2 or 3 hours. It is made by putting 200 grains of potassium chlorate in a large dry bottle, pouring on it 40 minims of strong hydrochloric acid, and setting aside, loosely corked, for 10 minutes; a pint of water is then added in 4 or 5 successive portions, shaking well. An equal quantity of water should be added to this solution before use. Great gentleness should be exercised if the nose be syringed; it is generally unnecessary. Ointment should be applied to the nares and upper lip to prevent excoriations.

Secondary tonsillitis is treated on ordinary lines, but care must be taken not to overlook diphtheria. If adenoids and enlarged tonsils delay convalescence, their removal gives good results. Cervical adenitis is treated by smearing glycerine on the neck and applying cotton wool. Poulticing is rarely called for; it appears to precipitate suppuration. Inflamed glands should only be incised when the presence of pus is assured. Care should be taken that the ears are clean. The pain of otitis may be mitigated by syringing with water as hot as can be borne and the application of hot, dry cotton wool, or a rubber hot-water bottle, to the side of the head. By some the instillation of a few drops of glycerin of carbolic acid and the use of fomentations are recommended. Incision of the tympanic membrane is the most efficient method. Discharging ears should be cleansed frequently with hydrogen peroxide and mopped dry with spirit but never plugged. After the fourth week of the fever, removal of adenoids and infected tonsils shortens the duration of discharge. Watch must be kept for mastoid tenderness and œdema.

Scarlatinal rheumatism is usually mild and transitory; salicylates, or acetylsalicylic acid give relief. When joint swellings persist, a mild pyæmic condition is often present, and may be associated with endocarditis. Some advise a cautious trial of intravenous scarlatinal serum in such cases. When the presence of pyæmic arthritis is suspected an exploratory aspiration under strict asepsis may be advisable. This may lead to subsidence.

Scarlatinal nephritis.—The importance of daily examination of the urine and avoidance of chill must be emphasised. No patient with albuminuria should be allowed up. During the acute stage of nephritis the diet should

be limited to milk, fruit juices and barley water. In very acute cases, water only may be given for 24 hours or even longer. The patient should be clothed in flannel and lie in blankets. The bowels should be regulated with salines or compound jalap powder: constipation is often troublesome. Action of the skin should be encouraged by simple diaphoretics and the use of hot bottles, hot packs or an incandescent electric bath, if available. Acetyl-salicylic acid is useful in promoting sweating. Thirty grains each of sodium citrate and bicarbonate should be given three times a day. For uræmia, free purgation and sweating should be induced; venesection is useful in older patients, coupled with saline infusion. Repeated uræmic convulsions call, in addition, for chloral or chloroform. Lumbar puncture may have a good effect. Morphine if used must be given with caution. Blood pressure should be watched and blood urea estimated.

Grave circulatory failure calls for strict recumbency. Strychnine in doses of gr. $\frac{1}{30}$ every 2 or 3 hours is often used, but even more effectual are injections of adrenaline or pituitary (posterior lobe) extract. Diffusible stimulants such as ammonia and ether mixture, and brandy or champagne, are of value. Oxygen inhalation, hot saline by the bowel, or glucose enemata (5 per cent.) are useful accessories.

The most promising treatment for *hæmorrhagic scarlet fever* is blood transfusion, preferably from an immune donor, or free administration of liver extract. Vitamin K or vitamin C may possibly prove of use.

TYPHOID FEVER

Synonyms.—Enteric Fever; Gastric Fever; Typhus Abdominalis.

Definition.—An infectious fever characterised by pyrexia of distinctive type, an eruption of rose spots, enlargement of the spleen, abdominal discomfort and bowel disturbance. Ulceration of the small intestine and enlargement of the mesenteric lymph glands and spleen are distinctive lesions. Typhoid is a septicæmia caused by ingestion of the *Bacillus typhosus* of Eberth, which is absorbed by the lymphoid tissue of the small intestine and carried to all parts of the body; it settles in the agminate glands (Peyer's patches) of the intestine, the mesenteric lymph glands, spleen, liver, gall-bladder and bone-marrow. Those organs which have excretory ducts, *e.g.* the liver and gall-bladder and the kidneys, as well as the intestinal tract, form the chief channels of elimination.

Ætiology.—The *Bacillus typhosus* (*Eberthella typhi*) is a flagellated, rod-shaped organism, about 3μ in length and 0·6 μ in thickness. It is actively motile and easily grown on artificial media. It belongs to the enteric group of organisms, a group which includes also the paratyphoid bacilli (*Salmonella typhi*). It grows best at blood heat and is quickly killed by boiling water, and within 15 minutes by exposure to a temperature of 60° C. (140° F.). It may survive for a considerable time in ice, and also in fresh or salt water. It resists drying, so that typhoid may be propagated by dust or by articles soiled by typhoid excreta. It has been found alive in the mantle-cavity and intestines of oysters, mussels and other shell-fish which have lived in sewage-contaminated water. It grows freely in butter and in milk.

The toxins are mainly intracellular. Inoculation of animals produces a

septicæmia without the intestinal lesions seen in man. Even in the latter the disease at times occurs without producing intestinal ulcers. The serum of patients has a specific agglutinative influence on cultures of the organism, a fact which is made use of in diagnosis, and at certain stages the bacillus can be cultivated from the blood. In man, infection is introduced by the alimentary tract, and is derived, directly or indirectly, from a human source.

Typhoid occurs in all parts of the world, but is most rife in tropical and subtropical countries. In Great Britain it is most prevalent in the months of September, October and November; in other countries the maximum incidence corresponds to the warm season. A hot, dry summer increases the prevalence in the autumn. An epidemic recrudescence is believed to occur every 5 or 7 years. Rather more males than females are attacked, and the greatest susceptibility is between the twentieth and twenty-fourth years. Infants are rarely infected. After the thirtieth year there is a progressive fall in its incidence. It is rare but not unknown in old age.

One attack confers immunity, which usually lasts for life, but second and third attacks have been reported. Where typhoid is endemic a proportion of the community acquires immunity without having passed through a recognisable attack. The supposed racial immunity of certain peoples may in reality be acquired through infection contracted in childhood. Fatigue and overwork are predisposing factors, and no condition predisposes so much as war to typhoid and paratyphoid infections, owing to the aggregation of susceptible subjects under conditions of defective sanitation, fatigue and exhaustion. Prophylactic vaccination has found its greatest triumphs under these conditions.

Propagation from the human source may be indirect or direct. Of indirect causes aerial infection, apart from the influence of wind-borne dust and of flies, is very doubtful. Drinking water supplies contaminated by sewage or the excretions of a carrier are the most common cause of widespread outbreaks. Milk and other articles of food may also act as diffusers of infection. Watercress and green vegetables, eaten uncooked, also spread the disease. Amongst shell-fish, oysters, mussels, cockles and periwinkles are dangerous. Fomites, enema syringes, bedpans, etc., which have been soiled by typhoid excreta undoubtedly act as infective agents. Laboratory workers have been infected by their cultures.

Direct contagion plays but a small part in the production of epidemics, but assumes importance in causing localised outbreaks, infection being conveyed by the fæces, the urine, the vomit, discharges from abscesses and possibly by the sputa. The chief danger arises with mild and unrecognised cases. Strict attention to personal cleanliness and proper disinfection of excreta, soiled linen, feeding utensils, etc., go far to eliminate infection, and prophylactic inoculation is a great safeguard. Of convalescents from typhoid, a small proportion, about 5 per cent., continue to pass bacilli, perhaps intermittently, in the stools for months or years. These are known as intestinal carriers. They may appear to be quite healthy, or may suffer from periodic intestinal disturbance or from symptoms referable to the gall-bladder. Typhoid bacilluria occurs in perhaps 25 per cent. of the cases of typhoid, but is as a rule quite transitory, urinary carriers being much less common but possibly more dangerous than intestinal carriers. Carriers are

particularly dangerous when they happen to be engaged in handling food, milk or water supplies.

The endemic occurrence of typhoid in certain localities is now attributed to the influence of human carriers rather than to the persistence of infection in the soil, although it is an undoubted fact that the typhoid bacillus may persist for a time and even multiply in sewage-infected earth.

Pathology.—The characteristic lesions are in the small intestine. Microscopically, proliferation of the large mononuclear phagocytes of the reticulo-endothelial system is the distinctive reaction. In the early stages the Peyer's patches are hyperæmic and swollen, the swelling attaining its height about the tenth day of the disease. The solitary follicles of the intestine are similarly affected and a diffuse catarrh of both large and small bowel may be present. Necrosis ensues in the inflamed lymphoid masses, and yellowish-brown sloughs are formed, the separation of which occurs during the third and part of the fourth weeks. In some cases, slow resolution may possibly take place without necrosis. The ulcers which result from sloughing of Peyer's patches are ovoid and lie along the long axis of the bowels. Those which arise in the solitary follicles are more circular. The edges of a recent ulcer are undermined, and the floor shows smooth muscular fibres, or sometimes the peritoneal coat. As the sloughs separate, perforation or hæmorrhage may ensue. Immediately above the ileo-cæcal valve irregular sinuous tracts of ulceration may be evident. Ulceration of the large intestine is rare. The ulcers of typhoid heal without contraction. A slaty pigmentation, often punctate, may persist. The time required for healing is a week or ten days. When perforation occurs it is usually in the lower ileum, where ulceration is most intense. It may, however, happen in other situations such as the colon, cæcum, appendix, or, on rare occasions, the jejunum.

The mesenteric lymph glands are hyperæmic and swollen. They rarely suppurate. The spleen is enlarged, softer and redder than normal, and the Malpighian tufts may be prominent. Infarction sometimes occurs, but rupture is rare. Parenchymatous degeneration occurs in the liver, and minute areas of focal necrosis are scattered through its substance. The gall-bladder may become infected and cholecystitis or gall-stones result. Pylephlebitis is a rare complication. Cloudy swelling of the kidneys is the rule, occasionally a parenchymatous nephritis ensues. In chronic urinary carriers inflammation of the renal pelvis or urinary bladder may be found.

The myocardium shows fatty and granular degeneration. Endocarditis is exceptional, but endarteritis may affect the aorta, coronary arteries and peripheral vessels. Hypostatic congestion of the lung bases is the rule with, it may be, distinct broncho-pneumonic consolidation. Lobar pneumonia is uncommon. Gangrene, abscess or infarction of the lungs is rare. Ulceration of the larynx may occur, the ulcers being found in the neighbourhood of the arytenoid cartilages, or at the base of the epiglottis. Necrosis of the cartilages sometimes ensues. Zenker's vitreous degeneration of muscle is particularly marked. It affects the straight muscles of the abdomen, the adductors of the thigh and the diaphragm. Rupture of muscle and hæmorrhage may result. Osteo-periostitis of the tibia, vertebræ and other bones may be due to primary infection with the typhoid bacillus or to secondary invaders. Superficial abscesses, degenerative changes in the central nervous

system or peripheral nerves, and venous thrombosis are also sequels of typhoid infection.

Symptoms and Course.—The period of *incubation* averages from 10 to 14 days, but may be as short as 5 days or as long as 3 weeks. During this period symptoms are generally absent, but ill-defined malaise or, more rarely, gastro-intestinal disturbance may occur.

The *onset* of the fever is generally insidious with chilliness, lassitude, loss of appetite and muscular pains. Symptoms which are particularly suggestive are frontal headache, epistaxis, slight bronchitis and disturbing dreams. The tongue becomes furred, the mouth dry and the bowels loose or constipated. The patient may not take to bed for a day or two. The temperature rises gradually, being a degree or more higher each succeeding night with morning remissions. By the end of the first week the patient's condition is very characteristic. The aspect is heavy and the cheeks are flushed. The lips and mouth are dry, and the dorsum of the tongue covered with a dirty white fur, the tip and edges being raw. The abdomen is slightly tumid, with gurgling in the right iliac fossa. The bowels are generally loose, several liquid motions like pea soup being passed in the 24 hours; sometimes, however, there is constipation. The spleen may be palpable. A characteristic feature is a moderately full but easily compressible pulse, the frequency of which is not increased in proportion to the temperature. The respiration is accelerated. The temperature will by now have attained a maximum of 103° to 105° F., still showing morning remissions of about 1°, and is unstable, reacting quickly to minor disturbances. The urine is high coloured and concentrated, and the skin usually dry. Thirst and headache are the chief complaints.

The rose spots usually make their appearance towards the end of the first week, sometimes on the fifth day, more often between the seventh and twelfth. Each spot is a circular, slightly elevated papule of a pale pink colour from 2 to 4 mm. in diameter, disappearing on pressure. The rash should be sought for on the abdomen, the flanks, the sides of the chest and the back, which should always be scrutinised. The spots appear in successive crops, each one fading in 3 or 4 days, and leaving a transitory brownish stain. Often the eruption is scanty, a few spots only being seen; occasionally it is very profuse, and involves the limbs as well as the trunk. The face usually escapes. Minute sudaminal vesicles occasionally cap some of the spots. The eruptive period lasts from 10 days to 3 weeks. A profuse rash does not necessarily indicate a severe attack. The spots are due to bacterial embolisms.

By the second week the fever (Fig. 2) has reached its fastigium. The temperature maintains its level with slight morning remissions, the headache may abate, but prostration increases and the other symptoms are more severe. The lips become cracked, sordes accumulate on the teeth, the abdomen becomes more distended and diarrhœa is often a marked feature, the stools being liquid, yellow in colour, alkaline and foul. They may be chocolate-coloured or red from admixed blood and small shreds of tissue, or actual sloughs may already be present. The evacuations are not accompanied by colic or tenesmus. The spleen is now larger. The pulse rate will have quickened to a frequency of 112 to 140. It is often dicrotic, and the heart sounds enfeebled. The bases of the lungs may now show signs of hypostatic congestion, and the respiration be more accelerated with slight lividity of the lips and face. Delirium of a muttering character disturbs the sleep, asthenia

is very marked and muscular wasting rapid . The urine may be albuminous. Patients may succumb during this period from toxæmia, or towards the end of the first fortnight from perforation of the bowel or intestinal hæmorrhage.

During the third week improvement should occur, the temperature becoming more remittent in type, the morning reading falling more rapidly than that of the evening. The tongue cleans and appetite begins to return. During the fourth week defervescence may be completed, the temperature usually remaining at a subnormal level for some time. In severe infections, however, the third week is a period of increasing anxiety. The symptoms increase in severity and the patient may pass into the "typhoid state," lying on the back in a semi-stuporose condition. The pulse and heart sounds become more and more enfeebled, the pulmonary congestion increases, the extremities become blue and cold, subsultus tendinum appears, and the evacuations are passed unconsciously. Sometimes there is retention of

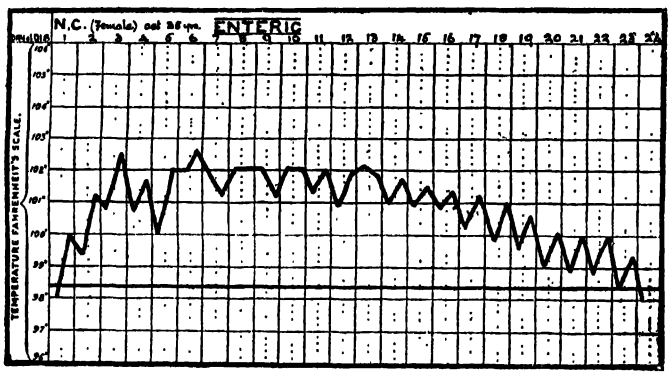


FIG. 2.—Typhoid Fever from the first day. Illustrating gradually rising temperature, a "continued" stage, and a typical lysis.

urine. Extreme abdominal distension may supervene, and the occurrence of perforative peritonitis or of hæmorrhage from the bowel is more than ever to be dreaded. In such severe cases the fever may be prolonged through the fourth and fifth weeks before any signs of defervescence appear. They are not necessarily fatal.

Convalescence after a severe attack is always protracted. The temperature is at first subnormal, and remains in a very unstable state. The heart sounds remain enfeebled, and the pulse is often rather fast or easily quickened by exertion or excitement. The effort of standing and walking is difficult and painful. The appetite, however, is good, and the weight rapidly increases. The aspect gradually becomes less anæmic. Slight peeling of the skin, loss of hair, and ridging or furrowing of the nails is often noticeable. During this period the feet and ankles may show slight œdema, and cutaneous abscesses or localised bone abscesses may occur. Femoral thrombosis sometimes appears; it is the chief complication of early convalescence.

Relapse.—Tendency to relapse is a marked feature, and shows itself in from 5 to 15 per cent. of the cases. The relapse may occur during actual

defervescence, but more commonly develops after an afebrile period of a week or a little longer. The symptoms are a repetition of those of the original attack, but in a mitigated form, the fever reaching its acme in a shorter time, and the whole duration being 10 days or a fortnight. The spleen enlarges again, a new crop of rose spots usually appears, fresh ulceration of the bowel occurs, and blood culture may again prove positive. On occasions, the relapse equals or exceeds the original attack in severity, and may even prove fatal. Spurious relapses are recrudescences of fever during convalescence, of short duration, and unaccompanied by definite symptoms. Their explanation is often obscure.

The fact that typhoid fever may show great variations in its clinical characters, and in the severity and prominence of different symptoms, has led to the description of many special types. Different epidemics may differ much in their salient features.

Variations in onset.—The onset of symptoms may be sudden, sometimes with rigors and vomiting. The temperature rises quickly, and delirium may supervene early. In such cases, death may occur during the second week, or the disease may gradually assume the ordinary type. In exceptional cases, severe bronchitis or pneumonia may mark and mask the onset, and the true nature of the infection may be overlooked. The prominence of meningeal symptoms may lead to confusion with cerebro-spinal fever, and the differential diagnosis only be possible by examination of the cerebro-spinal fluid. If typhoid meningitis is present, lymphocytes or polymorphs predominate, according to the severity of the infection, and the typhoid bacillus grows on culture. More commonly the fluid is under tension but clear; it is sterile and the meningeal symptoms quickly subside after lumbar puncture, to be succeeded by the more typical signs of typhoid fever. Yet another occasional mode of onset is with a primary acute hæmorrhagic nephritis. When acute gastro-intestinal symptoms signalise the invasion, appendicitis or irritant poisoning may be simulated.

The terms *pneumo-typhoid*, *meningo-typhoid* and *nephro-typhoid* have been used to designate some of the above-mentioned types.

Variations in course.—There is an ambulatory form in which febrile disturbance is generally slight, and the patient continues about during the whole or the greater part of the illness. Some such cases end in recovery; but others run a very severe course, the patient taking to bed about the end of the second week with aggravated symptoms, or succumbing to hæmorrhage from the bowel, perforation, acute delirium or circulatory failure. Mild and abortive forms of typhoid also occur in which the fever is insignificant, or, after a well-marked onset, ends in a rapid defervescence between the eighth and fourteenth day. An afebrile form is known, and is said particularly to occur in the enfeebled or those exposed to great hardships.

Variations due to age, pregnancy and other causes.—Typhoid fever is rare in infancy, but becomes more frequent in childhood, and then, generally, the symptoms are mild, the pyrexia of short duration and sometimes of a markedly intermittent or remittent type. Such complications as perforation or hæmorrhage are rare.

In the aged, particularly in those over sixty, typhoid tends to run an unfavourable course, hypostatic pneumonia and circulatory failure being common.

Abortion or premature delivery takes place in from 50 to 70 per cent. of pregnant women who contract typhoid. The fœtus is dead or, if born alive, usually succumbs to an acute typhoid septicæmia. The prognosis as regards the mother is not especially influenced.

In malarial patients the onset of typhoid may be sudden, with a typical rigor; but the severe symptoms proper to typhoid develop later. On the other hand, subtertian malaria may closely simulate typhoid in its commencement.

Chronic alcoholism exerts a very unfavourable influence. Pre-existing pulmonary tuberculosis is apt to advance rapidly during convalescence from the fever. In diabetes typhoid often runs a mild course.

Special Symptoms and Complications.—*Digestive system.*—Suppurative parotitis is attributed to duct infection, and occasionally leads to cellulitis. Attention to the cleansing of the mouth goes far to prevent it. Ulcers sometimes appear on the pillars of the fauces and the pharyngeal wall (Duguet's ulcerations). Diarrhœa is not a constant feature, some patients being constipated throughout the disease. The diarrhœa often disappears after a few days' hospital treatment, but in bad infections it may be severe and persistent.

Meteorism with a distended, tense, tympanitic abdomen signifies a virulent infection. It may or may not be accompanied by severe diarrhœa, and is often a harbinger of hæmorrhage or perforation.

Intestinal hæmorrhage occurs in about 7 per cent. of all cases, and is serious. It is most common at the time when the sloughs are separating, *i.e.* at the end of the second or beginning of the third week. The hæmorrhage may be slight, but more often is profuse. The evacuated blood is bright red in colour, unless it has been retained in the bowel. The signs of a severe hæmorrhage are a sharp fall in the temperature, a sensation of faintness, increased frequency of the pulse and, it may be, a transient rise in blood pressure with disappearance of dicrotism. The spleen may shrink rapidly. Sometimes the hæmorrhage is fatal before any blood is voided. There is a hæmorrhagic form of typhoid in which melæna may be an early sign, associated with petechiæ or bruises in the skin and hæmaturia. The outlook, then, is very grave.

Perforation of the bowel causes one out of every 3 or 4 deaths. Its incidence is something under 5 per cent. It is commonest towards the end of the third week, especially in cases characterised by severe diarrhœa or by meteorism. Its onset may be preceded by intestinal hæmorrhage. The perforation generally lies within the last 12 inches of the ileum, but may occur elsewhere. Shivering, with sharp pain in the right iliac fossa, is usually the first sign. Localised tenderness, localised rigidity and local immobility of the abdominal wall accompany the pain. The temperature may show a sudden drop to a subnormal followed by a rise; but sometimes no variation is detected. Both pulse and respiration rates are usually increased, and the former should be watched carefully. Obliteration of the liver dullness may occur; this sign is especially valuable when occurring in a rigid and retracted belly. Another sign is the occasional onset of irritability of the bladder. More reliance should be based on the local than on the general symptoms in making the diagnosis. After the first shock the patient may react and show deceptive signs of improvement, but before

many hours the signs of spreading peritonitis will assert themselves. Unless dealt with surgically with the utmost promptness perforation is almost invariably fatal. A polynuclear leucocytosis generally accompanies perforation, but is inconstant and not of great diagnostic value.

Other causes of abdominal pain in typhoid fever are acute cholecystitis or perforation of the gall-bladder, suppurative cholangitis, portal pyæmia, suppurating mesenteric glands, appendicitis and splenic infarction, but none of these is common. Thrombosis of the iliac veins may also cause abdominal pain and tenderness, but a clue to this condition may often be found by examining the veins of the lower limbs and by looking for slight œdema of the leg or foot. Gall-stones are a recognised sequel of typhoid infection, and may contain typhoid bacilli.

Respiratory system.—A mild bronchitis is present in most cases. In severe infections, hypostatic congestion of the lung bases occurs. Lobar pneumonia may supervene in the third or fourth weeks of the disease. Although typhoid bacilli may occur in the sputum, and be found in the lung, pneumococci are also present; the condition may be overlooked, as cough is often slight and rusty sputa absent. Embolic and pyæmic processes in the lungs during typhoid may give rise to abscess, gangrene and pneumothorax. Intra-pulmonary thrombosis, with infarction, is a very rare event.

Ulceration of the larynx is not infrequent in severe cases. It may be latent or give rise to huskiness of the voice, stridor and toneless cough. There may be pain on deglutition and laryngeal tenderness. The slighter symptoms may abate, but sometimes the process terminates in necrosis of cartilage and œdema or stenosis of the larynx.

Blood and circulatory system.—A slight polynuclear leucocytosis is sometimes seen in the first week of infection. More characteristic is anæmia associated with leucopenia, and a relative increase in the lymphocytes and large mononuclear cells. At the same time the eosinophils disappear to reappear with convalescence. The appearance of a polynuclear leucocytosis indicates the onset of inflammatory complications

Circulatory failure is a feature of severe attacks. The pulse rate, usually but moderately accelerated in typhoid, rises to 120 or more, dicrotism disappears, the cardiac sounds weaken, and the blood pressure falls. Acute collapse, with sudden drop of temperature, coldness of the skin, cyanosis and feeble or irregular pulse, may ensue. The collapse may be recovered from, but its occurrence is ominous.

Femoral thrombosis is apt to appear during early convalescence. It is usually left-sided, and sometimes appears to commence lower down in the veins of the popliteal space or calf or in the internal saphenous trunk. The symptoms are pain and tenderness at the site of the thrombosis, fever and swelling of the limb, usually moderate in degree. The affected vein may often be felt as a tender cord. In a few weeks the thrombus is absorbed, and the circulation re-established, but sometimes permanent obstruction and œdema result. The clot, if dislodged, may cause pulmonary embolism.

Arteritis, leading to occlusion, is an uncommon complication. The vessels affected are those of the lower limbs, sometimes those of the upper extremities, neck or brain.

Urinary system.—Febrile albuminuria is often present, but is transitory. Typhoid bacilluria occurs in some cases, the urine presenting a slightly

turbid, opalescent appearance; but a similar appearance may be due to the colon bacillus. Symptoms of pyelitis, pyelo-nephritis or cystitis may supervene. Urinary carriers continue to discharge typhoid bacilli for long periods. Acute nephritis is uncommon, but may occur either at the commencement or height of the disease. Retention of the urine may supervene during typhoid, but suppression is rare. During the fever the excretion of urea and of uric acid is increased, but the chlorides are diminished. A moderate oliguria is the rule. A considerable reduction, in spite of free fluid intake, is evidence of a severe attack. Polyuria occurs at the onset of convalescence, and is of good omen.

Generative system.—Orchitis and prostatitis have been observed. In females vulvitis and also mastitis may occur.

Nervous system.—Meningeal symptoms at the onset have already been mentioned. Delirium is often present and is usually of a quiet type. Drinkers may develop delirium tremens. Convulsions are rare. They may occur at the onset, or when occurring later may be due to cerebral thrombosis, encephalitis, or meningitis. Multiple neuritis or neuritis of such nerves as the ulnar may supervene, in the latter case often due to pressure. Acute tenderness of the toes during convalescence is also attributed to neuritis. During the course of the fever hemiplegia or aphasia may supervene. Sometimes there are signs of sclerosis of the lateral columns of the cord, the knee-jerks being increased, and an extensor plantar reflex present.

Mental disturbance is occasionally a sequel, taking the form of mania, melancholia or dementia. For many months after a severe attack the patient may remain in a fatuous condition but ultimately recover.

As regards the special senses, temporary deafness is often noticeable during the fever, and sometimes suppurative otitis. Double optic neuritis is a rare complication and may lead to blindness.

Osseous and muscular systems.—During convalescence localised osteo-periostitis of the tibia, sometimes of the femur, ribs or other bones may appear. It may terminate in suppuration with limited necrosis. The inflammation is chronic and relapsing. Typhoid bacilli may persist in the pus for long periods. A painful inflammatory affection of the ligaments and vertebral periosteum is the basis of the "typhoid spine." The lumbar and sacral regions are chiefly involved, with stiffness and pain on movement. The condition is chronic, but the ultimate outlook is said to be good. Arthritis of large joints is a rare occurrence; it may lead to dislocation of the hip.

Rupture of the rectus abdominis, sometimes of the adductors or other muscles, may take place. It is accompanied by local hæmorrhage. The resulting fluctuating and discoloured swelling may clear up or go on to suppuration.

Cutaneous system.—Abscesses and boils may prove troublesome. Lineæ atrophicæ may form in the skin of the abdomen and thighs. In severe cases pressure sores may appear on the sacrum, the heels or other pressure points. These bed-sores are a source of danger from septicæmia or pyæmia.

Diagnosis.—It is unnecessary to recapitulate all the symptoms already described as characteristic. Of the symptoms of onset, headache, slight epistaxis, disturbed sleep, a mild degree of bronchitis, abdominal uneasiness and some disturbance of the action of the bowels are very suggestive. Gradual daily increase in the pyrexia and its maintenance after the lapse of a week at a

steady level of 103° or 104° F., with slight morning remissions, is important. Relative slowness of the pulse and the presence of dicrotism are additional diagnostic points. The dry furred tongue, slightly tumid abdomen, moderately enlarged spleen and the appearance of rose spots are confirmatory.

Special Diagnostic Methods.—1. *Blood examination.*—Culture is particularly valuable in the first week before the agglutinative reaction has appeared or the rose spots are evident, but is also applicable during the second and third weeks and in relapse. Ten to 20 c.c. of blood drawn aseptically from a vein at the bend of the elbow are allowed to run directly into plenty of broth or peptone solution or, better, into a medium which contains filtered bile or bile salts. At the same time a blood count should show a characteristic leucopenia.

2. *Cultures from bone-marrow* obtained by sternal puncture are said to be more often and more persistently positive than blood cultures.

3. *Cultures from the stools.*—Owing to the presence of other intestinal bacteria this is not always an easy process, but by improved methods bacilli have occasionally been found during the incubation stage and in over 50 per cent. of the cases examined in the first week, a percentage increased to 70 or 80 in the third week. For methods, works on bacteriology should be consulted. Stool culture is also of value for the detection of intestinal carriers, and for determining whether a convalescent is fit to mix with other members of the community. The discharge of bacilli often being intermittent, more than one examination is necessary.

4. *Cultures from the urine.*—The typhoid bacillus hardly ever appears in the urine before the tenth day, and as a rule not before the fifteenth. The infected urine is generally opalescent and slightly albuminous. Cultures are made without difficulty and are useful not only for diagnosis but also for the detection of urinary carriers.

5. *Agglutination tests.*—Towards the end of the first week of the disease the blood serum becomes capable of agglutinating the typhoid bacillus. This power usually reaches its maximum about the eighteenth or twenty-first day. Blood is obtained from the lobe of the ear or a vein. The serum which separates is mixed in various dilutions with a young (18 to 24 hours) broth or agar culture of the typhoid bacillus and a hanging-drop preparation made. Controls are indispensable. Agglutination of 1 in 50 with a time limit of one hour is usually taken as the positive standard, but some prefer a titre of 1 : 100 especially if the macroscopic technique is adopted. The bacilli first lose their motility and then aggregate into small clumps. The macroscopic method of applying the test allows the bacilli to sediment in flakes at the bottom of small tubes; Dreyer's method in which standardised dead cultures are used is the best; it is quantitative. Normal blood serum does not show an agglutinating power greater than 1 in 10 or 1 in 20. Rising titres are highly diagnostic.

Corresponding to three types (H, O and Vi) of receptor or antigen in the infecting organism three kinds of agglutinin are found in the blood. The H antigen is specific and distinguishes the organism present. This antigen is present alone in Dreyer's formolised suspension. The O antigen, on the other hand, is common to the enteric group. The presence of its corresponding agglutinin in a patient's serum is proof only of infection by a member of the group; it does not identify it. The Vi antigen rarely occurs alone.

T.A.B. vaccine, in consequence of its mode of preparation, evokes H agglutinins chiefly, and these may persist for some years. The appearance of O agglutinins in an inoculated person shows an enteric infection. Blood culture or examination of the excreta may reveal its identity. A rising titre of H agglutination for a particular organism may also do this, but it is known that other, quite different, infections may also raise the H titre (*anamnestic reaction*).

6. *The atropine test of Marris.*—In typhoid and paratyphoid fevers atropine has but little power of accelerating the pulse. Marris's test is based on this fact, but is little used.

7. *The Diazo reaction.*—A saturated solution of sulphanilic acid in 1 in 20 hydrochloric acid and a fresh half per cent. solution of sodium nitrite are required. Equal quantities of urine and sulphanilic solution are mixed in a test-tube and a couple of drops of the nitrite added. By shaking, a froth is induced and ammonia is allowed to trickle down the side of the tube. If the froth becomes rose pink and the liquid turns crimson, the test is positive. The reaction may sometimes be obtained as early as the fourth day, and persists during the height of the fever. Unfortunately it also occurs in measles, typhus fever, scarlet fever, pneumonia, tuberculosis and erysipelas.

Differential Diagnosis.—Prominence of respiratory or bowel symptoms in typhoid fever may lead to the infection being overlooked. Conversely a deep-seated or apical *pneumonia* or, in children, *broncho-pneumonia* with intestinal disturbance, may simulate typhoid. Careful and repeated physical examination, blood culture and agglutinative reactions will lead to a correct diagnosis. When typhoid is prevalent, caution is necessary in arriving at a diagnosis of primary bronchitis, pneumonia, broncho-pneumonia, and, especially in children, gastro-enteritis.

Differentiation from *acute miliary tuberculosis*, from *tuberculous meningitis* and from *tuberculous peritonitis* is often difficult. Acute miliary tuberculosis may simulate typhoid in its insidious onset with malaise and headache, its rising temperature with morning remissions, its comparatively slow pulse, its bronchitis, and perhaps some enlargement of the spleen. But the temperature tends to be more irregular, sweats are present, the dyspnœa and cyanosis are suggestive, and signs of pleurisy may develop. There are no rose spots, and agglutinative tests and blood culture give negative results (tubercle bacilli are rarely found). Tuberculous meningitis is differentiated by such symptoms as vomiting, convulsions, the persistence of headache after the first week, or when delirium is established. A pulse hardly raised above the normal rate, stiffness and retraction of the neck, the presence of Kernig's sign and of retraction of the abdomen or the onset of ocular paralysis are very significant. The irritability and curled-up decubitus of meningitis contrasts with the apathy and dorsal decubitus of typhoid. Lumbar puncture will clinch the diagnosis; in tuberculous meningitis lymphocytes are in excess in the cerebro-spinal fluid, and sometimes tubercle bacilli may be demonstrated. The question of meningo-typhoid has already been discussed. Tuberculous peritonitis may resemble mild typhoid fever. The presence of tuberculous masses in the abdomen or the development of peritoneal or pleural effusions is significant. In cases with indefinite symptoms and no signs of tubercle elsewhere, negative blood culture and agglutination tests afford assistance.

Suppurative and pyæmic conditions may give rise to fever and constitutional disturbance bearing some resemblance to typhoid. Among these must be mentioned appendicitis and the intraperitoneal abscesses which may result from it, perinephric abscess, cholecystitis, pelvic, or puerperal infections, infective endocarditis and deep-seated osteomyelitis. The diagnosis is made by careful attention to the history of onset and course, thorough and complete physical examination, and the frequent presence of a pronounced polynuclear leucocytosis. Profuse sweats and rigors are more likely to occur, and the temperature chart is more irregular. The blood serum fails to agglutinate typhoid bacilli, nor can they be obtained by blood culture, which may, however, reveal the presence of other organisms.

Typhoid fever in its early stages is often mistaken for *influenza*, but in the latter the onset is generally sudden and the early symptoms are more severe. The temperature reaches its maximum much sooner. The pains in the limbs and the backache are more intense, and the headache, which has a neuralgic character, is frequently supra-orbital. Catarrh of the conjunctivæ and nose may be present, and perspirations are often marked. Defervescence usually takes place within a few days. A sharp drop of temperature after 2 or 3 days with a sudden rebound 12 or 24 hours later is very characteristic. If a supposed influenzal fever persist without definite cause, typhoid should be suspected.

A mild case of *typhus* may bear a close resemblance to typhoid, and severe typhoid with grave toxæmia, stupor and a profuse eruption may be mistaken for typhus. Points in favour of the disease being typhoid are a slower onset, the later appearance of the eruption, which is never petechial, and the presence of bowel symptoms. Typhus, on the other hand, has a sudden onset with high fever which sooner attains its maximum and does not show morning remissions. Conjunctival injection, contracted pupils and a drunken expression are the rule. The rash appears on the fourth day, becomes petechial and is accompanied by subcuticular mottling. Prostration is marked and there is a greater tendency to delirium and stupor. Crisis occurs about the fourteenth day. The Weil-Felix reaction is present, but agglutination tests for typhoid are negative except in inoculated persons (p. 88).

Undulant (Malta or Mediterranean) fever is distinguished from typhoid by its relapsing character, the prominence of arthritic pains and joint swellings, and the fact that the blood agglutinates the *Micrococcus melitensis*, which organism can also be recovered by blood culture. Closely allied to this is the fever produced by *B. abortus* of cows.

When *malarial fever* assumes the continuous type, which is likely to occur with the malignant infections, the diagnosis turns on known exposure to malaria, sudden onset, the detection of malarial parasites in the blood and the reaction to quinine. Malaria and typhoid fever, however, may coexist.

The fever of *secondary syphilis* is sometimes sufficiently severe to suggest typhoid, especially when accompanied by headache, malaise and muscular pains. Diagnosis depends on the history or detection of a primary lesion, the possible presence of a secondary roseolar eruption and on laboratory tests. Deep-seated malignant disease may also cause prolonged fever.

Amongst other diseases at times confounded with typhoid must be

mentioned psittacosis, kala-azar, glanders, trichinosis, fever due to *Ascaris lumbricoides*, scarlet fever in which pyrexia is prolonged, that type of glandular fever in which the glandular swelling is delayed, and especially fevers of the Salmonella group, *i.e.* paratyphoid A, B or C.

Prognosis.—Taking all ages, the death-rate varies from 5 to 25 per cent. It is higher in some epidemics than in others. The average hospital death-rate in London is 17 per cent. or a little less. Age has a decided influence on the mortality, which is least in children from 5 to 10, after which there is a steady increase with advancing years. Infants are believed to stand the infection very badly. Obesity, alcoholism, privation and fatigue are adverse factors. The influence of pregnancy has already been discussed. Indications of a grave attack are a pulse rate of 130 or 140, cyanosis with signs of failing circulation and hypostatic congestion of the lungs, marked delirium and subsultus or actual coma, persistent diarrhœa, tympanites, incontinence of urine and fæces. A temperature of 103° or 104° F. is not necessarily unfavourable unless it is sustained beyond the usual period or accompanied by signs of heart failure. Delayed appearance of the agglutinative reaction in some instances indicates a severe attack.

Of the complications, next to toxæmic circulatory failure, perforation is the most grave. Without operation it is almost invariably fatal. With operation the recovery rate is difficult to fix—some surgeons claim success in over 30 per cent., but the intervention must be immediate. The average recovery rate is very much lower. Hæmorrhage from the bowel is undoubtedly serious, especially if repeated. Such complications as meningitis, lobar pneumonia and acute nephritis are dangerous but fortunately not very common.

Sudden death sometimes occurs, either at the height of the fever or in convalescence. It may be caused by intense toxæmia and circulatory failure, cardiac or pulmonary thrombosis or pulmonary embolism. Rarely no definite cause can be assigned.

Treatment.—PROPHYLACTIC.—Patients should be isolated. Adequate disinfection of the fæces, the urine, the pus from abscesses, the vomit and the sputa is necessary. Blood discharged from the nose or bowel should also be looked upon as infectious. Equally essential is the disinfection of the bedclothes and personal linen of the patient, the feeding utensils, thermometer, bed-pan, urinal, spittoon and enema syringe. The stools and urine should be mixed with an excess of some such disinfectant as carbolic acid or corrosive sublimate, and allowed to stand for several hours before being thrown down a drain. The sputa should be received in small cloths which can be burned, or expectorated into a disinfectant solution. The clothing and bedclothes of the patient should be soaked in a 1 in 20 solution of carbolic acid before being sent to a laundry.

Nurses in attendance should submit to prophylactic inoculation and take special precautions for their own safety. Overalls will obviate soiling of the clothes. If the bath treatment is adopted, rubber aprons which can be carbolised are advisable. Rubber gloves may be worn when giving enemas or touching bed-pans and urinals, but always it should be realised that typhoid acquired by contact is a disease conveyed by unclean hands, and the danger may be obviated by washing with plenty of soap and water after touching the patient or anything which has been in contact with him. Everything

leaving the patient or used by him must be sterilised at once. Feeding utensils should be boiled after use.

In most cases the bacilli disappear from the excreta in convalescence, only persisting for a few weeks, but bacteriological examination several times repeated affords the only proof of safety. About 5 per cent. of those attacked become carriers. In most the carrier state is temporary and an arbitrary period of 3 months is allowed before the condition is deemed chronic. Intestinal carriers are more common than urinary carriers. In both the discharge of bacilli may be intermittent. Symptoms referable to the gall-bladder and periodic bowel disturbance occur in some intestinal carriers, and urinary carriers in like manner may suffer from kidney trouble or cystitis. Carriers do not necessarily give a positive Widal reaction.

Carriers are often responsible for the endemic persistence of typhoid in certain houses or localities and are particularly dangerous when employed in the preparation of food or in dairy work or in connection with water supplies. They should be prohibited from following these occupations. Since they may spread infection by contaminating their own hands during defæcation or micturition they should be scrupulous in washing after attending to the calls of nature and have towels reserved for their own use. Their soiled bed and body linen must be disinfected. Medical treatment by the use of intestinal and urinary antiseptics, surgical by excision of the gall-bladder, and treatment by autogenous vaccines have up to now alike failed to solve the problem of the chronic carrier. Preventive inoculation of contacts is the most effectual method of limiting their danger and is adopted in special circumstances. Some carriers give no history of an attack of typhoid and may themselves ultimately develop an attack of the fever or suffer from typhoid septicæmia after operations on the gall-bladder or kidney.

A pure water supply and an efficient system of drainage are important factors in the prevention of typhoid epidemics. When the disease is prevalent, drinking water and milk should always be boiled, and travellers in localities where it is endemic should adopt similar precautions. Uncooked vegetables and, in particular, radishes, salads, cress, tomatoes, cucumbers, strawberries and other fruits are liable to contamination. Oysters and other shell-fish should be avoided unless their source is known to be above suspicion. The disease has been contracted by bathing in sewage-contaminated water.

Prophylactic vaccination.—Immunity can be artificially induced by vaccination with typhoid vaccine. There are several methods of preparation of vaccine, one of which is to heat a 48-hour broth culture to 58° C., and complete the sterilisation by the addition of 0·5 per cent. lysol. Exposure to higher temperatures diminishes the potency of the vaccine. The number of bacteria in the first dose is 500 million, a double dose is given 10 days later and repeated 10 days later still. The injection is made subcutaneously and preferably not after a heavy meal or exposure to fatigue. A mild local reaction and sometimes constitutional symptoms may occur a few hours after injection, hence the patient should rest. If the patient is already infected the reaction may be more severe. The duration of the immunity conferred is said to average 1 to 2 years and to be proportional to the dosage employed. An individual inoculated at the beginning of the incubation

period of typhoid has a good chance of escaping the fever, but in rare cases the inoculation appears to aggravate its course. For army purposes, triple or quadruple vaccines of the organisms of typhoid and paratyphoid are largely employed.

CURATIVE.—In the absence of efficient sera or vaccines there is at present no specific. Skilful nursing and a suitable diet are of the first importance. The room should be kept at a temperature of 60° F., and the bed narrow and of a convenient height. A hair or rubber mattress is covered with two folds of blanket and a waterproof sheet over which is placed a sheet, and under the hips a draw sheet. A water-bed is unnecessary. A sheet and coverlet with a blanket over the feet are usually sufficient covering. Night and morning the patient should be sponged with tepid water, and parts exposed to pressure should be rubbed with surgical spirit, and dusting-powder applied. Rucking of bedclothes should be avoided. The urinal and bed-pan should be used in the recumbent position, and the buttocks sponged, dried and powdered after each motion. The mouth should be cleansed after each meal. From time to time it may be advisable to move the patient from the dorsal position to avoid hypostatic congestion of the lung bases. Stools and urine should always be reserved for inspection by the medical attendant, who should never neglect daily examination of the abdomen, and should also satisfy himself that the patient, especially if restless, had not retention of urine. The temperature pulse and respirations should be charted 4-hourly, and more frequently should complications be suspected.

Milk is the most suitable diet for patients in the acute stages. It should be given in measured quantities at 2- or 3-hourly intervals, the patient not being disturbed at night should he be sleeping. Three pints a day is, despite theoretical considerations, quite sufficient. The milk should be diluted with barley water or lime water, and plenty of plain cold water or fruit juice allowed between the feeds. Tea may be allowed or lemonade made with dilute hydrochloric acid and syrup of lemons. Should intestinal discomfort occur or curds appear in the motions the milk may be citrated or whey substituted. Beef-tea and meat extracts are to be avoided in diarrhœa or hæmorrhage. Carbohydrate can be added to the diet in the form of glucose or lactose. Junket and also apple-sauce are useful.

When the temperature has been normal for 3 days, cautious additions may be made, beginning with thin custard or grated bread-crumbs and milk, and then adding a small quantity of boiled or steamed fish, thin bread and butter, and so on.

High calorie diets are based on the belief that during the fever a daily intake of 4000 to 5000 calories is necessary to maintain nitrogenous equilibrium. Even in patients who are amenable this diet is prone to produce digestive upsets and meteorism, but mild cases can take a more liberal diet during the acute stage, *i.e.* milk puddings, custards, eggs, vegetable or meat soups strained and thickened with arrowroot or flour, finely minced lean meat, bread crumbs and mashed potato. Such feeding is said actually to diminish the tendency to perforation and hæmorrhage, and to hasten convalescence. It is not suitable in severe attacks or for patients with profound toxæmia and deficient digestive secretions. Alcohol is rarely necessary, but it is unwise suddenly to deprive alcoholic patients of all stimulants.

The antipyretic treatment of typhoid assumes that pyrexia itself is harmful. The cold bath is most efficient. Best suited to hot climates, it has never gained a great vogue in England. Whenever the temperature rises above 102°·3 F., the patient is lifted into a bath at 65° F. and immersed for 15 minutes, shivering being disregarded. The limbs and trunk are rubbed whilst in the bath. The patient is then removed, laid on a blanket, dried and lightly covered. A little alcohol is given immediately before or after the bath. Immersion is repeated every 3 hours unless the temperature remains below the point mentioned. Contra-indications are hæmorrhage from the bowel, severe abdominal pain, venous thrombosis or great prostration. The method needs good attendants, and can hardly be applied in private, but it is said to reduce the case mortality by a half or even two-thirds. In place of the bath, tepid, cold or ice sponging may be adopted when the temperature is high, or the cold pack used, especially when nervous symptoms are pronounced. The ice cradle is another useful means of refrigeration; the patient is covered with a sheet, and a cradle, in which small rubber bags of ice are suspended, is placed over the body, the whole being covered with a thin blanket. The cradle may remain in position indefinitely, the effect on the temperature being carefully watched.

Some advocate daily mild purges, such as calomel or drachm doses of castor oil, in the early days of infection, and claim that intestinal fermentation can be checked by the administration of various intestinal antiseptics.

Constipation should be met by a simple enema every second day. In defervescence liquid paraffin may be substituted. *Diarrhœa*, if accompanied by curds, calls for reduction of the milk. A starch and opium enema is useful, or 10 grains of Dover's powder by the mouth. In *hæmorrhage from the bowel* the most absolute rest is essential. Food should be reduced to a minimum or withheld for 12 or 24 hours. No stimulants or beef-tea are permissible. Ten minims of laudanum or a hypodermic injection of ¼ grain of morphine should be given, and an ice-bag applied to the right iliac region. A watch should be kept for signs of perforation. Intravenous saline infusion, or, better, transfusion of blood, may be necessary in severe cases. The injection of a solution containing 1 grain of calcium chloride in 10 minims of water into the gluteal region is worth a trial. *Perforation of the bowel* calls for immediate operation. *Meteorism* may be controlled by reducing the diet, administering enemata of hot water, and inserting the rectal tube. A turpentine stupe or ice-poultice may be applied to the abdomen. Turpentine by the mouth or by enema, and oil of cinnamon are useful. For *delirium*, *sleeplessness* and *headache*, the reduction of temperature by sponging or cradling and the administration of 10 or 15 grains of Dover's powder should be tried. Sometimes soluble barbitone (medinal) and aspirin are effectual. *Circulatory failure* is combated by strychnine or strychnine and adrenaline hypodermically, or by injection of nikethamide (coramine) or leptazol (cardiazol). Strophanthus and digitalis are of doubtful value. Alcohol is strongly advocated by some physicians. The supervention of *femoral thrombosis* calls for strict immobility of the limb. The intravenous injection of 5 or 10 ounces of a sterile 0·5 per cent. sodium citrate solution relieves the pain, and is said to arrest the progress of the thrombosis. *Bacilluria* and *cystitis* are treated by hexamine in 10-grain doses, 3 or 4 times a day; if persistent, sulphonamides may be effective. Of the suppurative and septic

complications, *periostitis* may be influenced by rest, local applications and typhoid vaccine, but suppuration calls for surgical intervention. *Parotitis* usually comes to incision. *Cholecystitis* may subside, and should be given a chance to do so, but if it persists operation becomes necessary. Crops of *boils* call for local treatment, and the appropriate vaccine or toxoid should the organism be identified. The intramuscular injection of colloidal manganese is useful in such conditions. The infectivity of purulent discharges should be remembered.

PARATYPHOID FEVER

Ætiology.—Paratyphoid fevers are, like true typhoid, ubiquitous in their distribution, but the prevailing type is different in different countries and in different climates. The infecting organisms belong to the group *Salmonella typhi*. Paratyphoid A is prevalent in India and other tropical countries. The experience of the War of 1914–1918 led to the suspicion that it may have been endemic, although unrecognised, in the Mediterranean area, and perhaps also in France, Flanders and Germany. In European countries, however, paratyphoid B is the more common type. Paratyphoid C occurs in the Balkans, and possibly there are also other varieties. *Bacillus paratyphosus* A and *Bacillus paratyphosus* B are organisms which under natural conditions only attack man, but it is stated that the intestines of domestic animals may contain the bacilli. *B. paratyphosus* C is by some considered identical with *B. suipestifer*, the hog-cholera bacillus.

The greatest incidence of paratyphoid is in the summer and early autumn, but it may occur at other seasons of the year. It is more prevalent in hot countries, and all ages are susceptible. In ordinary circumstances it affects both sexes equally.

The primary source is a patient suffering from an attack, or a carrier of the bacillus. Contagion, as with typhoid, may be direct or indirect through food, especially cream, drinking water, fomites, etc. The infection of water supplies is not so well established as in the case of true typhoid. The fact that infected meat, particularly pork, may induce symptoms resembling paratyphoid fever should be borne in mind.

Symptoms.—The *clinical manifestations* of paratyphoid infections are practically indistinguishable from those of typhoid fever, but the belief is generally held that paratyphoid differs from typhoid in its milder character and shorter course. This is on the whole correct, but marked exceptions occur. Occasionally paratyphoid infection is said to produce an illness which resembles acute irritant poisoning, or so-called ptomaine poisoning. But such infections are more likely to be caused by *B. aertrycke*, which in its agglutination reactions closely resembles *B. paratyphosus* B. In true paratyphoid the subsequent course is clinically unmistakable.

The septicæmic stage of paratyphoid is of short duration, rarely lasting more than a week, hence blood cultures for diagnostic purposes should be taken as soon after the third day as possible. The distribution of the infecting organisms in the body is similar to that of typhoid, and they are discharged in the fæces, the urine, the bronchial secretions, and the pus of suppurating foci. Residual foci of infection are said to be more common in paratyphoid than in typhoid infections.

The *incubation* period varies from 9 to 15 days, but may be shorter.

The *onset* is more often insidious than sudden, the invasive symptoms resembling those of typhoid, but a sudden onset is believed to be more common than in the latter disease. Shivering and vomiting are not infrequent symptoms of such invasion. Sometimes gastro-intestinal symptoms are for a time very prominent, and are particularly misleading in childhood. As with typhoid, influenza, appendicitis, meningitis, or pneumonia may at first be simulated. Sometimes the disease declares itself after several weeks of premonitory diarrhœa, or it may closely resemble dysentery.

The fever attains its maximum sooner than in typhoid, and may be at its height by the third or fourth day, by which time, if not before, the patient will have taken to bed with symptoms suggesting typhoid of a week's duration. The head aches, the patient is apathetic, and the spleen is generally palpable and sometimes tender. The liver may be slightly enlarged, and the gall-bladder tender if cholecystitis be present. The abdomen is generally somewhat tumid, but marked distension is uncommon. Diarrhœa may occur at the onset, but constipation is more common. Sweating is often a more pronounced feature than in typhoid. Rose spots are present in unusual profusion in some cases. They usually appear towards the end of the first week. In size, too, they often appear larger than those seen in ordinary typhoid infection, and the rash may continue to come out after the temperature has fallen. Pulmonary complications are mild, but bronchitis and broncho-pneumonia may occur. In the more severe cases, the heart may show signs of dilatation. It is exceptional for the patient to pass into the "typhoid state." The fever has a shorter duration and shows greater variations than in typhoid. Within a fortnight, sometimes sooner, it has generally fallen by rapid lysis to normal. The slow pulse and low blood pressure of typhoid are also seen in the paratyphoid variety. Relapse is said to be just as frequent.

Complications.—Intestinal hæmorrhage is much less common and less severe than in true typhoid. Perforation is rare. Thrombosis of the femoral or saphenous veins or their radicles is not uncommon, and broncho-pneumonia or pleural effusions may occur. Cholecystitis and catarrhal jaundice may be due to paratyphoid organisms, as also bacilluria, cystitis, pyelitis and even pyelonephritis. Orchitis is an occasional complication, and is believed to spread from the urinary tract. Other complications, which have mostly been observed in army practice, are laryngeal ulceration, parotitis, periostitis, sometimes suppurative, peritonitis without perforation of the bowel, and pylephlebitis, attributed to lesions of the appendix.

Diagnosis.—For the differentiation of paratyphoid from typhoid infections and of the varieties of paratyphoid from each other, recourse must be had to bacteriological methods, *i.e.* to blood culture, agglutinative reactions and cultures from the stools and from the urine. Of these methods, blood culture in the early stages is the most satisfactory. If agglutination occur in high dilutions with one of the paratyphoid organisms and little or not at all with the others and the organism of typhoid, the nature of the infection is evident; but in other cases the examination has to be repeated at short intervals and the results compared. A rising agglutination for one organism indicates it as the causal agent. Some infections with paratyphoid C fail to produce agglutinins in the patient's serum.

Prognosis.—The prognosis in paratyphoid infections is better than in those due to the *B. typhosus*, the proportion of severe infections being much smaller, and the mortality much lower. The causes of death are chiefly hæmorrhage, perforation, lung inflammations and toxæmia.

As regards differential diagnosis, prophylaxis and treatment, what has already been said with regard to typhoid applies.

CHARLES R. BOX.

DIPHTHERIA

Definitions.—A disease caused by the Klebs-Loeffler bacillus (*Corynebacterium diphtheriæ*), characterised by a membranous exudate at the site of infection and distinctive sequels of toxæmic origin, the chief being circulatory failure, paralysis, and albuminuria.

Ætiology.—Diphtheria is commonest in temperate climes. Human carriers are the cause of its endemic prevalence; local conditions being merely contributory. In its seasonal prevalence diphtheria resembles typhoid and scarlet fever, the maximum incidence falling in the autumn and late winter months. An epidemic tendency is noticeable in years of deficient rainfall. Formerly a disease of rural districts, diphtheria is now endemic in cities and shows a tendency to local epidemic outbursts. Its heaviest incidence is on children between the ages of 2 and 5 years. New-born infants are rarely attacked. Many cases occur in adults, and rather more females than males are affected.

Catarrhal conditions of the throat predispose to the infection; convalescents from measles and scarlet fever, and in less degree those recovering from whooping-cough and influenza, are liable to contract the disease, which in the case of recent measles or scarlet fever may assume a particularly severe form. A progressive increase in infectivity and severity is often noticed during epidemics. The immunity afforded by diphtheria is short-lived; relapses are rare. Second attacks may occur.

The disease is highly contagious, and infection is by direct or indirect contact. It is seldom air-borne even over a short distance. The organisms reside in the secretions from the nose and throat, in detached shreds of false membrane, and at times in discharges from the ears, the vulva, infected wounds or skin lesions.

Direct infection may result from kissing, or the reception of droplets of fluid ejected by speaking, coughing or sneezing. Indirect infection may be caused by eating or drinking utensils, handkerchiefs, towels, throat spatulas, clinical thermometers, toy trumpets, slate pencils and the like. The diphtheria bacillus readily grows in milk and produces no suspicious changes; milk thus may serve as a vehicle for spread of the disease. There is no evidence that it is conveyed by drinking water. The diphtheria of birds, cats and most other animals has not proved communicable to man and is due to a different organism, but virulent diphtheria bacilli have been found in nasal discharges and open sores of horses.

Diphtheria bacilli retain their virulence for long periods if protected from sunlight and from currents of air; hence the possibility of transmission by fomites. Sterilisation by boiling water or in the steam chamber is quite effectual.

Carriers.—Convalescents may harbour virulent bacilli in their throats, as also may others who have been in contact with the infection. Most are free from bacilli 4 or 8 weeks after the commencement of the disease, but in some the carrier state becomes chronic. The dangerous chronic carrier is usually an immune person, as shown by a negative Schick reaction. The presence of bacilli in the throat secretions of carriers is apt to be intermittent. All carriers are not equally effective distributors of the disease; intimate contact and addiction to such habits as kissing, sneezing, spitting and pencil-sucking are important in this respect. The nasal carrier is believed to be an especial source of danger. Among school children 80 per cent. of the carriers are between 5 and 8 years of age, and male carriers are two or three times more common than female. Throat and nose operations on carriers may be followed by clinical diphtheria. In the search for carriers, pallor, unhealthy tonsils, and nasal discharge are important indications, as also a history of recent sore throat. Skin carriers are the subjects of eczematous or impetiginous lesions or whitlows. The discovery of bacilli which morphologically resemble diphtheria bacilli does not necessarily prove they are virulent. Bacilli recovered from the throat are rarely harmless, but those recovered from the anterior nares, from discharging ears and from the skin often prove to be non-virulent when tested on guinea-pigs.

The Klebs-Loeffler bacillus is a non-motile, Gram-positive, non-sporing organism which grows as a diplo-bacillus and shows a great tendency to become segmented or clubbed. The bacilli are slender rods, straight or slightly curved, and of varying length and thickness. In films they often show a characteristic grouping which recalls the letters of the Chinese alphabet. Both long and short forms occur, the length varying from 2 to 6 μ. The segmented appearance of the protoplasm is relied upon for morphological identification. A rapid diagnosis may be made from smears prepared direct from the throat, but it should be confirmed by examination of a film made from a young (6 to 18 hours) culture on blood serum or Loeffler's medium. Diphtheria bacilli ferment glucose with formation of acid, but fail to ferment saccharose. The true bacilli have been divided into *gravis*, *intermediate* and *mitis* varieties, according to their virulence. Differences in growth on a special blood-tellurite medium, coupled with starch-fermenting power in the *gravis* type and a hæmolytic tendency in the *mitis* variety, are the chief distinctive features.

Pseudo-diphtheria bacilli, which, although identical in appearance, with diphtheria bacilli, are non-virulent, are frequently found in the nose and ear, more rarely in the throat. Another non-virulent organism of the same group is Hofmann's. This appears in smears as a diplo-bacillus, the elements of which are short, squat and wedge-shaped with apposed bases. It stains uniformly throughout, and is shorter than even the shortest varieties of the diphtheria bacillus. These distinctions apply only to young cultures. Hofmann's bacillus does not produce acid in glucose, or in saccharose media, and is thus further distinguished. The xerosis bacillus, obtained from the conjunctiva, also resembles the true diphtheria bacillus, but it produces acid both in glucose and in saccharose media.

The crucial test of the identity of the diphtheria organism is the prevention of the local or general action of an injected broth culture by the previous injection of diphtheria antitoxin into the test animal.

In the throat, diphtheria bacilli are often associated with streptococci, staphylococci, or the fusiform bacilli and spirilla described by Vincent. Of these, streptococci are most important, as cases of septicæmia have been found due to them. Diphtheria bacilli themselves rarely become disseminated in the blood stream or internal organs.

Pathology.—The constitutional disturbance caused by diphtheria is toxæmic, toxins but not bacilli being absorbed from the primary lesion, probably by the lymphatics. The extent, thickness, persistence and situation of the membrane determine the degree of toxæmia produced. In the formation of membrane, epithelial necrosis first occurs and is followed by inflammatory effusion from the subjacent tissues. This gives rise to the membrane in which stratified fibrin entangles epithelial cells, blood-cells and leucocytes. Nearly the whole of the process occurs outside the basement membrane. Bacilli are found in the false membrane and necrotic material, but not in the healthy tissues beneath. Recently formed membrane is firm in texture and has a glistening or somewhat gelatinous appearance. The tonsils are the common sites of the first membrane formation, but the faucial pillars, the soft palate, the pharynx, the epiglottis and the larynx may be implicated. Extension from the larynx along the trachea and main bronchi is not uncommon, but coherent membrane is rarely found in the bronchioles. Diphtheritic membrane is much more firmly adherent to the mucous membrane of the fauces than to the epiglottis, the larynx and lower air passages. Its appearance in the cavity of the mouth, on the tongue or lips is rare, and even more rare is its occurrence in the œsophagus, stomach or small intestine. The conjunctiva and occasionally the vulva, or a cutaneous abrasion or a surgical wound may become infected. In this connection it must be remarked that streptococci, pneumococci, and the virus of glandular fever can on occasion produce false membrane.

Apart from the membrane the morbid appearances in diphtheria are not distinctive. The condition, however, of the heart muscle is of peculiar interest. Even in cases in which the myocardium appears healthy to the naked eye, special staining will show extensive infiltration of the muscle fibres with minute granules of mobilised fat. In advanced cases, patches of myocardial degeneration and perivascular aggregations of leucocytes become apparent. The cavities of the heart may be dilated, the muscle flaccid and friable, and intracardiac thrombi, some obviously ante-mortem, may be found in the recesses of the auricles and ventricles, particularly on the right side.

The stomach may be acutely inflamed, with mucosal hæmorrhages and erosions.

The lesion in the kidneys is a degeneration of the epithelium of the tubules, but glomerular involvement may also be present.

Broncho-pneumonia is not uncommon in extensive faucial and in laryngeal infections, it is usually due to secondary invaders. Emphysema or pulmonary collapse may occur where respiratory obstruction is severe, and massive collapse of the lung may result from paralysis of the respiratory muscles.

In the nervous system, the essential lesion is a parenchymatous degeneration of the peripheral nerves which is patchy in its distribution. Chromatolytic changes are found in the vagal nuclei and in the anterior cornual cells of the cord. The cerebro-spinal fluid is normal.

The lymphoid tissues of the body often show a reaction, Peyer's patches being swollen and the spleen slightly enlarged. The liver, too, may be swollen from venous stasis and show slight toxic degeneration of its cells.

Petechial hæmorrhages in the skin, serous membranes, heart wall, and diaphragm are characteristic of hæmorrhagic diphtheria. Extensive effusions of blood sometimes occur.

Symptoms.—The incubation period may not exceed 24 hours, more commonly it is 3 or 4 days, but a carrier may harbour virulent bacilli for a considerable time before showing signs of infection. The fauces are most often the site of the disease, next in frequency come the naso-pharynx, the nasal passages, the larynx and trachea. Infection of the genital mucous membrane and of wounds is exceptional and of the intact skin rare.

Faucial diphtheria may occur in any degree of severity, from a mild catarrhal inflammation, the identity of which is only established by bacteriological examination, to a widespread infection in which membrane invades not only the whole throat but also the naso-pharynx, nose, larynx, and, rarely, the mouth, either simultaneously or in succession.

Invasion may be characterised by malais, headache, anorexia and soreness of the throat. Vomiting occurs occasionally and sometimes shivering; rigor is rare. In children, the onset is particularly insidious, discovery of membrane often being the first intimation of the disease. The exudate in mild cases is often limited to a patch on one or both tonsils, sometimes on the uvula or pillar of the fauces, sometimes on the soft palate. More rarely the posterior pharyngeal wall is first attacked. Special characteristics of the membrane are its elevation above the general surface, its well-defined edge, its glistening or pearl-grey colour, and its tendency to rapid spread. At first it is separable without bleeding, but later free oozing of blood occurs when it is forcibly detached. Multiple patches on the tonsils may, in the early stage, simulate follicular tonsillitis, but the patches tend to spread and fuse; limitation to one tonsil should always arouse suspicion.

Pyrexia is moderate or absent in mild infections, enlargement of the submandibular glands is slight, and early albuminuria so characteristic of grave attacks may be wanting.

When faucial diphtheria is severe it constitutes a very serious form of the disease with a high mortality. The grave form is more common in children than in adults and may develop very rapidly. The membrane is thick, tough, and adherent, sometimes much discoloured. It covers the swollen fauces and may extent widely over both aspects of the soft palate and on the pharyngeal wall. Nasal discharge points to implication of the naso-pharynx and nose. Rarely extension occurs along the hard palate and into the sulci at the sides of the tongue. Secondary invasion of the epiglottis and larynx is not uncommon. The cervical glands become swollen and tender, and periadenitis may extent and involve the neck in a collar of cellulitis (bull neck). The subcutaneous tissues may undergo widespread necrosis and the skin become thinned and much discoloured. A brownish or bloody nasal discharge excoriates the nostrils and the upper lip. Nasal respiration is obstructed and deglutition difficult. The breath has a sickening odour, and the face is puffy or becomes ashen in colour. The skin is dry and the extremities are cold. A slight general cutaneous œdema may make its appearance. The patient is restless and sleepless but apathetic. Bleeding

is easily induced by interference with the edges of the membrane, and epistaxis may occur. Fever is not proportionate to the gravity of the disease; in the worst cases the temperature is subnormal. Albuminuria is usually profuse and the quantity of urine secreted may be very small, but uræmic symptoms are rare. A steady and progressive circulatory failure, characterised by a falling blood pressure and feebleness of the heart's sounds, is an ominous feature. The pulse may become soft, irregular or quite imperceptible. Respiration is rapid and shallow. Vomiting often sets in before the end. Broncho-pneumonia can rarely be recognised by physical signs, but is often present. Death may occur within a week of the onset; sometimes, however, under the influence of antitoxin the membrane clears and the faucial swelling subsides, but acute circulatory failure may still be imminent, death often occurring during the latter half of the second week. In those who escape, widespread paralysis is a common sequel.

Laryngeal diphtheria.—Infection of the larynx may be primary, but is usually a sequel of faucial infection. Essentially occurring in childhood, its frequency increases up to the fourth year of life, after which it progressively declines. The presence of membrane, even in the smallest amount, on the tonsils or fauces will afford a positive indication of the nature of the laryngitis. Failing this a diagnosis is made by swabbing, not the tonsils, but the pharynx or larynx; but treatment must not be delayed pending the result. Hoarseness and croupy cough are early symptoms, soon followed by paroxysms of inspiratory dyspnœa due to laryngeal spasm, with characteristic stridor and recession of the chest wall. During the paroxysms the patient is agitated, sweating and perhaps cyanosed. The cough is loud and croupy. With relaxation of the spasm dyspnœa may cease and the child fall asleep from exhaustion. At first the paroxysms are mainly nocturnal, later they become more frequent and more prolonged, until finally obstruction is continuous and mechanical. Extraordinary recession of the sternum and lower ribs may then accompany the efforts to respire. The body assumes a leaden hue and death occurs from slow asphyxia. In rare instances the paroxysms of dyspnœa and cough culminate in the expulsion of membranous casts of the larynx, trachea or larger bronchi. The absence of toxæmic symptoms when membrane is limited to the larynx and lower air passages is very striking.

Laryngeal diphtheria may run its fatal course in a few days. In infants its duration may be less than 24 hours. In favourable cases the condition subsides under prompt treatment. Should obstruction persist after tracheotomy or intubation, the presence of membrane in the trachea or larger air passages should be suspected; when, however, the bronchioles are blocked, the character of the dyspnœa is quiet rather than violent. Laryngeal diphtheria in a mild chronic form is a rarity.

Nasal diphtheria.—A muco-purulent or blood-stained nasal discharge may be the only evidence of diphtheria in infants and fever convalescents. Infection may be naso-pharyngeal or purely nasal. The former is grave, as toxæmic symptoms may be pronounced, whilst localised nasal infection is more often benign. In such cases a small patch of membrane may, perhaps, be found on the septum. Possible implication of the nasal accessory sinuses should be remembered. As already mentioned, bacilli from the nose may prove to be non-virulent. Foreign bodies in the nose have been found associated with persistent nasal diphtheria.

Conjunctival diphtheria is usually the result of direct inoculation, but may extend from the nose. It may simulate a mild, simple conjunctivitis, or membrane may form on the inner aspect of the lids. There is a grave form with extreme inflammatory infiltration of the conjunctiva which may lead to sloughing of the cornea and destruction of the eye.

Vulval, vaginal and preputial diphtheria.—Vulval infection may be secondary to diphtheria of the fauces, infection being conveyed by the fingers, or it may be primary. Sometimes it is seen in puerperal women. It is of insidious onset, and the membrane looks like a slough on the inner surface of one or both labia. The inguinal glands are enlarged, and confusion with erysipelas, chancre or gonorrhœa is possible. Severe toxæmia may ensue. The vagina may be infected with the vulva. Preputial diphtheria may follow ritual circumcision. Infection of the puerperal uterus and of the male urethra is rare. Infection of the umbilicus may occur in the new-born.

Diphtheritic infection of wounds is not common, and membrane formation is not invariable. The wound may merely be dry and grey and the adjacent glands swollen. Bacteriological confirmation is necessary. Paralysis may be local in distribution.

Cutaneous diphtheria.—Slight infection of the macerated skin at the margins of the nostrils and mouth is frequent and diphtheritic whitlow is not rare, the finger possibly being infected by sucking. Sometimes the raw surfaces left by eczema, herpes, or impetigo, become secondarily infected, and membrane may form, but skin diphtheria may occur without this distinctive sign. Gangrenous varicella and extensive gangrene allied to noma has also been attributed to the action of the diphtheria bacillus. Before skin cases are accepted as genuine, rigorous bacteriological proof is essential.

Septic diphtheria.—The ordinary grave case of diphtheria may be looked upon as toxæmic or malignant. The septic type of case is characterised by pulpy discoloured membrane and great inflammatory œdema at the site of infection, accompanied, it may be, by ulceration, cellulitis, or even gangrene. The adjacent lymph glands are much swollen, periadenitis is marked and suppuration may ensue. Erythematous or measly rashes may appear on the extremities. Constitutional symptoms are severe and the prognosis grave, chiefly, it is alleged, because diphtheria antitoxin has no influence on the septic element, which may be a hæmolytic streptococcus.

Hæmorrhagic diphtheria.—Hæmorrhagic symptoms supervening during the acute stage indicate an infection of a severe type. Blood may ooze from the edges of the membrane, and epistaxis occur. This in itself is not necessarily serious, but the tendency to bleed may be more widespread, bruises appearing on the body and bleeding occurring around and along the track of the antitoxin needle. The conjunctivæ may become suffused with blood, and hæmorrhage may occur from the stomach or bowel. Hæmaturia is rare. Small cutaneous petechiæ are by themselves of most sinister omen. They are insignificant in appearance and easily escape detection on account of their smallness and tendency to occur on the neck and trunk where clothing conceals them.

Blood changes.—A polynuclear leucocytosis is common and reaches its acme at the height of the disease. Sometimes the red cells are in excess of normal and the specific gravity of the blood increased, indicating an oligæmia. Leucocytosis may be absent in very mild and also in very grave infections.

The presence of myelocytes is also characteristic, and their appearance in large numbers indicates a severe toxæmia and a bad prognosis.

Complications.—The chief are circulatory failure, paralysis, albuminuria and pulmonary inflammations. Relapse sometimes occurs.

Acute circulatory failure is a justly dreaded occurrence. Apart from asphyxia and from respiratory paralysis it is responsible for all the deaths. In diphtheria, excluding the mildest cases and those in which respiratory obstruction exerts its modifying influence, there is from the first a progressive fall of blood pressure, the systolic readings being affected earlier than the diastolic. Recovery is very rare when the systolic reading falls below 65 mm. The fall in pressure is said to be accompanied by a fall in volume and increased concentration of the blood. Vascular relaxation is believed to account for the early fall in pressure, the effect of myocardial weakness appearing later. The condition culminates in attacks of acute circulatory failure. Where systematic pressure readings have not been taken, minor irregularities and intermissions of the heart's action often afford the first warning. True respiratory or sinus arrhythmia, which is so common in childhood and often is exaggerated in diphtheria, should not be confounded with the condition now under consideration. Tachycardia and bradycardia are both disquieting signs. The heart sounds become modified, the first becoming short and soft and the second somewhat accentuated. Reduplication and gallop-rhythm may occur. Vomiting without obvious cause is always a danger signal. The characteristics of the acute attack are great irregularity and feebleness of the pulse, præcordial or epigastric pain, restlessness, rapid shallow respiration, slight cyanosis and a sub-normal temperature. The mind remains clear. Dilatation of the heart and increase in the size of the liver may be evident. Actual dropsy is rare, but sometimes slight œdema of the face, chest and feet appears. Albuminuria may supervene or, if already present, be much increased; partial suppression of urine occurs. Death often results with great suddenness, and should the first attack be survived, which is unlikely, a second or even a third may prove fatal. Rarely recovery ensues.

Death from circulatory failure is an early sequel of severe faucial infections, occurring at the end of the first or in the course of the second week. Cardiac failure occurring at a later stage of the disease is often associated with severe paralytic phenomena, and in some cases, at all events, is believed to be of nervous rather than myogenic origin. Extra systoles, heart-block and auricular fibrillation have at times been demonstrated. The absence of residual valvular or myocardial lesions after diphtheria is remarkable.

Diphtheritic paralysis occurs in from 15 to 20 per cent. of cases. It is more often localised than general, and rarely complete in degree. Children suffer more frequently and more severely than adults. As a general rule the extent and severity of the palsy are proportional to the amount of membrane which was present. Exceptionally, paralysis of diphtheritic type occurs in the absence of recognised infection. The usual time of onset is the end of the third or beginning of the fourth week of the disease, but in grave infections it may even set in before the fauces are clear of membrane. Widespread paralysis rarely declares itself before the end of the fourth week, and paralysis of the ataxic type, which is rare, often does not appear until the second or even third month. For a detailed description see pages 1781–1783.

The limited form of diphtheritic paralysis is transitory, its duration being measured by days or weeks, but the more widespread paralysis may last for months or the best part of a year before recovery is complete.

Hemiplegia sometimes occurs in diphtheria and is due to occlusion of the middle cerebral artery, usually by an embolus. In most cases this paralysis is more or less permanent. Much more rarely an embolus from the heart lodges in a main artery of a limb, producing gangrene.

Albuminuria is of common occurrence, but in mild or doubtful cases its absence is not sufficient to negative the diagnosis. It is most likely to be found about the tenth day, but appears earlier and in greater quantity in grave cases. In those who recover, its presence is transitory and no grave damage to the kidneys results. At times casts and a little blood may be found in the urine, particularly in toxic or asphyxial cases. Acute circulatory failure greatly increases the albuminuria and may lead to actual suppression of urine. Acetone often appears in the urine during severe attacks.

Pulmonary Complications.—Bronchitis and broncho-pneumonia may accompany severe faucial diphtheria, but are more common when the larynx is implicated. The cause is more often a secondary infection than the diphtheria bacillus. Febrile disturbance, great dyspnœa, cough, and lividity are the signs which should suggest implication of the lung. Auscultatory signs are often equivocal, owing to laryngeal obstruction or the presence of a tracheotomy tube. Massive collapse of the lungs may occur in paralytic patients and is often mistaken for acute circulatory failure, pneumonic consolidation or pleural effusion. Some degree of acute emphysema is usually present when the larynx is obstructed, and surgical emphysema of the mediastinal and subcutaneous tissues may follow a difficult tracheotomy. As sequels of diphtheria, lobar pneumonia, pleural effusion and empyema are rare.

Otitis media is exceptional and seldom serious. In this respect it stands in sharp contrast to the otitis of scarlet fever. Diphtheria bacilli recovered from the discharge are often non-virulent (perhaps in 50 per cent. of the cases). Diphtheritic membrane is sometimes formed in the auditory meatus.

Relapse of diphtheria is rare. It occurs in little over 1 per cent. of the cases and usually is mild, the membrane being limited to the tonsils and rarely spreading to other parts.

Diagnosis.—Every inflamed throat, or nasal discharge, particularly in a child, should be regarded with suspicion, and clinical diagnosis supplemented by bacteriological examination before antiseptics are applied. Definite membrane on one or both tonsils or adjacent parts of the throat is characteristic of diphtheria. Tonsillar inflammation, if accompanied by hoarseness or rhinorrhœa or albuminuria, is highly suggestive. Some diphtheritic throats are very œdematous and painful, but as a rule pallor of the mucous membrane and absence of pronounced fever and pain are striking features of the disease.

The differential diagnosis between scarlet fever and diphtheria is discussed on p. 73. Simple tonsillitis is usually bilateral, and the exudate, which is soft and crumbling rather than membranous, is follicular and limited to the surface of the tonsils. Pyrexia and constitutional disturbance are more pronounced than in diphtheria, and the tongue is heavily coated.

Peritonsillar abscess is more characteristic of simple tonsillitis and the secondary tonsillitis of scarlet fever. It seldom occurs in diphtheria.

Vincent's angina may produce a greyish film of exudate on one or both tonsils, and even invade the adjacent parts of the faucial pillars and the soft palate, but the process is rather a shallow necrosis than a true membrane formation. Ulceration may be evident at the centre of the deposit; sometimes it is widespread and destructive. The mucous membrane of the gums and cheeks may also be attacked. The breath has a peculiar and offensive odour, but diagnosis should never be based on this alone. The large fusiform bacilli and spirilla described by Vincent can be demonstrated.

Double infections with diphtheria and Vincent's organisms are not at all rare. Thrush, which produces an exudate like milk curd, is recognised by detection of the characteristic mycelium. It is a disease of infants and greatly enfeebled adults.

Membranous angina may occur in glandular fever, leukæmia, or agranulocytosis. For the differentiation of these, blood-counts as well as throat swabbings are necessary.

Syphilis.—Both in adults with the acquired and children with the inherited disease the inflamed throat of secondary syphilis is a cause of confusion. The throat is painful and full of mucous secretion. Filmy patches appear on the tonsils and pillars of the fauces. The tonsillar glands are swollen and there is little or no fever. The rapidity with which ulceration and perforation of the palate occur in some cases is striking. The diagnosis is made from the history, the presence of other signs of syphilis, failure to find diphtheria bacilli, a positive Wassermann reaction and prompt response to vigorous anti-syphilitic treatment.

Other conditions which simulate faucial diphtheria are erysipelatous inflammation, herpes of the soft palate and lesions due to steam, boiling fluids, caustics or tonsillectomy.

Laryngeal diphtheria.—Croupy cough, hoarseness, and stridor in a child will always suggest diphtheritic infection. Examination may show membrane on the fauces. By forcible depression of the base of the tongue with a spatula, the epiglottis may often be seen and membrane possibly recognised on its edge or surface. Rarely fragments of membrane are ejected on coughing, or there may be a history of contact with the disease. All doubtful cases should be treated freely with antitoxin, pending confirmation by examination of a swab taken from the pharynx as near the glottic aperture as possible.

Other forms of laryngitis have to be differentiated. They are (1) the laryngitis of early measles, distinguished by history, catarrhal symptoms, and Koplik's spots. (2) Simple catarrhal laryngitis; in this bacteriological examination is most essential. The voice may be hoarse, and the cough croupy; nocturnal spasms of dyspnœa may occur. Enlarged tonsils and adenoids are often present, and sometimes the history of previous attacks is obtained. (3) The glottic spasm of laryngismus stridulus is also definitely paroxysmal, but although the child crows the voice is not hoarse nor is the stridor persistent. Rickets, tetany and convulsions are the accompaniments in many cases.

Retro-pharyngeal abscess, when low down, produces considerable laryngeal obstruction. Digital examination of the back of the pharynx reveals its presence; sometimes the bulging may be seen on inspecting the fauces.

Rare causes of laryngeal obstruction are congenital laryngeal stridor, congenital syphilis, œdema of the glottis in renal disease, or resulting from inhalation of steam or other irritants, foreign bodies in the larynx, and papillomatous growths. These forms of obstruction are differentiated from diphtheria by the history, by careful inspection of the fauces, followed by digital examination, by general examination of the patient and by the negative results of bacteriological examination. In adults the laryngoscope will give useful information. Direct laryngoscopy is of great value.

Prognosis.—The important indications yielded by determination of the extent and position of the membrane have already been mentioned: the more extensive and more persistent this is, the greater is the risk of severe toxæmia. Cases where the membrane is limited to one, or to parts of both tonsils are likely to be mild; when both tonsils are completely covered the attack is more grave, but recovery is still probable; when the fauces and naso-pharynx are extensively involved, the outlook is very serious. The great mortality of laryngeal diphtheria is due to asphyxia and broncho-pneumonia, absorption of toxin from this region being small. Diphtheria limited to the nose and not involving the naso-pharynx has a low mortality.

Enlargement of the cervical glands is more or less proportional to the extent of the lesion in the fauces and naso-pharynx, and has the same prognostic importance. The efficiency of antitoxin treatment and the day of its first administration have a most important influence. The mortality is almost negligible when antitoxin is administered on the first day of the disease, but it increases progressively to 18 or 20 per cent. if administration is delayed to the fifth or subsequent days.

Age also has a great effect, the disease being very fatal to children in the first year of life, and much more serious in children under 5 than in those over that age. Septic attacks with much pallor, copious nasal discharge, considerable glandular enlargement and profuse albuminuria have a very bad prognosis.

Hæmorrhagic symptoms, other than slight bleeding from the edge of the membrane and possibly epistaxis, are grave; particularly so, minute cutaneous petechiæ. Cases such as these hardly ever survive. Repeated vomiting after the initial stage, and signs of acute circulatory failure are most ominous. The chief danger of paralysis, when this ensues early, is its association with acute circulatory failure, but paralysis of the bulbar type is in itself very fatal. Failure of the muscles of respiration and liability to broncho-pneumonia and pulmonary collapse constitute the chief dangers of generalised paralysis. If the patient survives, paralysis terminates in complete recovery, but hemiplegia, which is of vascular origin, may be permanent.

Treatment.—PROPHYLACTIC.—Convalescents should be isolated for not less than 4 weeks from the commencement of the disease, or until three negative bacteriological examinations at intervals of a week have been obtained. The presence of inflammatory conditions or discharges from the throat, nose, eyes or ears is an indication for further detention. Skin eruptions and whitlows should be carefully treated.

The period of quarantine advised is 12 days. This may be supplemented by bacteriological examinations. Children from an infected house should not be allowed to attend school. Contacts in the home or school often become carriers, and should be bacteriologically examined. Clothing and

utensils which have been in contact with the sick should, of course, be disinfected.

When diphtheria breaks out, contacts should be examined for unhealthy conditions of throat, nose, ears or skin, and bacteriological examination made in all instances, if possible. Opinion with regard to the desirability of prophylactic injections of antitoxin is not unanimous. The *symptoms* of diphtheria may be prevented in contacts by the injection of 500 units of antitoxin, but this method fails if the subject is already incubating the disease, and only affords protection to others for some 3 or 4 weeks. It should be realised that antitoxin does not prevent *infection*, but only the toxic results of infection. It militates against active immunisation, and may produce a condition of hypersensitiveness to serum, which may have to be used subsequently.

For these reasons, the best authorities are against prophylactic injections of antitoxin in contacts and in favour of repeated examinations for signs of development of the disease, when antitoxin can be administered at once. Meantime, immunisation of susceptible contacts (*vide infra*) can be initiated, since there appears to be no negative phase induced.

In the Schick test we have a means of determining whether an individual is susceptible to diphtheria. If a local inflammatory induration from 1 to 2 cm. in diameter follows the injection of a minute quantity of diphtheria toxin *into* the skin, susceptibility to the infection is indicated. One-fiftieth of the minimum lethal dose (M.L.D.) of toxin for a guinea-pig of 250 grammes weight, in 0·2 c.c. of normal saline is the standard dose. At the same time, but at another spot, an intradermic injection of heated, and therefore inactive, toxin is made, to discount a " pseudo " reaction due to the foreign protein in the solution of toxin. The absence of a reaction to the active toxin indicates the presence of more than one-thirtieth of a unit of antitoxin per c.c. in the blood, and is a sign of immunity. The injections are usually made into the skin of the forearms. The reaction takes 24 to 36 hours to develop, and another week to subside. Four types of reaction are possible : (1) Negative, (2) Positive, (3) Negative and Pseudo, and (4) Combined Positive and Pseudo. These must be discriminated with care. The best time for reading the test is 36 hours after injection, and again at the end of a week when false reactions will have faded and late positive reactions will be detected.

For immunisation, diphtheria toxin, guarded by antitoxin, was originally used. Later, toxin, converted to toxoid by incubation with formalin (*anatoxine*), replaced this. Toxoid-antitoxin floccules, precipitated by interaction of toxoid and antitoxin produce little or no reaction and are effective. For the immunisation of children, alum-precipitated toxoid (A.P.T.) is now recommended. Two doses (of 0·5 c.c.) are given intramuscularly, with an interval of 4 weeks between, the first dose acting both as an antigen and as a detector of sensitive individuals. For adults, who are more liable than children to reactions, toxoid-antitoxin floccules (T.A.F.) are preferable, three injections (1 c.c., 1 c.c. and 1·5 c.c.) being administered, with intervals between them of 3 or 4 weeks. Susceptibility to reaction may be detected by intradermal injection of 0·2 c.c. of diluted toxoid (Moloney test). The development of active immunity takes about 6 weeks. This immunity is protracted, but its exact duration cannot yet be specified. Most children under 6 years are susceptible and the ideal time for immunisation is in the

pre-school period, after the first year of life. When the proportion of vaccinated children in a community reaches 70 to 80 per cent. a great reduction of incidence of diphtheria, perhaps to zero, may be expected.

When dealing with outbreaks of diphtheria in wards or institutions, swabs should be taken from the throats and noses of the inmates, and Schick tests performed. The negative reactors are then isolated. They will probably include a dangerous chronic carrier as proved by the virulence test. The positive reactors may be immunised with A.P.T. Virulent bacilli in the Schick positive group indicate precocious carriers or who will soon sicken with the disease.

Chronic carriers are a great source of difficulty. The bacilli cannot be eradicated by local application to the throat or by the administration of antitoxin or vaccines. If the tonsils are unhealthy, they should be enucleated and adenoids removed; this is often successful. Carriers should spend as much time in the fresh air and sunlight as possible. Before condemning a carrier to isolation, the virulence of the organisms should be tested.

CURATIVE.—The patient should be isolated and strict recumbency enjoined. Diphtheria antitoxin must be injected without delay, the result of bacteriological examination not being awaited in any case in which the diagnosis is reasonably certain. It is very important the patient should receive the first dose of serum not later than the third day of the disease; the earlier it is given the better the result, but at whatever stage the presence of membrane indicates prompt dosage. The amount required depends, not on the age, but on the duration of the disease, the extent of the membrane and the degree of toxæmia. For mild cases on the first or second day 8000 units are sufficient; in more severe cases the dose should be 20,000 units. In severe faucial and naso-pharyngeal diphtheria and in infections of the larynx, 20,000 units should be the initial dose, repeated in 12 hours if the membrane still shows a disposition to extend, or the laryngeal symptoms are not relieved. Cases coming under observation after the third day of illness require larger doses than those seen earlier. In very severe infections and those complicated by pulmonary lesions, enormous doses have been recommended; The advocates of these larger doses claim a diminished mortality, a reduction of paralytic complications and a speedier convalescence.

Antitoxin should never be given by mouth or rectum. Intramuscular injection is more effectual than subcutaneous, and should replace it. In severe, advanced, and hæmorrhagic infections, the antitoxin should be given intravenously, undiluted and at blood heat. Injection should be very slow, through a fine needle. The patient is then wrapped in warm blankets, hot water bottles applied, and the foot of the bed raised, since rigor and collapse may follow. Fifty thousand or more units may be given in this way, followed by intravenous injection of 20 grammes of anhydrous dextrose in the form of a 50 per cent. solution in normal saline, supplemented by 20,000 units of antitoxin intramuscularly into the buttock or outer side of the thigh. In cases which do not respond the injection is repeated after 12 hours. Strict aseptic precautions should always be observed.

Antitoxin treatment may be followed by certain sequels due to horse serum. These are less frequent when concentrated antitoxin is used. They usually occur a week or more after injection and take the form of erythematous, morbilliform, or urticarial eruptions, appearing first in the vicinity of the

puncture. Fever, vomiting, arthritic pains or slight joint effusions may accompany the rash. The tonsils may again become inflamed (*angina redux*) and albuminuria may occur. The rashes and other symptoms are transient but may recur. Aspirin often affords much relief, and the cutaneous irritation may be allayed by weak carbolic lotions. On rare occasions rigor, dyspnœa and collapse follow the injection immediately, and death has been known to occur. These symptoms are anaphylactic in nature and may occur if the patient has been sensitised by injection of serum a few weeks previously, or quite apart from this. Asthmatics are said to be particularly liable to them. When it is necessary to administer antitoxin in such circumstances, a preliminary injection of 5 minims should be given and the effect watched. If no symptoms occur within an hour the full injection may be employed, otherwise desensitisation is necessary.

Absolute recumbency is essential in the treatment of diphtheria. For the mildest case a fortnight is not too long, in the average case at least a month, and for severe infections longer. When the patient is first allowed to sit up in bed the effect on the pulse should be carefully noted. No patient should be allowed to sit up whose pulse is irregular or who has recently vomited. The detection of paralytic symptoms is also an indication for rest.

Local applications to the fauces and nose are of minor importance. In cases characterised by fetor the free chlorine lotion is of use. When douching is resisted it is better to omit it altogether.

In laryngeal diphtheria prompt administration of antitoxin and the use of a steam tent will generally obviate the necessity of operative interference; but tracheotomy, intubation or laryngeal aspiration should not be postponed, if restlessness, dyspnœa and recession of the chest wall are present, or paroxysmal dyspnœa has supervened.

Intubation is suitable for the milder type of case, but constant skilled supervision is necessary, as the tube may be ejected. As a rule, tracheotomy is preferable, especially if the fauces and naso-pharynx are much involved. Tracheotomy as a sequel to intubation has a very high mortality on account of the class of case in which it becomes necessary. After tracheotomy or intubation the patient is usually placed in a steam tent and the arms secured by light splints or other means. Cough on swallowing is obviated by using thickened foods or by nasal feeding. A method of feeding with the head lying lower than the body is often successful in intubated patients. If all goes well an attempt should be made to dispense with the tracheotomy or intubation tube on the third day, sometimes even sooner. Patients must be watched constantly when the tube is first removed. In cases where the tracheotomy is dry and no secretion occurs, an alkaline spray is useful.

Circulatory failure is treated by removing all pillows, raising the foot of the bed on blocks and applying a binder to the abdomen. The most absolute rest and perfect quietude are essential. A combination of atropine, strychnine and adrenaline has the best reputation as a circulatory stimulant in these cases (atropine sulphate, gr. $\frac{1}{200}$; strychnine sulphate, gr. $\frac{1}{100}$; adrenaline solution, 1 in 1000, min. 5). The solution is made up to 10 minims with sterile water and injected every 4 hours or more often if necessary. At the same time, as vomiting often precludes feeding by the mouth, a 5 per cent.

solution of glucose in hot normal saline should be given by the bowel. Other circulatory stimulants and brandy are also advocated. When marked acetonæmia is present, 10 grains of sodium bicarbonate dissolved in 1 ounce of water should be given by mouth or rectum every 4 hours.

Paralysis calls for careful nursing and feeding, with avoidance of muscular exertion, but patients with palatine paralysis only may be allowed up after 10 days if the condition is stationary. Massage and electricity may be useful during convalescence, but should be avoided in the early stages. Hypodermic injection of strychnine is possibly of some use. The administration of vitamin B_1 (aneurine hydrochloride; thiamine hydrochloride, U.S.P.) is said to expedite recovery. The daily administration of antitoxin in doses of 1000 to 2000 units is advocated, but is of very doubtful utility. Extensive respiratory paralysis necessitates artificial respiration with a Drinker or Bragg-Paul apparatus. Active collapse of the lung in diphtheria may be mistaken for acute circulatory failure if its special diagnostic signs are not borne in mind.

During the acute stage of diphtheria and also when albuminuria is present, milk is the best food. Solids may be allowed quite early in convalescence. When swallowing provokes coughing, the milk should be thickened with isinglass or cornflour. When pharyngeal paralysis is present, the patient should be fed by rectum, or better, through a large soft œsophageal tube or by nasal catheter.

The occurrence of anaphylaxis after injection of antitoxin is treated by injection of adrenaline, and by artificial respiration; by some adrenaline is given before injection of serum, as a prophylactic.

WHOOPING-COUGH

Synonym.—Pertussis.

Definition.—An acute specific disease of high infectivity, characterised by catarrh of the respiratory tract, combined with periodically recurring laryngeal spasms of distinctive type and other signs of nervous excitability.

Ætiology.—Whooping-cough is mainly a disease of temperate climates, being rarer and less severe in hot countries. Spring and autumn are the seasons of its maximum prevalence, and also of its greatest mortality, chiefly owing to respiratory complications; but the disease may also occur in the warmer months, even in epidemic form. It is more prevalent in cities and industrial centres than in the population of rural districts. Persons of all ages, if unprotected by a previous attack, are susceptible to the infection; a number of cases have been recorded in patients over 60 and a few in patients over 80 years of age, but whooping-cough is essentially a disease of childhood. Moreover, it shows a stronger tendency to attack children under 2 years than does any other specific disease, and the death-rate is highest for this group, especially in infants of the first year. Most attacks occur before the age of 10 years. The fœtus *in utero* has been known to contract the infection from its mother, and to show the characteristic symptoms soon after birth. More females than males are attacked. The frequency with which whooping-cough follows an attack of measles is noteworthy.

Infectivity is greatest during the catarrhal and early paroxysmal stages;

but its exact duration is a matter of dispute. On rare occasions convalescents are said to have acted as carriers of the disease.

The infection is usually direct, being conveyed by the mucous droplets expelled by the cough. Since the bacillus can resist drying for several weeks the disease may also be conveyed by fomites, but this is uncommon. One attack almost invariably confers lifelong immunity.

Bacteriology.—Of the various organisms which have been alleged to be the causal agents, the bacillus of Bordet and Gengou (*Hæmophilus pertussis*) has the strongest claims to acceptance. This is a minute, slender rod closely allied to the bacilli of the influenza group. It is Gram-negative, and only flourishes on artificial media which contain blood or serum. It grows best at blood heat. Cultures are most easily obtained from the small pellets of viscid mucus which are expectorated at the end of a paroxysm of coughing. The blood of convalescents agglutinates the bacilli.

There are no post-mortem appearances which are distinctive, the changes found after death being due to complications. Of these, congestion of the air-passages and broncho-pneumonia are the most common, and are accompanied by general acute vesicular emphysema. The tracheo-bronchial lymph glands are usually soft and swollen.

The paroxysmal cough is attributed to hyperæsthesia of the respiratory mucous membrane and to heightened excitability of the vagus nerve.

Symptoms.—The incubation period is difficult to fix with accuracy, owing to the insidious nature of the onset and the delayed appearance of the characteristic whoop, but it is most probably 13 to 15 days. Extremes of 3 days and over 3 weeks have been claimed. During a typical attack three stages may be recognised—the catarrhal, the paroxysmal, and the convalescent.

The catarrhal stage lasts from seven days to a fortnight—it is febrile, and in many ways resembles a somewhat severe respiratory catarrh; but the cough is more troublesome and generally accompanied by some sonorous and sibilant rhonchi. Recognition of the disease at this stage is difficult unless the patient is known to have been exposed to the infection. Suggestive signs towards the end of the period are a tendency of the cough to assume a paroxysmal character, with greater severity at night, giving rise to suffusion of the face and occasionally culminating in vomiting. Bacteriological investigation by cough plate and the detection of lymphocytosis will assist early diagnosis.

When the paroxysmal stage is reached the disease is unmistakable. Fever will usually have subsided; but the cough occurs in paroxysmal bouts, often spontaneous, but frequently the result of external stimuli, such as excitement, draughts, the ingestion of food or examination of the throat. Several paroxysms may occur in quick succession with longer or shorter intervening periods of freedom. The victim knows when the cough is impending, and may attempt to suppress it. If lying in bed a child will sit up, if about he may run to his mother or nurse. A brief, deep inspiration is followed by a rapid succession of short coughs, with open mouth and protruded tongue, which are continued until the chest is almost emptied of air. The face becomes congested or livid, the superficial veins are engorged, and the eyes fill with tears. The eyeballs protrude, the skin is bathed in sweat, and suffocation appears imminent; but relief is suddenly afforded by relaxation of the laryngeal.

spasm and the occurrence of the whoop, a long-drawn crowing inspiration, which refills the lungs with air. The paroxysm then recurs, and may be repeated several times, leaving the child perspiring and exhausted. The bout often terminates with the discharge from the air-passages of a pellet of viscid, transparent mucus. A quantity of thin sticky secretion, which is sometimes blood-stained, may also flow from the mouth and nose. During the fits of coughing, which often last for 2 or 3 minutes, the child may faint or become convulsed and insensible. The contents of the stomach are often ejected, and the urine may be voided; in some instances incontinence of fæces occurs. Epistaxis is not uncommon in the more severe attacks. Subconjunctival hæmorrhage may occur, and petechiæ appear in the skin of the eyelids and other parts. Rarely the membrana tympani is ruptured, and blood escapes from the ear In infants asphyxia may occur and call for artificial respiration.

In the early paroxysmal stage the cough is only occasional, but its frequency soon increases, and in a case of moderate severity from 15 to 20 paroxysms occur in the 24 hours; in some attacks, however, they are much more numerous. They are characteristically most frequent and most severe at night.

Physical examination of the chest at this stage will still reveal signs of diffuse bronchitis; but this is now accompanied by a greater or less degree of acute emphysema and a moderate degree of abdominal distension is not uncommon. The forcible protrusion of the tongue over the lower incisor teeth often produces a shallow ulcer on the frænum linguæ.

The duration of the paroxysmal stage is from 3 to 10 weeks, and after this convalescence begins. Whooping-cough is more prolonged in winter than in summer, and its duration is increased if complications ensue. After the whoop has ceased a fresh attack of respiratory catarrh may cause it to reappear; but this should not properly be regarded as a relapse, and does not render the patient again infectious.

The blood shows a leucocytosis even in the early catarrhal stage. Both polymorphonuclear cells and lymphocytes share in the increase; but the lymphocytes are increased out of proportion to the other cells; a typical count would be 15,000 to 25,000 white cells per c.c. with from 50 to 70 per cent. lymphocytes. Myelocytes may also make their appearance. The leucocytosis is said to be increased after each paroxysm of coughing, and the highest counts to be found during convulsions. The supervention of pneumonia increases the polymorphonuclear cells.

Course.—Attacks vary in their severity and duration. Mild infections may run their whole course in a week or two, whilst severe ones may last several months. As mentioned above, the number of paroxysms in 24 hours is some measure of the severity. The danger of supervention of complications is broadly proportional to the severity of the attack. When whooping-cough occurs in the adult the whoop is much less conspicuous, and may be entirely absent, the disease being characterised by violent fits of coughing with a sense of impending suffocation. Cyanosis, vomiting, and even temporary attacks of unconsciousness may occur and subcutaneous ecchymoses appear. The legs may become œdematous and muscle rupture may ensue from the violence of the cough, which retains its paroxysmal character and nocturnal severity. In infants, too, the whoop may be very imperfectly developed.

Complications.—These belong mainly to the paroxysmal stage of the disease—they are partly mechanical and partly inflammatory in nature. The most serious are excessive vomiting, broncho-pneumonia and convulsions.

When the paroxysms of coughing are frequent and severe, excessive vomiting may lead to great emaciation and exhaustion. Diarrhœa and ileo-colitis may also occur, mainly in younger children, and during the summer months.

Pulmonary complications are frequent, and are more common during the winter. A mild general bronchitis with general, but temporary, acute emphysema is the rule, and is of but little moment. Capillary bronchitis or broncho-pneumonia, with pulmonary collapse, is much more serious. It usually occurs at the height of the paroxysmal stage, and is responsible for two-thirds of the deaths. Interstitial emphysema of the lung may result from rupture of an air cell during coughing, but is only likely to be recognised when it overflows into the root of the neck and the connective tissue of the chest wall. Bronchiolectasis is an occasional sequel of the disease.

A single convulsion may prove of little importance, but convulsive states in the form of *whooping-cough eclampsia* constitute a deadly complication, which is seen chiefly in infants and young children. The convulsions occur after prolonged paroxysms of coughing or as a terminal event, but on occasions they may precede a paroxysm or occur in the intervals. Their cause is much disputed. It is tempting to associate them with the encephalitis of measles, mumps, small-pox, and other infectious diseases. Degenerative changes have been found in the nerve cells of the cornu ammonis and basal ganglia, and also in the Purkinje cells of the cerebellum.

Coma or paralysis of varying duration and extent may follow convulsions. Hemiplegia, aphasia, paralysis of ocular nerves, or defects of sight, hearing and intelligence sometimes supervene, and bulbar paralysis and polyneuritis have been recorded. Defect in vision is sometimes due to retinal hæmorrhage or detachment.

The strain of the recurrent paroxysms of coughing may induce dilatation of the right ventricle of the heart, subconjunctival hæmorrhages, cutaneous petechiæ, epistaxis, bleeding from the mouth or ears, hæmoptysis, and hæmorrhage on the surface or less commonly in the substance of the brain. Other results are the appearances of herniæ and prolapse of the rectum.

True nephritis is rare, but albuminuria may appear. Glycosuria is occasionally seen.

An unhealthy condition of the naso-pharynx may persist after the cough has subsided, and no other disease except measles has such a bad reputation as whooping-cough as a forerunner of tuberculous manifestations.

Diagnosis.—In the absence of known exposure to infection, diagnosis may be impossible until the whoop is heard; but the significance of a paroxysmal cough, worse at night and terminating in vomiting, should not be overlooked. The disproportion between the violence of the cough and the accompanying physical signs in the chest is also noteworthy. When broncho-pneumonia does supervene the whoop may cease. In infants the

cough may be paroxysmal and asphyxiating, but the whoop not developed; in such cases, as also in adults when the whoop is absent, the diagnosis may be cleared up by the occurrence of infection in contacts.

Bacteriological diagnosis may be effected by receiving the invisible droplets ejected during a natural paroxysm of coughing on a modified Bordet-Gengou culture medium in a Petri dish, held 6 inches in front of the mouth. The medium consists of defibrinated blood-agar, human blood being used by preference. The growth should be recognisable in 48 to 72 hours as small glistening colonies of minute ovoid, Gram-negative rods or cocco-bacilli, frequently paired. More than one exposure may be necessary. A negative result does not necessarily exclude whooping-cough. The bacteriological method may also be applied to determine the cessation of infectivity, three negative results on successive days being accepted as satisfactory.

The spasmodic cough of bronchial gland irritation and of adenoids is apt to be paroxysmal, but the whoop is wanting. The same observation applies to the obstinately recurrent coughs of influenza and bronchiolectasis. In children, laryngeal inflammation of catarrhal or of syphilitic origin may induce paroxysms of cough and laryngeal spasms, but the tone of the cough at once indicates its laryngeal origin. Conversely, whooping-cough in its early stages, if accompanied by an unusual amount of laryngeal catarrh, may be confused with the laryngitis of measles or of diphtheria.

In the catarrhal stage the malaise, cough, pyrexia and slight fullness of the abdomen with perhaps some irregularity of the bowels, may arouse unfounded suspicions of early general tuberculosis.

The leucocytosis of whooping-cough, which is considerable in the early stages, may prove of assistance in the early diagnosis of the disease, especially if combined with sputa teeming with slender Gram-negative organisms like influenza bacilli. The count should, of course, be compared with that normal for the child's age. An authentic history of a previous attack puts whooping-cough for all practical purposes out of court, second attacks being excessively rare.

The presence of the sublingual ulcer is only to be expected after the incisors have appeared. Occasionally it is seen in other conditions of persistent cough.

Prognosis.—Whooping-cough is a much more serious malady among the children of the poor, and in those suffering from malnutrition, rickets, tuberculosis, or a predisposition to chest troubles, than it is to healthy children in comfortable circumstances. Apart from this, age constitutes the most important prognostic factor. Infants and children under 3 years of age suffer a considerable mortality, which for the first 12 months of life is estimated at 25 per cent. The mortality decreases rapidly after the third year, and after 10 years of age is insignificant. Hence it is found that more than two-thirds of the deaths from whooping-cough occur during the first year of life, the younger the infant the worse being the outlook. Of complications, broncho-pneumonia causes most of the deaths, occurring chiefly in the winter months. In the summer, ileo-colitis comes into prominence.

Convulsions, especially if repeated, are of grave omen. Death at times occurs suddenly from asphyxia due to sustained laryngeal spasm, or from heart failure or intracranial hæmorrhage. When tuberculous lesions are

present these may be stirred into activity by the infection, and especial care is necessary.

A cautious prognosis should be given with regard to paralytic sequels, since in a number of cases these prove permanent.

Treatment.—Isolation should be enforced. Free ventilation with abundance of fresh air is desirable, and gives better results than confinement in a close room and the inhalation of medicated vapours. In the absence of fever, older patients may be allowed up and out as much as possible, provided isolation can be maintained. In suitable weather continuous open-air treatment may be adopted even for those patients who are confined to their beds. It is especially valuable in broncho-pneumonia. A light binder should support the abdomen, and the clothing be loose and not too heavy. When lung complications are present a jacket of gauze tissue should be worn. The diet should be light and digestible, excess of starchy and saccharine food being avoided. When vomiting is persistent it is a good rule to administer food in small quantities shortly after the paroxysms of coughing. Overloading the stomach may aggravate the cough. A diet of milk or whey may be considered in some instances. Orange juice with glucose may be given freely. Rectal feeding is very unsatisfactory. The chest may be rubbed as a routine with some stimulating liniment.

As regards drugs, there is no specific, although quinine or euquinine in large doses have been recommended. During the catarrhal stage simple expectorant mixtures are sufficient, and later the paroxysms may be modified by such sedatives as bromide, belladonna, phenazone, bromoform, chloral, paregoric and heroin, all of which have their advocates. Perhaps belladonna in increasing doses (2 or 3 minims four-hourly cautiously increased until the pupils are widely dilated) and phenazone are the most generally useful; the latter may be given to a child in doses of 1 or 2 grains with small doses of potassium iodide and expectorants every 4 or 6 hours. Remarkable amelioration of the cough and vomiting may be effected by the use of repeated heavy doses of sodium bicarbonate, the urine being made and kept fully alkaline. It is claimed that intramuscular injections of ether in doses of 1 or 2 c.c. given every 2 days reduce the number of paroxysms. Vaccine treatment with the Bordet-Gengou bacillus is still on its trial. Its prophylactic is greater than its curative value. Attention should be paid to the condition of the nose and throat, and adenoids removed as soon as possible, since they tend to maintain the cough. During convalescence, tonics and a change to the seaside are advisable.

Complications should be treated on general lines. Obstinate vomiting needs careful feeding, and hydrochloride of cocaine in quarter-grain doses 3 times a day, or intramuscular injections of soluble phenobarbitone (gardenal sodium, luminal sodium). Gastric lavage with 0·6 per cent. solution of sodium bicarbonate may help. Asphyxial attacks may be treated by pushing forward the lower jaw and applying artificial respiration. Inhalation of CO_2 is said to be of good effect. Intubation has been practised in some very severe cases. Convulsions call for the mustard-bath or hot pack, with chloral and bromide by the rectum, or an enema of paraldehyde in olive oil. A whiff of chloroform may give relief, and sometimes lumbar puncture with free escape of cerebro-spinal fluid is effective. In broncho-pneumonia sulphonamides may prove effective.

The injection of the serum of convalescents, on the same lines as in measles and in similar doses (*q.v.*), has been advocated as a prophylactic but has proved disappointing.

Although the infectivity of the paroxysmal stage, especially of its latter part, is problematical, patients should be isolated for 5 weeks from the commencement of the whoop, provided the paroxysmal cough and whoop have ceased for a fortnight; or, better, until the infecting organism has disappeared, which may occur after 3 weeks of illness, or a week or two later. The quarantine period for non-immune contacts is 21 days. Disinfection of rooms and clothing is desirable.

CHARLES R. BOX.

BACILLARY DYSENTERY

Definition.—An acute inflammation of the colon sometimes culminating in coagulation necrosis of the mucosa, caused by specific dysentery bacilli and characterised clinically in the acute stages by fever and frequent, small, mucoid, muco-sanguineous, or muco-purulent stools associated with tenesmus and griping.

Ætiology.—No country is exempt, and natives and Europeans of all ages and both sexes are susceptible. Overcrowding, intercurrent disease, deficient dietary, and malnutrition predispose. Even in Europe Flexner or Sonne dysentery bacilli cause epidemics in military barracks, prisons and asylums, and along with Morgan's bacillus No. 1 are responsible for certain outbreaks of summer diarrhœa in children. Dysentery is prevalent in the tropics, especially during the early summer, rainy season, and autumn months, and is spread by fæcal contamination of food or water, either directly from an infected individual or indirectly by the house fly.

Dysentery occurring in epidemic form is always of bacillary origin. Boyd, who has recently reclassified the organisms causing bacillary dysentery, recognises two non-mannitol fermenting bacilli, *B. dysenteriæ* Shiga and *B. dysenteriæ* Schmitz. Of the mannitol fermenting dysentery bacilli there is *B. dysenteriæ* Sonne, which is a late lactose fermentor, and two groups of non-lactose fermenting organisms which include six types of *B. dysenteriæ* Flexner, *i.e.* I, II, III, IV, V and VI, and three types of *B. dysenteriæ* Boyd, *i.e.* I, II and III. The latter types have been found in India, and probably have a much wider geographical distribution.

Pathology.—The large intestine is the site of an acute inflammatory reaction, especially involving the sigmoid flexure, rectum, and cæcum, and in fulminating Shiga cases the mucosa may be converted into a greyish-white or greenish gangrenous membrane. Rarely the ileum is involved. Initially there is redness, injection of vessels, hæmorrhages and muco-purulent exudation; the mucosa becomes infiltrated with fibrin and in severe cases coagulation necrosis results. Localised exfoliation leads to multiple superficial ulcers, often situated transversely on the mucosal folds and separated by congested, red, œdematous mucous membrane. Generally, healing takes place without scarring and recovery is complete. Occasionally chronic dysentery occurs, and then there is considerable thickening and rigidity of the bowel wall with decrease in its lumen. Ulcers may be found, but more

frequently a chronic granular proctitis and colitis, especially involving the distal portion of the gut, result.

Symptoms.—The clinical features vary with the resistance of the patient and the type of invading organism, Sonne infections being often mild, Shiga infections severe. Flexner infections vary in severity but may be rapidly fatal in infants in whom frequent greenish fluid stools are passed containing typical cytological exudate. Toxæmia and dehydration play an important rôle in the clinical picture. Catarrhal, acute, and fulminating types are encountered, as well as entero-dysentery and chronic dysentery. The incubation period is 1 to 7 days, and in acute cases the onset is generally sudden, with fever, possibly preceded by a chill. Nausea, retching, vomiting, and headache are common. Colicky abdominal pain occurs, and there are frequent, small dysenteric stools associated with straining and tenesmus due to sphincteric spasm. The bowels may be opened from five to fifty times daily. As toxæmia increases the cheeks become flushed, the expression anxious, the temperature higher, the pulse more rapid and the tongue coated and yellow. Restlessness, mental confusion, and even delirium may ensue. Dehydration produces an increase in the nervous symptoms, associated with thirst, pinching of the features, sunken eyes, dry brown tongue, decrease in urinary secretion, increase in blood urea, collapse of the peripheral veins, and in infants depressed fontanelles. If acidosis develops the breathing becomes rapid, deep and often irregular. The severest cases may die in a state of collapse with subnormal temperature and cold, blue extremities. Mild catarrhal cases may show neither fever nor any serious indisposition, mild transient diarrhœa with brown fluid stools being the only sign. In the ordinary acute cases the stools rapidly lose their fæculent character and consist of odourless, gelatinous mucus admixed with bright red blood; later they become muco-purulent, and as recovery ensues bile-stained fæcal matter reappears. In the early stages the abdominal muscles may be held rigid, but later the contracted sigmoid may be palpated; localised pain and tenderness are infrequent owing to the absence of peritoneal involvement. The temperature, at first remittent, may become intermittent later, but with appropriate treatment it generally subsides in 1 to 2 weeks. Persistent fever means persistent infection and calls for rigorous treatment.

Entero-dysentery is associated with involvement of the terminal ileum, and if, as rarely happens, the rectum and sigmoid escape, tenesmus may be absent and the mucoid stools less typically dysenteric than usual. The onset is sudden, vomiting is severe, toxic features are marked, there is a high temperature, the mouth and tongue are covered with sordes, and a typhoidal state develops. In the worst cases watery, choleraic-like stools appear, and the patient may die early with collapse symptoms and a subnormal temperature.

Complications and Sequelæ.—Dysentery bacilli do not penetrate deeply or invade the blood stream, and local complications, such as perforation and stricture, are not met with. Joint and eye complications are attributable to dysentery toxins, and filtrates of Shiga cultures produce similar lesions when injected into animals. Acute conjunctivitis, irido-cyclitis and iritis may occur, while generalised peri-arthritis and effusions into the joints are not uncommon, especially in convalescence from Shiga infections; their duration is variable, but, though arthritis and fever may persist for several weeks or even months, permanent deformity is rare. Neuritis, terminal intussuscep-

tion, especially in children, and parotitis and broncho-pneumonia due to secondary coccal infection, may be encountered. Colonic dysfunction following acute dysentery may take the form of constipation in some cases, while in others post-dysenteric diarrhœa or looseness of the bowels due to an " irritable colon " is found : the latter is distinguished from chronic dysentery by an absence of cellular exudate and the negative sigmoidoscopic picture.

Course.—Fulminating Shiga cases may die rapidly of toxæmia and dehydration, but with appropriate treatment the temperature generally becomes normal in less than two weeks. The natural tendency in all types of dysentery is toward complete recovery, the bowel being restored to a normal condition. Rarely chronic dysentery develops.

Chronic Dysentery.—There is a history of typical acute dysentery, often inadequately treated, from which the patient has never really completely recovered. The stools remain more frequent than usual, are foul-smelling, and contain mucus, muco-pus or blood. During exacerbations fever may recur ; such patients become miserable and emaciated ; in some instances they develop anæmia, œdema of the lower limbs, and are liable to succumb from intercurrent disease. The abdomen is scaphoid, and the spastic, thickened, descending colon palpable. Dysentery bacilli are isolated with difficulty, even during exacerbations, and Cunningham was only successful in finding them in 26·7 per cent. of his Indian cases.

Diagnosis.—The clinical history and physical examination of the patient generally suggest the diagnosis, while the more acute onset, severer pyrexia, greater urgency of the bowel symptoms, and the character of the mucoid stools containing bright red blood, help to differentiate it from amœbic dysentery. Immediate microscopic examination will show an absence of *Entamœba histolytica*, a predominance of polymorphonuclear leucocytes, and frequently the presence of non-motile macrophage cells which must not be confused with amœba. Stools for culture must contain mucoid exudate, be absolutely fresh, uncontaminated by urine and antiseptic, and these, if examined in the first few days of illness, yield a high proportion of positive results. Treatment, however, should never be delayed pending cultural findings in a severe case.

Sigmoidoscopy is indispensable in the diagnosis of chronic dysentery. During the acute stages this examination is rarely indicated, and the slightest pressure of the instrument on the inflamed mucosa causes bleeding. If, however, the bowel be examined at that time uniformly diffuse reddening and hyperæmia of the mucosa associated with blood-stained mucus will be found, while in severe cases the greenish-white necrotic membrane is diagnostic. Later, as the membrane separates, shallow, serpiginous ulcers may be observed, located transversely on the mucosal folds, and surrounded by congested, red, œdematous mucous membrane. In chronic dysentery these ulcers may persist, but more commonly the mucosa, which is largely replaced by granulation tissue, shows a red, hyperæmic, granular surface, bleeding readily on instrumentation, which is rendered more difficult by the thickened, rigid, spastic condition of the bowel wall.

Prognosis.—Dysentery, particularly Shiga infection, is a serious disease which demands prompt treatment, and in some epidemics the mortality rate is very high. Infants and young children, the aged, and people who are semi-starved or suffering from intercurrent disease, do badly.

Treatment.—PROPHYLACTIC.—As the disease is spread by water and food, contaminated either directly from a patient or healthy carrier or indirectly by flies, prophylactic measures similar to those adopted in enteric fever are indicated. Unfortunately no satisfactory prophylactic vaccine is available.

CURATIVE.—Treatment is directed towards conserving the energy of the patient, resting the bowel by a low residue dietary, relieving intestinal and systemic toxæmia and dehydration. Rest in bed is essential, and if a bed pan proves too exhausting the buttocks should be well padded with tow. Special attention should be directed to the hygiene of the mouth and to preventing bed sores. *Diet*: Warm feeds (5 to 10 oz.) should be given two-hourly. Only water is permitted for the first day, followed by albumin and barley water, expressed meat juice, clear soups, and jellies. Later, sprulac, arrowroot and sago pudding are allowed. Lactose is useful. Milk is not well borne and alcohol is contra-indicated. *Aperients*: a preliminary dose of castor oil (min. 240) with tinct. opii. min. 15 is given, followed by sodium sulphate (gr. 60),every two to three hours until the stools lose their dysenteric character. Enemata of 1 per cent. saline or 1·5 per cent. sodium bicarbonate (2 pints) are also useful in eliminating toxic material. *Anti-dysenteric serum* is only of value early in the disease, and in severe Shiga infections it should be immediately injected intravenously. A potent monovalent anti-Shiga serum should be used, but the optimum dosage expressed in international units has not yet been determined. Bacteriophage treatment has been disappointing. Dehydration is treated by intravenous injection of Rogers' hypertonic saline, normal saline, or 5 per cent. dextrose in physiological saline (1 to 2 pints). Adrenaline (0·5 c.c. of 1/1000 solution) may be added in cases of collapse. *Symptomatic treatment*: griping and tenesmus may be relieved by hot fomentations, turpentine stupes, morphine suppositories, and starch and opium enemata; animal charcoal and kaolin may be useful for gaseous distension. Complications are treated as they arise.

For chronic bacillary cases treatment is often unsatisfactory. A high calorie, high vitamin, low residue diet is advisable, and autogenous streptococcal vaccines may be tried. Rectal lavage with saline, sodium bicarbonate and chiniofon (quinoxyl, yatren) (1/40), silver protein (1/500), potassium permanganate (1/5000), and eusol may prove useful. Alternatively a 5 per cent. suspension of bismuth subgallate in 4–8 oz. of olive oil may be injected daily. Iron and whole liver may be used for the anæmia, and blood transfusion is sometimes most helpful. As a last resort, appendicostomy, cæcostomy, or even ileostomy, may be advisable in intractable cases; lavage with antiseptic solutions is thus permitted, while, in addition, the last two operations rest the large bowel and so aid healing.

For *Amœbic Dysentery*, see p. 264.

CHOLERA

Definition.—A specific disease due to Koch's comma vibrio, characterised clinically by violent vomiting, painless diarrhœa with copious rice-water stools, dehydration, cramps and urinary suppression.

Ætiology.—Cholera exists endemically in certain far Eastern countries, and especially in India, where Rogers has demonstrated three main endemic

foci from which epidemics spread in the spring and summer through movements of pilgrims who acquire the disease from infected water. Deficient rainfall results in scanty and bad water supplies, and generally precedes epidemics in India. Herding of people in famine camps also favours outbreaks. Occasionally cholera has reached Europe. People of different race, sex and age are all susceptible. The disease itself is generally water-borne, and is caused by the *Vibrio comma* described by Koch (1883). Carriers, who pass vibrios in the stools, need not necessarily have had clinical cholera. Flies also disseminate the disease by contaminating food, milk, etc., with infected fæces. Cholera vibrios occur in great numbers in the rice-water stools, but disappear in over 90 per cent. of patients within 10 days. Phage is said to be absent from the stools of the most virulent cases, and present in mild and convalescent cases. It is also claimed that bacteriophage may convert virulent highly agglutinable vibrios into non-agglutinable ones.

Pathology.—After death rigor mortis sets in early, and a post-mortem rise of temperature is common; the blood is thick and tarry. The small intestines are collapsed and shrunken, the mucosa is denuded of its epithelial lining, congested, perhaps hæmorrhagic, and the lymphoid follicles enlarged. The stomach and liver are congested, and the gall-bladder distended with viscid, thick bile, difficult to expel—hence absence of bile in the intestine. The kidneys show swelling, congestion and ecchymoses, the spleen is small and shrunken, and the lungs collapsed and dry. The comma vibrio is readily isolated from the contents of the small intestine and occasionally from the urine, gall-bladder and lungs.

As a result of denudation of intestinal epithelium fluid pours out from the blood vessels into the lumen of the bowel, and cholera endotoxins are absorbed into the circulation. This toxæmia and fluid loss underlie the pathological findings and clinical picture. Diarrhœa and vomiting lead to chloride depletion, to decrease in blood volume with increased viscosity of the blood, and to tissue dehydration. Biochemical investigations show reduced blood chloride, diminished plasma alkalinity, phosphate retention and increased blood urea. A polycythæmia of 6 to 8 million red corpuscles per c.mm. and a leucocytosis of from 15,000–20,000 per c.mm. are found; hæmatocrit estimations have shown an average loss in serum of 35 per cent. in mild and 64 per cent. in severe cases. Finally the weakened heart may prove incapable of pumping the viscid blood through the damaged kidneys and anuria may result.

Symptoms.—The incubation period is 2 to 5 days. Castellani and Chalmers describe 5 clinical types. (1) *Ambulatory* cases. (2) *Choleraic diarrhœa.* (3) *Cholerine*: the patient suddenly develops severe abdominal pains, passes numerous fæculent motions, then typical rice-water stools followed by rapid recovery. (4) *Cholera sicca*: the patient becomes rapidly collapsed and dies before the typical gastro-intestinal features develop. (5) *Cholera gravis*: typical cholera, constituting 95 per cent. of the cases in most epidemics. When cholera is prevalent the only safe rule is to treat every case of diarrhœa as suspect until proved otherwise. Laboratory confirmation in all atypical cases should be sought. Three more or less well-defined stages are described. (1) *The preliminary diarrhœa*: In this stage—infrequent in Indian epidemics—colicky abdominal pain, looseness of the bowels, headache, vomiting and mental depression may be present for 24 hours.

(2) *The collapse stage*: Once diarrhœa has really started, all fæcal matter rapidly disappears, to be replaced by copious, colourless, rice-water stools containing flakes of epithelium. Watery vomiting also occurs and several quarts of fluid may be lost in a few hours. Cramps, starting in the hands and feet, now appear and soon involve the extremities. Thirst, restlessness and collapse become extreme, the skin is cold, blue and wrinkled, and the face pinched. The voice becomes husky, the respiration rapid, the temperature subnormal, the blood pressure markedly lowered (systolic 55–70 mm.), the peripheral veins depleted and collapsed and the pulse imperceptible. The urine is diminished, contains albumin and casts, and uræmia with suppression and acidosis may follow. Collapse is extreme and only prompt treatment can save the patient. (3) *Period of reaction*: With recovery, the temperature rises, the heart's action and blood pressure improve, the urine increases, diarrhœa decreases and abdominal pain disappears. In less favourable cases, especially where the collapse stage has been prolonged, the circulatory recovery may not be sufficient to restore renal function and fatal uræmia results. Or again, the improved circulation may lead to an overwhelming absorption of cholera toxin from the damaged gut with hyperpyrexia and death.

Complications and Sequelæ.—Cardiac failure in convalescence, persistent cramps, broncho-pneumonia, enteritis, nephritis and cholecystitis may require special medical treatment; parotitis and abscesses need early surgical incision. Abortion and premature delivery are not infrequent, and formerly, before dehydration could be effectively treated, sloughing of the cornea and gangrene of the toes, fingers, penis and scrotum were encountered (Rogers).

Diagnosis.—During an epidemic little difficulty arises, but in atypical and sporadic cases the diagnosis will largely depend on a positive culture. Cholera nostras of temperate climates, the choleraic forms of malaria and dysentery, ptomaine, arsenic and perchloride of mercury poisoning have all to be differentiated.

Prognosis.—The mortality rate has varied in different epidemics from 30 to 80 per cent., being most fatal at the start. Modern treatment has reduced it to about 20 per cent. Over 90 per cent. of cases admitted with a blood pressure above 70 mm. recover. Young children, pregnant women, aged and debilitated people, alcoholics and chronic nephritics do badly. A severe and prolonged collapse stage, uræmic symptoms and hyperpyrexia are unfavourable, but with modern treatment these can often be avoided.

Treatment.—PROPHYLACTIC.—During epidemics cholera vaccine is valuable, affording temporary immunity (6 months). When feasible 1,000,000 dead vibrios in 1 c.c. are inoculated, and a week later this dose is doubled. Unboiled milk and water and uncooked foods, salads and raw fruit must be avoided. Wells should be disinfected immediately an outbreak occurs. Houses should be fly-proof, food covered, and drinking vessels and eating utensils cleaned in boiling water and dried by heat. The value of cholera bacteriophage, both in prevention and treatment, is uncertain. Many different types of phage have been isolated, but no unanimity of opinion has yet been reached.

CURATIVE.—The patient is kept strictly in bed and practically starved for the first few days, but water with or without glucose and barley water are freely given. Efforts may be made to destroy cholera toxin by calcium

permanganate (grs. 2 every ½ hour for 8 doses, then half-hourly), and large doses of kaolin *per os*. The Japanese claim to have used cholera antiserum with benefit. Essentially treatment consists, as Rogers points out, in replacing fluids and salts lost from the blood by appropriate intravenous injections whenever a rise in the specific gravity of the blood above the normal 1056–1058 occurs. A blood pressure below 70 mm., especially if associated with cyanosis, restlessness, cramps and cold extremities, also necessitates transfusion. Rogers advocates two solutions: (*a*) Hypertonic saline (sodium chloride, 120 grs.; calcium chloride, 4 grs.; water, 1 pint) for reinforcing blood volume and chloride loss, and (*b*) an alkaline solution (sodium bicarbonate, 180 grs.; sodium chloride, 90 grs.; water, 1 pint) to counteract acidosis and uræmia. More recently physiological saline, 0·9 per cent., has yielded excellent results. During the *collapse* stage 1 pint of (*b*) is first given and the total quantity as estimated from the specific gravity is made up with Rogers' hypertonic saline solution. Thus a specific gravity of 1063–1064 calls for three pints, and between 1065–1070 for 4 to 6 pints, the aim being to keep the figure below 1060. Injections must be repeated as often as the specific gravity of the blood rises to or above 1063, or the blood pressure falls to 70 mm. As much as 31 pints of saline has been given in the course of 4 days, with recovery. If the rectal temperature is elevated, the temperature of the injected fluid should not exceed 80° F. (room temperature in the tropics) to avoid hyperpyrexia. In the *reaction* stage cold sponging is advisable whenever the temperature exceeds 103° F., and while the blood pressure remains below 100 mm. pituitary (posterior lobe) extract (1 c.c. t.i.d.) is useful. Threatened uræmia is treated by dry cupping, alkaline solution per rectum, and by injections of 5 to 10 per cent. dextrose intravenously. Complications are dealt with as they arise. As the patient improves farinaceous foods are allowed, but proteins and extractives must be withheld until renal function is quite normal.

LEPROSY

Definition.—Leprosy is a chronic bacillary disease of low infectivity peculiar to man, caused by the *Mycobacterium lepræ*, and associated with characteristic lesions involving the skin and mucous membranes (nodular type), and the nerves (anæsthetic type). Infection, however, may remain latent and clinical manifestations never appear.

Ætiology.—The disease has a widespread geographical distribution, occurring in Egypt, Asia, Africa, West Indies and the Pacific Islands, etc. It is not hereditary, and individuals of any age, sex and race may be attacked. Children are more susceptible than adults. The *Mycobacterium lepræ* was discovered by Hansen in 1874; it is a non-motile, acid-fast bacillus occurring in large clumps in skin lepromata, septal ulcers and nasal mucus, and has never been cultivated with certainty. The mode of spread is unknown, but intimate contact with lepers is essential; a history of attendance on lepers, of living in the same house, sleeping in the same bed, or sexual connection is frequently obtained. Only 3 per cent. of people, however, living with lepers develop the disease.

Pathology.—Leprosy bacilli spread through the lymphatics of the corium and subcutaneous tissues, producing granulomata of the skin and infection

of lymph glands; the nasal and buccal mucous membrane, the eye, larynx and internal organs, such as the liver, lungs and testicles, may be similarly involved and bacilli found. The nerves may swell, turn a reddish-grey colour, and undergo an axonal degeneration; scanty bacilli may be demonstrated in the endo- and perineurium. Paralysis, muscular atrophy and deformity follow.

Symptoms.—There are three main types of the disease—(1) nodular or cutaneous leprosy; (2) anæsthetic, neural or nerve leprosy; (3) mixed leprosy. The incubation period is uncertain, being 1 to 5 years in most cases, though occasionally persons develop it a few months after coming into an infected area. Often bacilli remain latent for years, and intercurrent disease may be necessary to precipitate clinical leprosy.

1. Nodular or Cutaneous Leprosy.—This is the low resistant type, in which there is gross infection of both skin and nerves; the neural signs are mild, since the invading organisms fail to elicit any marked response from nerve tissue (Muir). Prodromata, which are marked, include leprotic fever, rigors, sweating, progressive weakness, diarrhœa, alternating dryness and hypersecretion of the nasal mucosa and epistaxis. The first positive evidence is the primary exanthem, involving especially the face, buttocks, legs or arms, commencing as a slightly raised erythematous macule which later shows dissociation of sensation and absence of sweating; it may disappear, leaving some brownish discoloration, but soon fever recurs with a fresh eruption, and bacilli may be found in the blood. After one or two recurrences reddish-brown elastic nodules appear, often at the site of the old macular rash, and these may become more generalised. Only the dorsal surfaces of the hands and feet are affected. The face acquires a leonine aspect from the enlarged nose, lobes of the ear and pendulous cheeks. The hair is often lost, especially on the outer third of the eyebrows, the nipples become prominent, the breasts may hypertrophy, and the mucous membrane of the nose, pharynx and larynx may be affected. Leprotic nodules often involve the cornea and iris. The further history varies; the nodules may remain stationary, disappear or break down and suppurate. Ulcers may form on the eye, causing blindness, and the larynx and pharynx may be destroyed.

2. Anæsthetic Leprosy.—This is a highly resistant type, in which the infection of skin and nerves is less, yet the neural signs are more prominent since the reaction in nerve tissue is more marked (Muir). Prodromata consist of mental depression, chilliness and malaise with neuralgic pains and paræsthesias, involving the ulnar, peroneal and facial nerves. Numbness of the hands and feet, anæsthesia of ulnar distribution, and maculæ, giving rise to flat, anæsthetic patches resembling ringworm may be the first indications. These anæsthetic patches may commence as erythematous or pigmented or depigmented areas and ultimately become dry and hairless. A quiescent stage may now set in until definite nerve lesions appear. Demonstrable fusiform enlargement, especially of the ulnar and great auricular nerves may develop, and wasting of the hypothenar eminence associated with contraction of the third and fourth fingers is often seen. Muscular palsies and trophic lesions of the skin, nails and bones, including perforating ulcers, are common, and atrophies and contractures like claw hand may ensue. Necrosis or interstitial absorption of the small bones occur, and fingers and

toes may disappear. The fifth and seventh cranial nerves are sometimes attacked, and ectropion of the lower lid, followed by corneal ulceration, is common.

3. MIXED LEPROSY.—Many cases ultimately become mixed in type, the nodular and nervous features either developing together or following one another. Tuberculoid leprosy—so called owing to its histological resemblance to tuberculosis—is encountered in patients with a high resistance. The lesions consist of raised plaques or of macules with raised margins: anæsthesia is well marked, and the nerve branch supplying the area is often thickened.

Diagnosis.—Clumps of lepra bacilli which have to be distinguished from tubercle can often be demonstrated in nasal mucus, in scrapings obtained from nasal ulcers using a speculum, and in the serous exudate from granulomata of the skin. The "snip method" of removing a small piece of skin with curved scissors, especially from the lobe of the ear, and making smears from its under-surface, is valuable. Gland puncture may also reveal bacilli. In pure nerve cases they can rarely be found unless portions of the nerves be examined. The differential diagnosis includes in nodular leprosy, lupus vulgaris, skin tuberculosis, syphilis and yaws; and in the anæsthetic type, syringomyelia, Morvan's disease, progressive muscular atrophy, peripheral neuritis, cervical rib, ainhum, scleroderma, and Raynaud's disease.

Prognosis.—This is by no means good in more advanced cases, though with earlier diagnosis and modern treatment the disease may be arrested, the expectancy of life increased and cases sometimes cured. Muir states that if the patient can tolerate maximal treatment and maintain a sedimentation rate below 10 a good prognosis can generally be given. Nodular leprosy is particularly prone to such complications as tuberculosis, renal disease and pneumonia, and laryngeal and visceral involvement are serious.

Treatment.—PROPHYLACTIC.—Lepers must be excluded from acting as cooks, waiters, etc., and segregation properly and humanely carried out is best for all parties concerned. Contacts who have lived in the same houses as lepers should be bacteriologically examined every few months for at least 5 years.

CURATIVE.—As in tuberculosis, the first essential is to increase the general resistance of the patient by good food, fresh air, regulated exercise, and to eradicate intercurrent diseases such as ancylostomiasis, malaria, etc. The confidence and active co-operation of the patient are essential. According to Muir the erythrocyte-sedimentation test affords a valuable index to the patient's resistance, slow sedimentation being favourable. Only when the resistance is high, and the general state of health satisfactory, should special drugs be used with the object of clearing up lepromata, otherwise lepra reactions, with increase in the local lesions, fever and bacillæmia in nodular leprosy and agonising pain in nerve cases, may develop. Too large and too frequent treatments with special drugs are dangerous, the aim being to avoid lepra reactions and to keep the health of the patient at the highest level. Special drugs: the oils of the hydnocarpus and chaulmoogra group have been in use for centuries. Chaulmoogra oil (oleum chaulmoograe) is expressed from the fresh ripe seeds of *Hydnocarpus Kurzii* (King N.O. Bixiniæ), that of hydnocarpus from *Hydnocarpus Wightiana* and *H. anthelmintica*. The crude oil is given by the mouth in 10 minim doses t.i.d., being gradually increased to 60 to 120 mins. per day. Intramuscular injections may be given,

but penetration of a vein may lead to a fatal fat embolism. Antileprol, a mixture of the ethyl esters of the various unsaturated acids of chaulmoogra, is given in capsules, each containing 1 gram, the dosage being 1 to 3 grams daily after meals. McDonald and Dean have used weekly intramuscular injections of Moogrol (ethyl chaulmoograte), beginning with 1 c.c. and increasing by 1 c.c. every third injection up to a total of 6 c.c. Alepol (sodium hydnocarpate), 1 to 5 c.c. of a 3 per cent. solution, can be given subcutaneously or intramuscularly without pain; for intravenous injections a 1 per cent. solution is used. The latest treatment advocated by Muir consists of the intradermal injection of the skin lesions with sterilised *H. Wightiana* oil, which is heated to 55° C. before use to reduce its viscosity; the injection is made with a short guarded needle inserted at an acute angle for 2 or 3 mm. The dosage varies, according to the tolerance of the patient, from 0·5 to 5·0 c.c. once or twice a week. From 0·03 to 0·06 c.c. is injected at each puncture, and some 80 to 100 punctures are required to inject 5 c.c. Six months may be necessary to infiltrate once all the affected skin, while another disadvantage is the pain it may produce. Hydnocarpus oil injected intradermally is stated to act as a local irritant stimulating phagocytosis and possibly antibody reaction from the absorption of lepromatous material, while protein shock effects may also be so induced. Whatever its action, the dosage must be carefully graded and only given when resistance is high.

Any erythematous or raised appearances of the skin or thickened and tender nerves indicate activity of the disease, and cases should be free from *Myco. leprœ* for at least 2 years before discharge; even then it is not possible to say whether the condition is really cured or merely arrested, for leprosy is notoriously a disease of remissions.

Lepra reaction should be treated with diaphoretics such as aspirin, phenacetin, hot drinks, and calcium and alkalis in large doses; small doses of tartar emetic (0·02 to 0·04 gram every second day) and protein shock may be useful; in nerve leprosy the agonising pain may be relieved by adrenaline intramuscularly or ephedrine given orally or by infiltration of the nerve.

Potassium iodide is a dangerous drug, but Muir uses it in the late stages of treatment when the resistance is high and the case has become bacteria-free. Diathermy is of value in subacute and chronic nerve lesions. If the ulnar nerve is bound down to bone—especially at the elbow—freeing adhesions and linear incision of the sheath with or without removal of fibrous tissue may bring relief. Abscesses occurring in the ulnar or other nerves should be incised; drainage is rarely needed.

MELIOIDOSIS

Definition.—A fatal disease, resembling glanders in symptoms and pathology, caused by *Bacillus whitmori*; it has been found in Burma, British Malaya, Cochin China and Ceylon, and is primarily a disease of rodents; the mode of human infection is unknown.

Pathology.—The characteristic lesions are small caseous nodules which sometimes coalesce, forming large honeycombed abscesses in the viscera. The lungs, liver, spleen and, less commonly, the intestines and kidneys may

be implicated, while pustules and bullæ may involve the skin. *B. whitmori* is readily cultivated from these lesions as well as from the blood during the septicæmic stage, but the safety-pin-like bipolar staining organisms are scanty in smears of the pus obtained from the nodules.

Symptoms.—In severe cases the vomiting, purging and collapse may simulate cholera, and death from septicæmia may occur in 3 days; other cases may show remittent and intermittent pyrexia for weeks and months. The clinical picture varies with the organ predominantly attacked, and according to Stanton and Fletcher the clinical types may resemble: (1) plague; (2) broncho-pneumonia; (3) typhoid or malaria; (4) liver abscess; (5) infective endocarditis or general tuberculosis; (6) pyelitis.

Diagnosis.—This is always difficult clinically, and is dependent on the cultivation of the organisms from the blood, sputum, urine, cerebro-spinal fluid or material aspirated from the liver or spleen. Only 10 per cent. of cases have been diagnosed during life.

Treatment.—In man the disease is almost invariably fatal, only two cases having recovered. Autogenous vaccines are worth a trial, but neither vaccines nor anti-sera possess protective power in infected animals.

PLAGUE

Definition.—Plague is primarily a disease of rodents caused by the *Pasteurella pestis*. Transmitted to man by rat fleas, it runs a rapid course with high fever, and a marked tendency to septicæmia and tender enlargement of lymphatic glands. More rarely a pneumonic form develops.

Ætiology.—Plague may occur anywhere; it is more common in sub-tropical regions, but towards the equator tends to die out. High temperatures and a dry atmosphere or high saturation deficiency reduce its incidence in the hot weather in India by killing the flea vector. It spread from Hong-Kong to India, Egypt and Japan in 1896, and 3 years later to the Philippines and South America. People of any race, age or sex are susceptible. The plague bacillus, *Pasteurella pestis*, was isolated by Kitasato and Yersin in 1894. It is readily cultured, and is a short, Gram-negative rod showing bipolar staining. Guinea pigs and other laboratory animals are susceptible. Rat fleas, especially *Xenopsylla cheopis*, which have fed on the blood of infected rodents such as the large grey rat (*Rattus norvegicus*) and the smaller black rat (*Rattus rattus*), desert these animals after death and inoculate man by regurgitating *Past. pestis* during the act of biting and sucking blood. Epidemics in rats invariably precede human epidemics, and an extension of plague to man can be accurately foretold 2 or 3 weeks beforehand from a rising curve of infection in the rat population. Pneumonic plague, on the other hand, is intensely infectious, being directly transmitted by droplet spray infection from person to person. Doctors and nurses often acquired the disease during the Manchurian epidemic.

Pathology.—At the site of entrance, especially in resistant cases, plague bacilli may occasionally produce a primary vesicle. Generally the adjacent chain of lymph glands are acutely inflamed (primary bubo) while others are secondarily involved. Frequently bacilli enter the circulation, producing various degrees of septicæmia and in the most fulminating cases

primary buboes may be absent altogether. The toxic substances elaborated by *Past. pestis* also affect the endothelial lining of the blood vessels, giving rise to congestion and hæmorrhage in the mucous and serous membranes and skin, while the cardiac muscle shows fatty degeneration and the right heart is dilated. On section the primary bubo shows intense congestion and hæmorrhage, with periglandular, gelatinous and hæmorrhagic œdema matting adjacent glands together. More distant glands, secondarily implicated, are congested and greyish-red in colour. Bacilli are numerous in the early stages and also often occur in the spleen and blood. The liver and kidneys are congested, showing cloudy swelling and fatty change, and fibrinous thrombi may be present in the Malpighian tufts. The spleen, which is 2 or 3 times its normal size, is hyperæmic and often hæmorrhagic. The meninges are very congested and hæmorrhages may occur in the brain. Pneumonic plague starts as a broncho-pneumonia, but later may involve the entire lobe; pleural ecchymoses, congestion of the bronchial tree and involvement of the bronchial glands are characteristic.

Symptoms.—The incubation period varies from 2 to 12 days, generally being 3 to 4 days. In severer infections there is a marked tendency toward septicæmia and in the types of pestis major a sudden onset with chill or rigors, irregular high fever, nausea, vomiting, cardiac weakness and great mental prostration is characteristic. Splenomegaly and also hæmorrhagic rashes may occur, hence the ancient synonym "black death." Nine clinical types have been described.

(1) BUBONIC.—Prodromata include backache, pains in the limbs, and mental depression, but generally the onset is abrupt and the constitutional features severe. The blurred speech, reeling gait, and mental dullness may suggest alcoholic intoxication. Examination reveals fever, injected conjunctivæ, rapid soft pulse; the urine contains albumin, and the blood count shows a moderate leucocytosis. On the second or third day a tender primary bubo appears, the affected group of glands (femoral and inguinal = 70 per cent.; axillary = 20 per cent.; submaxillary and cervical=10 per cent.) rapidly swelling to the size of a hen's egg or larger. Pain is severe and suppuration generally occurs during the second week. Death usually eventuates between the third and fifth day; with recovery the symptoms gradually ameliorate, but convalescence tends to be protracted. Secondary broncho-pneumonia may occur, and the sequelæ include sepsis, carbuncles, etc.

(2) SEPTICÆMIC.—The disease is rapidly fatal; there may be splenomegaly and slight general enlargement of lymphatic glands, but no bubo. Frontal headache, fever and vomiting are characteristic, but in the severest cases there may be only a slight rise of temperature. Cutaneous petechiæ and melæna may be noted. The diagnosis is made by a positive blood culture.

(3) PNEUMONIC.—Chill and a rapid rise of temperature occur at onset, followed by headache, dizziness, pains in the limbs, clouding of consciousness, pain and tightness in the chest, with cough and expectoration of a copious, sanguineous, watery sputum teeming with plague bacilli. Dyspnœa with cyanosis, crepitations, and possibly areas of diminished resonance are found. Cardiac failure is common and death almost invariably occurs within 4 days.

(4) INTESTINAL.—A rare form, described by Wilm in the Hong-Kong

epidemic of 1896, as an intestinal disorder with vomiting, incessant purging, and liquid, offensive, bile-stained stools often mixed with blood. Buboes were absent, but pathological lesions were present in the intestine.

(5) CEREBRAL.—In this type, which may resemble cerebral malaria, the mental hebetude characteristic of ordinary bubonic plague progresses to delirium, convulsions and coma. Definite plague meningitis has also been recorded, and may run a chronic course.

(6) CELLULO-CUTANEOUS.—Carbuncles appear having a necrosed and ulcerated centre, with a hard edge surrounded by a red areola, sometimes covered with minute vesicles. The condition is distinguished from coccal carbuncle by the demonstration of *Past. pestis*.

(7) VESICULAR OR VARIOLOID.—In this form the vesicles and pustules may be so abundant as to simulate varicella. *Past. pestis* is readily isolated from the vesicles.

(8) ANGINAL OR TONSILLAR.—Cervical buboes may implicate the tonsils, or violent plague tonsillitis and pharyngitis, with secondary cervical adenitis, may arise from killing vermin with the teeth—a habit of Indians in Ecuador.

(9) ABORTIVE OR AMBULATORY (*Pestis minor*).—Such cases are common in all epidemics: buboes develop and may suppurate or be absorbed without serious indisposition or fever, or the lymph glands may simply swell and become painful, associated with transient headache.

Complications.—Acute bubonic cases may develop plague septicæmia or pneumonia with fatal results, or after the fever has disappeared the local buboes may become indolent and take many weeks to heal. Broncho-pneumonia and septic complications such as subcutaneous abscesses, cellulitis, adenitis and parotitis sometimes ensue.

Diagnosis.—Bubonic plague early in an epidemic may need to be differentiated from climatic bubo, chancroid or syphilitic buboes, rat-bite fever, and possibly tularæmia. Gland puncture reveals bipolar bacilli on culture or in smears, the crucial test being transmission of plague to the white rat by smearing infective material on its skin. In pneumonic plague herpes is absent and the sputum is sanguinolent and watery, not viscid and rusty as in pneumonia: furthermore it is teeming with plague bacilli. Septicæmic plague is diagnosable only by positive hæmo-culture.

Prognosis.—Pneumonic and pure septicæmic plague are practically always fatal. In bubonic plague the mortality rate is much higher in natives (75–80 per cent.) than in Europeans (25–30 per cent.), and axillary buboes are less favourable than inguinal ones. Positive hæmo-culture is of serious significance, and Liston showed that where the bacilli exceed 40 per 1 c.c. of blood, death almost invariably resulted.

Treatment.—PROPHYLACTIC.—This consists essentially in the destruction of rats and fleas, in preventing their coming into contact with man, and in increasing individual resistance by Haffkine's prophylactic vaccine, which gives an immunity lasting 6 to 12 months or more. The building of rat-proof houses and grain stores, rat destruction by poisoning and trapping, fumigation of ships with sulphur dioxide and hydrocyanic gas, and evacuation of infected villages and houses during epidemics are all important measures in controlling the spread of plague.

CURATIVE.—Bed rest, liquid diet, and careful nursing are essential. Specific treatment, with large doses of antiplague serum intravenously during the

first two days has been advocated (Yersin and Lustig), and recently workers at the Haffkine Institute, Bombay, have produced a potent antiplague serum from horses which is yielding promising results. It is given in doses of 20 c.c., and repeated till a total of 60–160 c.c. are administered. Treatment with sulphapyridine (M. and B. 693) and sulphathiazole (M. and B. 760) is under trial; preliminary experiments on animals suggest they may be valuable. The buboes should be treated by hot fomentations, kaolin poultice, or belladonna and glycerin applications with early incision when suppuration occurs. Morphine may be necessary for the pain. Stimulants and cardiac tonics should be used early, and intravenous injections of dextrose may be of value.

UNDULANT FEVER OR BRUCELLIASIS

Synonyms.—Malta or Mediterranean Fever; Abortus Fever.

Definition.—An endemic or epidemic disease characterised clinically by prolonged fever with a tendency to long wavy relapses, splenomegaly, transient painful swellings of the joints, neuralgia and secondary anæmia. In Malta *Brucella melitensis*, conveyed in goat's milk, proved the causative organism, but indistinguishable diseases of widespread geographical distribution may be caused by the bovine and porcine strains of *Br. abortus*.

Ætiology.—Undulant fever of caprine origin is endemic in the Mediterranean basin, in the Red Sea littoral, in South and West Africa, and in the goat-raising regions of Texas, Arizona and New Mexico. In the East it is found in India, Assam, Hong-Kong and China; in the West in the West Indies, Porto Rico, and northern countries of South America. The indigen population sometimes appears to have a certain immunity to the dis ous as in Malta, where the Maltese, prior to the boiling of goats' milk b ease, garrison, were less affected than English soldiers and sailors. All agev the both sexes appear equally susceptible, and in Malta, at least, the ds and proved more prevalent in the dry summer months. isease

Bruce, in 1886, isolated *Br. melitensis* from cases of undulant fever and experimentally reproduced the disease in monkeys. Eighteen years later it was proved that infection was conveyed in goats' milk. The organism causes a bacteriæmia and may be isolated from the blood, bile, fæces, urine and milk. Primarily it is a disease of goats which, while themselves showing few symptoms, may yield a good quality milk containing large numbers of *Br. melitensis*. Other varieties include the bovine and porcine strains of *Br. abortus*, and are only distinguishable by agglutinin-absorption tests. The latter organism, which infects the chorionic cells, causes contagious abortion of swine and cattle, and produces a disease in man indistinguishable from undulant fever; it has been reported from the United States, Europe, Southern Rhodesia, South Africa, etc., is of bovine or porcine origin, and is contracted from cow's milk or contact with carcases, infected animals or their excreta.

Pathology.—The disease is essentially a bacteriæmia and organisms may be isolated from the blood, spleen and lymph glands at autopsy. The spleen is constantly enlarged, averaging about 20 ounces in weight. Sometimes the mesenteric glands appear swollen, but there is no ulceration of

Peyer's patches. The liver, kidneys and pulmonary bases show congestion, and occasionally broncho-pneumonia and glomerular nephritis are found.

Symptoms.—The incubation period is about 14 days, but may last a longer or shorter period. Monkeys develop fever 5 days after subcutaneous inoculation, and 15 days after ingestion of infected material. Five clinical varieties are recognised by Hughes: (1) Ambulatory; (2) Undulant; (3) Intermittent; (4) Continuous; (5) Malignant.

(1) AMBULATORY OR MILD.—In some cases the symptoms are so slight that infected persons go on with their work as usual; in others there are slight fever and minor symptoms which disappear rapidly, serum tests alone indicating infection. Out of 525 dock hands examined by Shaw in Malta, 79 gave positive agglutinin reactions, whilst 9 out of 22 of those specially tested showed the organism either in the blood or urine or both. Such cases constitute human carriers.

(2) UNDULANT OR ORDINARY.—The onset is generally insidious like typhoid, and the symptoms often resemble those seen in other fevers, but the temperature chart is characteristic. Bouts of fever lasting 2 or 3 weeks alternate with periods of remission, so producing the typical undulant fever chart. Illness in the ordinary case lasts 3 to 4 months, the extremes being 3 weeks to several years. The fever is often associated with profuse sweating, lassitude, secondary anæmia, debility and transient painful swelling of the joints resembling rheumatic fever, but not responding to salicylates. Enlargement and tenderness of the spleen and liver also occur, and neuralgic pains, especially involving the intercostal and sciatic nerve, are common. The tongue has a central white fur, and anorexia, flatulence, abdominal discomfort and constipation are often troublesome features. The leucocyte count is generally normal, but there is a relative lymphocytosis; the urine may contain albumin. After running a more or less chronic course, the remissions become more prolonged, the febrile exacerbations less high, and recovery gradually ensues. No patient should be regarded as convalescent, however, until the temperature and pulse have been normal for at least a fortnight and all other symptoms have disappeared. Neuritis, debility and anæmia may persist for a considerable period.

(3) INTERMITTENT TYPE.—There is a swinging temperature resembling benign tertian malaria, a normal morning temperature being succeeded by a sudden afternoon rise to 105° F. or higher, accompanied by chilliness and a definite rigor; by evening the temperature falls again with drenching sweats. The condition is differentiated from malaria by the absence of parasites.

(4) CONTINUOUS TYPE.—Here there is continuous fever for a period of from one to three months.

(5) MALIGNANT TYPE.—The patient is attacked suddenly with high fever, severe generalised pains, diarrhœa and vomiting. Broncho-pneumonia, cardiac weakness and a typhoidal state frequently develop, while hyperpyrexia may percede death.

Complications.—These include bronchitis, broncho-pneumonia, neuritis, parotitis, orchitis in the male and mastitis in the female. Purpura and suppurative osteitis have also been described. Menorrhagia, abortion or premature labour may also result.

Diagnosis.—The differential diagnosis includes the enteric fevers, acute rheumatism, malaria, kala, azar, tuberculosis, subacute bacterial endocarditis, thoracic lymphadenoma associated with the Pel-Ebstein syndrome, amœbic abscess of the liver and occult pyogenic infections. Macroscopic agglutination reactions are of great diagnostic value after the first fortnight of fever, the serum being tested in an ascending series of dilutions (1/25–1/1000) against dead Brucella emulsions. Absorption of agglutinin may be necessary to distinguish infections with *Br. melitensis* and *Br. abortus* respectively. Blood culture in liver infusion broth is often positive for *Br. melitensis*, and the period of examination should extend over a fortnight before reporting the result as negative. *Br. abortus* must be grown in an atmosphere of 10 per cent. carbon dioxide or, better still, 1 c.c. of suspected blood is inoculated into the peritoneal cavity of a guinea-pig, culture from the peritoneal cavity being generally positive in about a week and from the spleen at a later date. Burnet's intradermal test is frequently positive; it is characterised by the development of localised redness and œdema some six hours after inoculation, the reaction lasting 1 to 2 days.

Prognosis.—Mortality rates of from 2 to 9 per cent. have been recorded. Death generally results in malignant cases during the first three weeks of fever. At any time, however, fatal recrudescence may occur, a typhoidal state, broncho-pneumonia, cardiac failure and hyperpyrexia being grave signs. Chronic cases may present great debility, emaciation, anæmia and neuritis.

Treatment.—PROPHYLACTIC.—Laboratory workers should be very careful in handling Brucella cultures for, as in tularæmia, infection is easily acquired. Adequate boiling of goats' milk renders it safe, but its prohibition in endemic centres and the destruction of infected animals are more effective. Cream and cheese may also convey infection. In the case of *B. abortus* the disease may arise from cows' milk or the carcasses or excreta of bovines and porcines.

CURATIVE.—Careful nursing and a nourishing dietary which should include milk puddings, eggs, fish, fruit juice, yeast and other vitamin-containing foods, are desirable. Cool sponging is indicated whenever the temperature exceeds 103° F. Specific therapy is still under trial. Anti-undulant fever serum has been favourably reported on, as has also immune-transfusion in the form of a direct transfusion of 500 c.c. of compatible blood from a recovered case. Autogenous vaccines are of doubtful value. A course of sulphapyridine terminates the fever in some cases, but recurrences are not infrequent. Cures are recorded following T.A.B. vaccine intravenously, commencing with 50 millions and working up to 250 millions, injections being given every fourth day. Various symptoms and complications, such as sleeplessness, headache, arthritis and orchitis, should be treated on general principles as they arise.

BARTONELLOSIS

Two clinical forms of Bartonellosis are now recognised, namely, (1) Oroya fever, in which there is a generalised infection with *Bartonella bacilliformis*; and (2) Verruga peruviana, in which there are local lesions in the skin.

Oroya Fever

Synonyms.—La Maladie de Carrion; Carrion's Disease; Generalised Bartonellosis.

Definition.—An acute infectious disease caused by *Bartonella bacilliformis*, characterised by irregular remittent fever, headache, tenderness over the bones and a severe anæmia of megalocytic type; fatalities are frequent.

Ætiology.—Oroya fever is limited to valleys on the western slopes of the Peruvian Andes between 1800 and 9000 feet. Both sexes are susceptible and children may be attacked. Carrion (1885) inoculated himself from a verruga nodule and died of Oroya fever a month later. Barton (1909) found rod-like organisms in the red cells in this disease; they were also numerous in the endothelial cells of the lymphatic glands. Noguchi (1926) cultured the organism and subsequently experimentally infected monkeys, the susceptible animals developing a condition like Oroya fever, the most resistant ones, lesions of verruga peruviana only. The disease is most prevalent from January to April, when insect life is most plentiful. Transmission is probably by sand-flies of the species *Phlebotomus noguchi* and *P. verrucarum*.

Pathology.—The skin is yellow, the lymphatic glands, liver and spleen are enlarged, and the long bones filled with red marrow. The heart shows fatty degeneration, the liver zonal necrosis, while endothelial cell hyperplasia is common. Petechial hæmorrhages occur in the skin and serous sacs.

Symptoms.—The incubation period is about 3 weeks, the onset being fairly rapid with malaise and headache. Irregular remittent fever somewhat similar to paratyphoid, pains in the joints and tenderness over the long bones are characteristic, while the spleen and lymph glands may be enlarged. Grave anæmia of hæmolytic megalocytic type rapidly develops, in the severe cases the red cells falling as low as 1,000,000 per c.mm. The colour index often exceeds 1·0, and polychromatophilia, poikilocytosis, normoblasts, erythroblasts and even megaloblasts are evident in blood smears. The indirect van den Bergh reaction shows hyperbilirubinæmia. Unlike pernicious anæmia it presents a marked leucocytosis with a shift to the left, myelocytes and meta-myelocytes being present, lymphoblasts, Turck cells and the Reider type of lymphocyte are also common (Monjl and Weiss). Œdema of the legs, cardiac murmurs and retinal hæmorrhages may occur, while hæmorrhagic manifestations of the skin and gums, and coma with subnormal temperature are met with in severe cases. The acute stage of the illness lasts some two weeks, and may either terminate fatally or pass on into the eruptive stage with chilblain-like nodules, *i.e.* verruga peruviana.

Diagnosis.—The rod-shaped bacilli are only demonstrable in the blood smears in severe infections, and Noguchi preferred culturing *Bartonella bacilliformis* for this reason. The limited geographical distribution and the rapid onset of a febrile megalocytic anæmia are important features in diagnosis, but malaria, paratyphoid, rheumatic fever and tuberculosis may need to be differentiated.

Prognosis.—A great variation in the intensity of the infection in different patients is noted. Mild cases recover, but in well-established cases of Oroya fever the mortality rate is from 30 to 40 per cent.

Treatment.—Sand-fly bites should be avoided by sleeping under netting with a 22-inch mesh.

Specific treatment with an arseno-antimony compound, Sdt. 386B, is now available. This drug, introduced by Kikuth, is given intravenously in a dosage of 0·1–0·3 g. on three or more occasions. Bartonella rapidly disappears from the blood, and the anæmia improves. In some cases a total of 5·7 g. was tolerated without untoward effect.

Verruga Peruviana

Synonym.—Localised Bartonellosis.

Definition.—This is the eruptive stage of Oroya fever in which host resistance is high; miliary and nodular lesions may result which show a marked tendency to ulceration and hæmorrhage.

Ætiology.—The disease may be transmitted by local inoculation from monkey to monkey, and Noguchi has successfully cultured *Bartonella bacilliformis* from the local lesions. Only specially susceptible animals show the systemic manifestations associated with Oroya fever.

Pathology.—The pathological lesion is a very vascular, infective granuloma showing a marked tendency to ulceration and hæmorrhage. The endothelial lining of both lymphatics and capillaries proliferates. Plasma cells and fibroblasts appear in an œdematous, delicate reticulum containing numerous blood vessels around which angioblasts undergoing mitosis may accumulate; the late appearances may simulate fibrosarcoma.

Symptoms.—The incubation period varies from 2 to 5 weeks, when rheumatic-like pains develop in the limbs and joints associated with moderate fever which generally subsides within a few days. Subsequently an eruption of tubercles and nodules occurs. The *miliary type* of lesion commences as a red macule which gradually develops into a flat or pedunculated wart-like structure about the size of a small pea; the lesions occur most frequently on the face and extensor surfaces of the arms and legs, but similar ones may involve the mucous membranes of the eyes, nose, pharynx and larynx, giving rise to cough, hoarseness, epistaxis and even sudden death. The *nodular type* of lesion may attain the size of a chestnut; these tumours often ulcerate, forming large, bleeding, fungating masses situated in the flexures of the joints and appearing in successive crops. Little difficulty is experienced in diagnosis and fatal results are rare, though the disease may last 2 to 3 months.

Treatment.—When the nodules ulcerate they should be dressed with antiseptics, and if they undergo necrosis or hæmorrhage severely they may be excised. Intravenous injections of Sdt. 386B, should be administered.

G. Carmichael Low.
N. Hamilton Fairley.

PNEUMOCOCCUS INFECTIONS

Lobar Pneumonia (see p. 1225).
Broncho-Pneumonia (see p. 1237).

BOTULISM (see p. 401).

B. DISEASES CERTAINLY, OR ALMOST CERTAINLY, OR POSSIBLY DUE TO FILTRABLE VIRUSES

INTRODUCTION (see pp. 8–10)

THE COMMON COLD

Synonyms.—Acute Coryza ; Cold in the Head.

Definition.—An inflammatory process affecting the upper respiratory tract in which the air sinuses and tubes in connection therewith may also be involved.

Ætiology.—Colds are very common in the damp variable weather of the autumn, winter and spring in temperate climates. Susceptibility to infection tends to diminish with age, yet shows great variation amongst different individuals and even in the same individual under different conditions. Both sporadic and epidemic forms are met with, and infection may spread through a community with great rapidity. Amongst important predisposing causes are frequent changes of atmosphere, as by entering and leaving hot, stuffy, ill-ventilated, crowded rooms ; the presence of a focus of chronic infection in the upper respiratory tract, *e.g.* adenoids, infected tonsils and chronic cranial sinusitis ; structural anomalies which interfere with free ventilation of the nose, *e.g.* deflected septum, and polypi ; and chronic irritation of the mucosa by smoke, dust or chemicals in sprays, etc. Very little is known of the exact pathogenesis, but there would appear to be at least two factors. A filtrable virus seems to be primarily responsible, aided by other organisms which set up a secondary infection, either severally or together. The virus is air borne, and spread is by droplets expelled from the nose and naso-pharynx by sneezing, speaking, coughing, etc. The portal of entry is the nasal or pharyngeal mucosa and, possibly, the conjunctival sac ; infection develops locally via the submucous lymphatics to neighbouring areas, all or one of which may bear the brunt of the inflammation, the resulting clinical picture being an acute rhinitis, sinusitis, pharyngitis, laryngitis or tracheitis. The secondary infection may be by organisms already present as normal inhabitants on the inflamed mucosa, *e.g.* pneumococcus, streptococcus viridans or micrococcus catarrhalis ; or pathogenic bacteria generally conveyed by droplet, *e.g.* hæmophilus influenzæ, streptococcus hæmolyticus, staphylococcus pyogenes. It is impossible to be dogmatic as to which signs and symptoms are consequent on the primary or the secondary infection respectively ; it may be that variations in symptoms and the degree of the accompanying toxæmia in different individuals in the same epidemic are due to variations in the secondary infection. Local infection induces vasodilatation and œdema in the spongy submucous tissues and engorgement of the mucosa, with outpouring of mucoid secretion, which soon becomes muco-purulent in character. The swelling may cause obstruction to the outlet of an air cell, particularly in the ethmoid or sphenoid, or to the duct of the frontal sinus ; absorption of air behind such an obstruction may be responsible for a " vacuum headache," or if

the Eustachian tube is involved to deafness and vertigo; when an air sinus is implicated in the inflammatory process and its opening is obstructed, local pain and "distension headache" are prone to follow.

Clinical Features.—The incubation period varies considerably but is usually between 12 and 48 hours; it would appear to be shortened by chilling of the body or exposure to wet. The first symptom is often a stuffiness in the nose, which is soon accompanied by a pricking sensation and sneezing; a profuse discharge, at first mucoid but which within 12 hours becomes mucopurulent, may lead to excoriation of the anterior nares. Taste and smell are impaired. Pharyngitis and tonsillitis are common, and there may be some follicular exudate on the tonsils. If the inflammation spreads to the larynx, the voice becomes hoarse, and a tracheitis will induce a painful irritating cough which may be paroxysmal, especially at night, and retrosternal soreness. Symptoms are confined in the main to the respiratory tract. Constitutional disturbance is usually slight, though in some epidemics the temperature may reach 102° F. for 48 hours. In such cases pain in the back and limbs, and a sense of exhaustion may be experienced. The catarrh slowly subsides, and the patient is usually free from symptoms in from 4 to 7 days. Immunity is shortlived.

Complications and Sequelæ.—When these arise, they are consequent on the secondary infection. Some suffusion of the conjunctivæ is common. Herpes around the nostrils and on the lips may be extensive during the acute stage. Suppuration in the accessory sinuses or an acute otitis media may occur. Bronchitis, especially in those patients liable to that disease, may flare up and persist for a long time. Broncho-pneumonia is the most serious complication, and not a few cases of pulmonary tuberculosis follow a "neglected cold."

Treatment.—PROPHYLACTIC.—The avoidance of infection in the community is well-nigh impossible, but much may be done by efficient ventilation and fresh air. When knowingly exposed to infection, it is a good rule to keep the mouth shut as far as possible, and on leaving some individuals have faith in taking a pinch of snuff into each nostril. A full dose of quinine is certainly sometimes of value when symptoms threaten: *e.g.* liq. quininæ ammon., min. 120, tinct. opii camph., min. 60, spir. ammon. aromat., min. 60, in half a tumbler of water; which may be repeated in 4 hours if necessary. Stock anti-catarrh vaccine undoubtedly has a prophylactic value in some seasons; though the results of inoculation may appear encouraging through one winter, they may be disappointing the next, or *vice versa*. If inoculation is to be employed in this country it is recommended that four doses ($\frac{1}{4}$, $\frac{1}{2}$, $\frac{3}{4}$ and 1 c.c.) of the St. Mary's Hospital vaccine should be given subcutaneously at weekly intervals during September, followed by 0·5 c.c. once a month throughout the winter. In those patients in whom recrudescence, relapse or repeated re-infection appear to be associated with a chronic inflammatory focus in the upper respiratory tract, that focus should be eliminated by surgical means; in these conditions vaccine therapy is not included in the first line of attack.

Discharge from the nose and throat during the first 48 hours is highly infective; handkerchiefs, pillow-cases and other materials likely to be soiled should be soaked in disinfectant.

GENERAL.—Though isolation is, in theory, admirable both for the pro-

tection of the patient and for limiting the spread of the disease, in practice it can be enforced but seldom. If there is much constitutional disturbance, if the patient suffers from the frailty of old age, or active pulmonary disease, or diabetes mellitus, or subacute nephritis, or heart failure, the common cold must be taken seriously and the patient confined to bed until free from symptoms for 48 hours.

Treatment is entirely symptomatic. In the early stage stuffiness of the nose and throat may be relieved by inhalation for 10 minutes from a jug containing boiling water ¾ pint and cold water ¼ pint (or a pint of boiling water allowed to stand for 7 minutes), tr. benzoini co., min. 60, and menthol grs. 2. This should not be done just before the patient goes out of doors. A solution of 2 per cent. silver nitrate or colloidal silver may be used as a spray. Amphetamine (benzedrine) and ephedrine may give temporary relief to symptoms by shrinking the congested nasal mucosa ; they should not be used to excess. Hoarseness of voice and the retrosternal soreness of tracheitis may be helped by local counter-irritation ; a piece of active mustard plaster the size of half a crown applied to either side over the thyroid cartilage for 20 minutes, or heat in some form, may serve to restore a lost voice. Diaphoresis is encouraged by aspirin, Dover's powder and a hot drink at bedtime. Drugs of the sulphonamide group should not be administered as a routine ; only when a pyogenic complication develops should the appropriate drug be given, and in full dose.

HORDER.
A. E. GOW.

MEASLES

Symptoms.—Morbilli.

Definition.—A specific infectious fever, characterised by catarrh of the respiratory passages, the presence of Koplik's spots on the mucous membrane of the cheeks, a distinctive papular eruption on the skin and a special liability to pulmonary complications.

Ætiology.—Measles is of universal distribution. Both sexes are equally liable. It is extremely infectious, and there is little evidence that natural immunity ever occurs, but a temporary active immunity may be acquired during epidemics without an overt attack. When introduced among unprotected communities it spreads with appalling rapidity to persons of all ages, and causes many deaths. More than half the attacks of measles occur in the first 5 years of life, but there is a temporary passive immunity of the newborn child, possibly due to maternal immunity, gradually waning after the first 3 months, and infants under 6 months rarely take the disease. Early incidence is most pronounced in poor and crowded communities ; among the middle classes it is delayed to school age or later. Seven-eighths of all cases occur in children under 10. When measles occurs in a pregnant woman abortion or premature delivery often results, and the infant may also exhibit the rash, usually in the same stage as the mother (*Congenital Measles*). The disease is endemic in large cities, and cases are numerous from December to March, again increasing in May and June. Epidemics recur every two or three years, and every tenth year an especial incidence is said to be noticeable.

The virus resides in the secretions of the respiratory tract and direct infection is the rule, very intimate contact is not essential. Infectivity may be present 5 days before the appearance of the rash, possibly longer, and then rapidly declines. Only on rare occasions do intermediaries convey the infection, and rooms and fomites do not retain it for more than a short period. There is no evidence incriminating water, milk or other articles of food.

Pathology.—The causal agent is a filter-passer, but has not been positively identified. A small diplococcus, which forms green colonies on blood-agar, isolated by Ruth Tunnicliff, was at one time suspect. The disease has been reproduced in man and monkeys by inoculation with blood, bronchial secretions or tears. The most striking visceral change is broncho-pneumonia. Secondary infections chiefly with hæmolytic streptococci are common. Catarrhal or ulcerative laryngitis may be found. The bronchial glands are inflamed and the lymphoid aggregations of the small intestine may be very conspicuous. Active tuberculous lesions are not uncommon.

Symptoms.—The rash appears on the fourteenth day of infection, sometimes a day earlier or a day later, but it may be delayed in patients who have been injected with the serum of convalescents. This interval is more constant than that which elapses between infection and the first catarrhal symptoms. Reckoning to the onset of fever and catarrh 9 or 10 days usually pass. In some cases the incubation period is slightly febrile and a transitory feverish catarrh with fleeting rash has occurred even a few hours after exposure to infection (Goodall's *illness of infection*). A polynuclear leucocytosis is characteristic of the incubation stage. Slight enlargement of the cervical, inguinal, axillary and other glands may precede the eruption. Koplik's spots on the buccal mucosa may precede the rash by 2 or 3, sometimes by 5, days. Prodromal rashes are not uncommon ; a precocious macular eruption is the commonest, but a punctate scarlatiniform erythema is the most important, since it simulates scarlet fever. It is apt to appear on the second day of invasion. An urticarial rash may also occur.

Invasion.—This is characterised by catarrh of the respiratory tract, fever and the outbreak in the mouth of Koplik's spots. It culminates in the appearance of the skin eruption. Sneezing, irritating cough, watery eyes and conjunctival injection are the early signs. There is chilliness, and the temperature may reach 103° F. by the end of the first day. Photophobia and sharp diarrhœa may occur. In the early stage of invasion slight blotchiness of the skin about the mouth and nose may be evident. The cutaneous rash usually appears on the fourth day, and a deceptive remission of symptoms and fall of temperature sometimes occur just before its outbreak. In some instances laryngeal symptoms are marked during the invasive stage, and give rise to suspicion of diphtheria ; exceptionally, catarrh is insignificant, and an attack of severe simple tonsillitis is simulated.

Koplik's spots are of great importance in the early diagnosis, since they are recognisable some 72 hours before the rash, with the appearance of which they rapidly disappear. They are minute superficial specks of a bluish-white tinge, and show a tendency to aggregate into small clusters or granular patches. Their common site is on the inner aspects of the cheeks, opposite the line of apposition of the molar teeth ; but they may be more widely scattered over the buccal mucous membrane, on the inner surfaces of the

lips, and also on the conjunctivæ. Sometimes they are surrounded by a bright red areola. In addition, the mucous membrane of the mouth becomes congested and dusky, and a decided blotchy enanthema may here precede the cutaneous rash.

Period of eruption.—With the approach of the rash the symptoms become aggravated. The temperature (Fig. 3) rises sharply, it may be to 104° or 105° F. The hurried respiration and slight cyanosis may suggest broncho-pneumonia. Diarrhœa may persist, and sometimes urinary irritation is noticeable. The nasal and conjunctival discharges become more purulent. The eruption makes its first appearance about the brow, behind and below the ears, and in the circumoral region. Rarely, it appears first on other parts, such as the buttocks, thighs or wrists. It spreads rapidly, sometimes after a short hesitation, over the face, neck, trunk and extremities, and is usually fully out on the fifth or sixth day of the attack. Small brownish macules are the first elements, but they soon become papular, and show a tendency to fuse into groups with irregular sinuous outlines. Profuse eruptions may become confluent on the face, neck, back and extensor aspects of the limbs. Petechial hæmorrhages in the rash are not uncommon. The skin is usually moist and exhales a peculiar musty smell. Rarely, it is hot and dry. Itching or burning sensations may accompany the rash. The eruption fades in the order of its appearance, and usually disappears in the course of two or three days; but brownish staining may persist for some time, particularly on the back. A fine branny desquamation speedily follows. At its first appearance, the rash may fail for a time to spread; retrocession is also sometimes observed. A badly developed and retarded rash is characteristic of some severe attacks, and in asphyxial states the rash may be quite cyanotic. As the rash develops, the temperature continues to rise, reaching its maximum with the climax of the attack in from 24 to 48 hours. When the rash begins to fade, the temperature falls more or less abruptly by a crisis which is rather prolonged. The pulse-rate is increased in proportion to the fever, but the respiration is disproportionately rapid. The catarrhal symptoms also reach their greatest intensity at the height of the eruption. Headache, slight delirium, insomnia

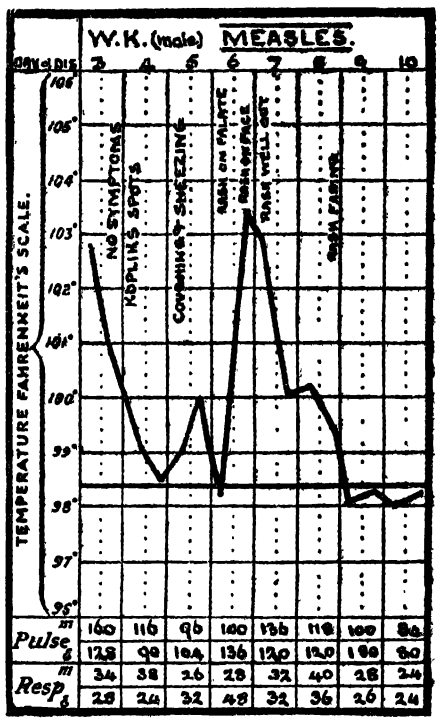


FIG. 3.—Measles. Showing the remission in invasion stage and the abrupt termination.

and a feeling of intense wretchedness are characteristic of this period. The throat may be sore, and the glands at the angle of the jaw tender. The tongue at first is heavily coated, but before long red papillæ are evident, and when peeling is complete a clean, red papillated tongue, very like that of scarlet fever, may often be seen. With the crisis rapid amelioration of all symptoms should occur.

The blood now shows a leucopenia with a high percentage of large lymphocytes. All complications induce a polynuclear leucocytosis.

The urine presents the ordinary febrile characters. Transitory albuminuria may occur. Ehrlich's diazo-reaction is nearly always present, and is most marked when the temperature begins to fall. An acetone reaction is obtained in most cases.

VARIETIES.—Attacks may be mild or severe. Some of the mildest attacks are abortive, the rash failing to appear, and only Koplik's spots giving a clue to the disease. Severe attacks are classified as toxic, pulmonary and hæmorrhagic. The *toxic type* includes those cases in which the patient may succumb during the eruptive period without evident complication. Ill-defined rashes, high fever, muscular tremor, delirium, dyspnœa and circulatory failure are characteristic features. In the *pulmonary type* the infection falls with especial stress upon the lungs. The temperature is high, the respirations rapid and hissing, and the condition suggestive of slow asphyxia. Consolidation of the lungs cannot be detected, but rhonchi are present everywhere, accompanied by fine crepitations. A stuporose condition may precede death or terminal convulsions may arise. The true *hæmorrhagic type* of measles is rare. The patient may bleed from the mucous membranes with hæmorrhages into the skin and subcutaneous tissues. Recovery takes place in some instances. Hæmorrhage *into* the rash has not the same grave significance.

Complications.—These are numerous, but those involving the respiratory tract, the middle ear and the bowel are the most important.

Laryngitis may accompany the onset, develop during the eruption, or appear early in convalescence. Arising in the invasive stage it may simulate laryngeal diphtheria. Laryngitis is more common during the eruptive period, and may persist for some days—it may be complicated by laryngeal ulceration, sometimes by œdema of the glottis; but necrosis of the laryngeal cartilages and abscess formation are rare. Severe laryngitis developing during convalescence should always arouse suspicion of diphtheria.

Bronchitis is often present during the eruptive stage, but broncho-pneumonia is a much more serious complication, and is a common cause of death. Its incidence is favoured by climatic conditions, overcrowding and contact with similar cases. It is generally attributed to secondary pneumococcal or streptococcal infection; but, especially when occurring early in the infection, it is rightly regarded as due to measles itself. This early broncho-pneumonia is associated with a high temperature and considerable toxæmia. It is suffocative in type, and the lung signs are rather those of capillary bronchitis than of consolidation. During the eruptive stage, broncho-pneumonia should be suspected if the temperature fails to fall with subsidence of the rash, and the pulse remains quick and respiration rapid. It may clear up in a week or ten days, but often persists for weeks, or relapses. The temperature chart often shows remarkable daily remissions and exacerbations which may lead to suspicions of tuberculosis. The mortality is serious, since

one-third or one-half of the children attacked are said to die. Feeble infants succumb rapidly, and in those who recover convalescence is protracted. True lobar pneumonia is uncommon. Massive collapse of the lower lobe of a lung has been described; its onset is sudden with intense dyspnœa, cyanosis and cardiac failure. It is distinguished from pneumonia by the feebleness of the breath sounds, upward displacement of the diaphragm and dislocation of the heart towards the affected side. Rarely mediastinal and subcutaneous emphysema have occurred. Effusions into the pleura have been noticed in some epidemics, and empyema may follow. Fibrosis of the lung and bronchiectasis may originate in the broncho-pneumonia of measles.

Pericarditis or endocarditis sometimes develops; and may be associated with chorea. Arthritis with rheumatic pains is sometimes pronounced.

Blepharitis and phlyctenular ulcers of the cornea are common sequels. In cachectic children intense conjunctivitis may arise and lead to ulceration and even perforation of the cornea with destruction of the eye.

The catarrhal stomatitis of measles occasionally persists and becomes ulcerative. A gangrenous form (noma) may attack the lips, cheeks, vulva or other parts. A discoloured patch appears on the mucous membrane and quickly ulcerates, extending both in depth and breadth. A zone of inflammatory induration surrounds the lesion, and a fetid odour is given off. Noma is terribly destructive both to soft parts and bone, and is very fatal. It occurs in debilitated and feeble children, and is attributed to secondary infection. Vincent's spirilla and fusiform bacilli are often present. It is said to be sometimes due to the Klebs-Loeffler bacillus.

Otitis media is frequent. It may be catarrhal or suppurative; the suppurative form is more common in children, and is responsible for much chronic ear disease. Mastoid inflammation may occur, and deafness may result.

Cutaneous eruptions of eczematous, impetiginous or pustular type are common. Sometimes they are widespread, and very resistant to treatment.

Enlargement and suppuration of the cervical glands, entero-colitis and ascites are rarer complications.

Encephalo-myelitis may occur towards the end of the first week, with a course which is either rapidly fatal or tends to spontaneous recovery. Meningeal symptoms or convulsions may signalise its onset. Hemiplegia, aphasia, coma or mental defect are rare. Myelitis, sometimes of the ascending form, has been known to occur; also symptoms suggestive of disseminate sclerosis. Sometimes the cranial nerves are attacked. Paralysis of extra-ocular muscles, papillœdema and optic atrophy have all been encountered. The peroneal type of muscular atrophy may follow measles.

Measles especially favours the development of tuberculosis hitherto latent in the bronchial glands or elsewhere. Caseous broncho-pneumonia, miliary tuberculosis of the lungs, or general tuberculosis with meningitis may follow measles immediately or occur after a quiescent period. Measles often occurs in close association with whooping-cough, diphtheria and scarlet fever.

Relapse in measles is rare. Second attacks, although uncommon, undoubtedly occur, and some unfortunate individuals never appear to

acquire any lasting immunity. Fourth, and even seventh, attacks are known.

Diagnosis.—In the prodromal stage, measles may be mistaken for ordinary naso-pharyngeal catarrh. If laryngitis is pronounced, and the child croupy, diphtheria may be simulated. Mastoid operations, operations on the tonsils and even on the appendix sometimes are performed precipitately before the true nature of the infection is recognised. Febrile symptoms and loss of weight during the incubation stage may be erroneously attributed to tuberculous infection. The prodromal scarlatiniform rash may lead to confusion with scarlet fever. These errors may be avoided by bearing in mind the possibility of measles, inquiring for possible exposure to infection, and particularly by a careful search for Koplik's spots, and shottiness of the posterior cervical glands. The pre-eruptive fall of temperature and recession of the catarrhal symptoms before the appearance of the rash should be borne in mind, and not lead to premature relaxation of precautionary isolation.

In the eruptive stage, the fevers with which measles may be confused are rubella, small-pox, and perhaps typhus.

Rubella is distinguished by the trivial nature and brevity of its prodromal symptoms; the slightness or absence of catarrh and cough; the insignificant fever; the absence of Koplik's spots and of stomatitis; and the presence of tender enlargement of the posterior cervical, mastoid and occipital glands. The rash of rubella is smaller, pinker and more discrete; but a scarlatiniform stage may supervene. The patient never feels or appears so ill as in ordinary measles.

Small-pox may be heralded by a prodromal rash of morbilliform character, which may have a similar distribution to that of measles, save perhaps on the face. Catarrh, stomatitis and Koplik's spots, however, are absent, and the onset is more abrupt than that of measles, and more likely to be signalised by such symptoms as backache, acute shivering, vomiting and prostration.

Measles may, on the other hand, be mistaken for the early eruptive stage of small-pox, for in both an illness for a few days may precede the appearance of a papular rash on the face and upper parts of the body. Catarrh, Koplik's spots and distribution of the rash about the ears, forehead and margins of the hairy scalp are in favour of measles. The temperature, too, continues to rise until the maximum efflorescence, whilst that of small-pox falls with the appearance of the rash. As the rash develops, the shottiness of the small-pox papules and the peculiarities of their distribution become apparent.

Typhus fever may be simulated by measles when the rash of the latter is receding and dusky, and lung complications are present; but the rash of typhus rarely invades the face, which is always affected in measles. The Weil-Felix reaction also is valuable.

Septic rashes in scarlet fever are often morbilliform; but their distribution does not conform to that of the measles rash. *Serum rashes, food rashes* and *drug eruptions* may assume a measly character; but these rashes often prove to be polymorphic when the whole body is examined, as it should be, and, besides, other signs of measles are wanting.

The *macular syphilide* is distinguished by the absence of respiratory catarrh and of Koplik's spots. History of exposure to venereal infection, a

chancre and the accompanying throat symptoms afford a clue. The Wassermann test should be employed.

Prognosis.—In different epidemics the death-rate may vary from 1 or 2 to over 50 per cent. Measles is most fatal to infants and young children, 70 per cent. of the mortality occurring in children under 3 years of age. After the fourth year the death-rate is low. Rickets, tuberculosis, congenital syphilis, malnutrition and chronic bowel complaints are unfavourable factors, and the disease is more fatal among the poor. In the cold season of the year the tendency to respiratory complications is more marked. When the infection occurs in conjunction with whooping-cough or chronic lung disease the mortality is high. Diphtheria is apt to assume the laryngeal form, and is an especially fatal complication. Considerable toxæmia with high fever, cyanosis, muscular tremor and diarrhœa point to a severe attack. Laryngitis, capillary bronchitis and broncho-pneumonia are serious. Cerebral symptoms, such as prolonged stupor or convulsions, are of bad augury. Remarkable recovery has been noticed in some cases of ascending myelitis.

Treatment.—PROPHYLACTIC.—Measles is chiefly disseminated by schools. The difficulty in controlling outbreaks of measles arises from the fact that it is extremely infectious, and the infectivity is present in virulent form for 4 or 5 days before the rash appears. Notification and school closure have been tried with poor results. The best method is to make provision for the early recognition of suspicious symptoms in contacts or to exclude those who have not had measles previously, for a period covering the ninth to the sixteenth day after the occurrence of the first case.

As regards the home, when measles occurs those who have had the disease need not be excluded from school—save from infant classes, but those presumably susceptible should either be excluded for over 16 days from exposure to infection, or, if allowed to attend, be subjected to daily examination.

In ward outbreaks children who have not had measles should be passively immunised, and if possible isolated or, at all events, segregated in small groups.

Serum prophylaxis.—Intramuscular injection of the blood serum of healthy convalescents from measles into susceptible contacts produces a *passive* immunity, which lasts about a month. Injection during the first 5 or 6 days of the incubation period prevents measles if the dose is adequate. Injection after the sixth and before the ninth day will modify the severity of attack, and allow the development of an *active* immunity which is lasting.

The dose is 2 c.c. for each year of a child's age up to a maximum of 10 c.c.; more is needed for adults or if the serum is injected late. In children under 3 years of age it is better to prevent the attack altogether. The most potent serum is obtained from the sixth to the ninth day after defervescence. The donor must be free from syphilis, malaria and tuberculosis, and must not be incubating any other infectious disease. The serum of adults, presumed to have had measles, but not recently, is of some value, but the dose should be doubled. A placental globulin extract has been prepared for use in the same way.

If measles follows the subcutaneous injection of immune serum the rash fails to erupt at the site of injection; this is the *Debré phenomenon*. Immune

serum does not blanch the developed rash. A disquieting feature is the occasional occurrence of infective hepatitis after the administration of convalescent measles serum, sometimes after so long an interval as 3 months.

Systematic taking of temperatures and examination for Koplik's spots and catarrh facilitate early detection of the disease, when patients are under close observation. The wilful exposure of children to the contagion of measles is unjustifiable, as the nature of the resulting attack can never be predicted.

Sixteen days' quarantine from the date of last exposure to infection is usually deemed sufficient, but, owing to the trivial nature of the prodromal symptoms it is better, in the case of schools, to allow a period of 3 weeks to elapse, especially if serum prophylaxis has been attempted. Convalescent patients in the absence of complications are quite free from infectivity at the end of a fortnight from the appearance of the rash.

CURATIVE.—The patient must be confined to bed during the febrile, and also during the prodromal stage, if this be recognised in time. The sick-room should be kept at a temperature of 60° to 65° F., and ventilation effected by means of open windows ; an open fire is also an advantage. The photophobia calls for the avoidance of direct light. Clothing should be light and consist of a flannel or woollen nightdress ; this is sufficient to prevent chill, allows the respiratory muscles full play, and encourages the evaporation of perspiration. Strict attention should be paid to cleansing the mouth and teeth, and the regulation of the bowels. During the febrile stage the diet should be restricted to milk, diluted if necessary with barley water. Tea may be allowed, and fruit juices or barley water given to assuage the thirst.

Twice a day during the febrile period the patient should be washed with tepid water ; but should the attack assume a toxæmic form, accompanied by high fever and delirium, cold sponging or the use of the cold pack is advisable. Amidopyrin, given early, is said to abort the disease, but has its dangers. The hot mustard bath is useful for children when pyrexia is accompanied by indications of circulatory failure.

Laryngitis in the early stage is relieved by steam and the use of a simple expectorant mixture, to which a sedative may be added. The croupy symptoms usually subside without necessitating tracheotomy or intubation. The possibility of the presence of diphtheria renders a bacteriological examination essential.

Laryngitis which persists after the eruption may be alleviated by the inhalation of compound tincture of benzoin or lysol in the strength of 60 minims to the pint of boiling water. The cough is relieved by a simple linctus, or one containing $\frac{1}{8}$ grain of morphine or other sedative. Late laryngitis if diphtheritic needs antitoxin. Bronchitis and broncho-pneumonia call for prompt treatment. A jacket of Gamgee tissue should be applied. If the cough is dry and irritating, steam often relieves. An expectorant mixture containing ipecacuanha and a small quantity of potassium iodide is useful. Sulphonamides may prove valuable. Sometimes a single mustard and linseed poultice gives great relief. As the cough becomes looser, steam should be discarded and free ventilation arranged. It is well to separate cases with broncho-pneumonia from others, as the condition is believed to be infectious. Treatment of the broncho-pneumonia of measles in the open air, where circum-

stances and weather permit, gives excellent results. Oxygen is valuable where there is much respiratory distress and cyanosis. Cardiac dilatation is an indication for the application of leeches. Frequent small meals are preferable to overloading the stomach.

Conjunctivitis should be met by bathing the eyes with boric lotion and the application of boric ointment to the lids. In severe cases, drops of silver nitrate solution, 2 grains to the ounce, should be instilled night and morning, or a 2–10 per cent. solution of silver protein used. Should the cornea ulcerate, atropine drops should be employed and oculent hydrarg. oxid. applied. Eye bandages are undesirable.

Stomatitis usually subsides quickly; the mouth should be cleansed with a lotion containing chlorate of potash (10 grains to 1 fl. ounce). In the presence of ulceration due to Vincent's organism, neoarsphenamine should be injected or applied locally. The supervention of noma calls for bacteriological examination and antitoxin or surgical interference in the way of cauterisation or free excision. Entero-colitis is managed on the same lines as infantile epidemic diarrhœa.

Convulsions and encephalo-myelitis are treated by sedatives and lumbar puncture, repeated if the cerebro-spinal fluid is under increased pressure. Intramuscular, intravenous or intrathecal injection of 10 c.c. of blood serum from a recently recovered case with this complication, if obtainable, seems worthy of a trial.

In an uncomplicated case of measles the patient may be allowed up 2 or 3 days after the temperature subsides. Supervision should be exercised during the convalescence of severe cases, and the possibility of later tuberculosis borne in mind. Ear discharges call for skilled treatment, as they may become chronic.

RUBELLA

Synonyms.—German Measles, Rötheln.

Rubella is quite distinct from ordinary measles and from scarlet fever. It protects only against itself. Amongst the exanthemata it is characterised by its long incubation period, its short invasive stage, its benign course and its seasonal prevalence.

Ætiology.—The infectivity is less than that of measles and of short duration. Like measles it is infectious for a day or two before the eruption appears. Infection is facilitated by close contact and there is no evidence that the disease is spread by fomites. Infection through an intermediary cannot be considered proved. The infective agent is unknown, but a filtrable virus has been suspected.

Rubella is prevalent in the first half of the year. Cases increase from January to a maximum in May and June. After that an abrupt fall ensues. A series of local outbreaks usually occurs, determined by the aggregation of a number of unprotected young adults. A more or less pronounced epidemic wave occurs every third or fourth year. The maximum incidence is at a later age period than that of measles, but even the youngest infants have been known to take the disease. Its frequency much diminishes after the age of 30. Sex is without influence.

Symptoms.—The incubation period, although variously stated to be from 7 to 22 days, is usually 17 or 18 days.

Premonitory symptoms are mild or altogether absent, but a short catarrhal stage usually occurs, the rash making its appearance within 24 hours. Rarely a longer prodromal period of ill-defined illness occurs before the eruption. The characteristic adenitis of the mastoid, occipital, cervical or other lymph glands can, more often than not, be detected for a day or two, exceptionally even a week or longer, before the appearance of the rash.

The rash is often dimorphic. Macular, slightly papular and morbilliform in its progress, it frequently fuses and becomes scarlatiniform in its second stage. Discrete spots first appear on the face or neck; they invade the circumoral region and may be found behind the ears and on the scalp. Sometimes they are first found on the wrists, chest, shoulders, or even on the legs. They are smaller than the papules of measles, pale pink in colour, and tend to cluster in small groups. The rash quickly extends to the trunk and limbs and in most cases as quickly fades. On the second day the face is no longer spotty but appears diffusely erythematous ("sunburnt"). Sometimes the outbreak of the eruption is halting in its progress. The scarlatiniform stage is not developed in all attacks; it is due to the fusion of the discrete elements, and is generally best marked on the trunk, especially so on the back. It becomes most apparent on the second day of the eruption. The rash rarely lasts more than 72 hours and hardly stains the skin, thus contrasting with measles.

The mucous membrane of the mouth is not inflamed, and Koplik's spots never occur. The tonsils may be slightly swollen and reddened, sometimes a follicular exudate is present. Some degree of pharyngeal catarrh is evident, and the tongue may be lightly coated. A fine vesiculation and congestion of the soft palate are often seen, and the orifices of Stenson's ducts may be vividly injected. The gums may be injected and tender. The conjunctivæ are pink and the eyes slightly suffused. Photophobia is rare. Fever is slight, even when the rash is intense. Often there is no fever at all. The pulse and respiration rates are only increased in proportion to the febrile disturbance.

A tender adenitis is very distinctive. The mastoid and occipital glands may rapidly attain the size of peas; the posterior cervical glands are also enlarged, frequently too those in the axillæ and groins. The enlarged glands are firm, tender and discrete; suppuration never occurs. As a rule resolution takes place rapidly when the rash subsides. The urine presents no special characteristics.

As in the case of morbilli, a leucocytosis occurs during the incubation period, but a leucopenia with a relative increase of lymphocytes is found in the eruptive stage. More distinctive is a high percentage of plasma cells and Türck cells.

Convalescence is remarkably speedy. Slight furfuraceous desquamation may occur.

Complications.—Complications and sequelæ are for all practical purposes non-existent. When they do occur they are trivial and take the form of mild recurrent sore throat, slight laryngitis, slight bronchial catarrh, rheumatism, rarely acute, or transient albuminuria. Otitis is very rare, and meningeal symptoms, encephalo-myelitis, or polyneuritis, rarer still.

On occasions, epidemics of rubella of more severe type, approximating in symptoms and sequelæ much more closely to measles, have been described.

Diagnosis.—The disease has a similarity to measles and scarlet fever, especially when the latter occurs in a mild form. In addition, the rash of rubella must be distinguished from toxic and drug rashes, from the eruption of secondary syphilis, from glandular fever, and from certain skin diseases.

Measles is differentiated by the following points. The incubation period is shorter, being 14 days from exposure to the appearance of the rash; cough and catarrhal symptoms are marked, the mucous membrane of the mouth is inflamed and Koplik's spots are present. The rash appears later, is darker, more persistent, and stains. There is no late scarlatiniform stage. Fever is more pronounced, and the mastoid and occipital glands are not especially enlarged. Pulmonary complications are much more likely to occur.

Rubella is often mistaken for scarlet fever. Distinctive points in favour of the latter are: the short incubation period; the occurrence of such initial symptoms as vomiting, marked faucial inflammation, shivering or severe headache. The fever is high at onset and the pulse disproportionately rapid. The circumoral region is free from rash, and by the fourth day the tongue has peeled. The occurrence of such sequelæ as arthritis, cervical adenitis and nephritis, also typical pinhole or lamellar desquamation, will clinch the diagnosis. Even in the scarlatiniform stage of rubella, discrete measly elements may generally be detected about the edges of the rash on the forearms, wrists, legs and ankles. An eruptive fever which simulates measles at its onset and scarlet fever later, is generally rubella. Occasionally glandular fever (*q.v.*) resembles rubella.

Toxic, enema and drug rashes may bear a resemblance to the rash of rubella, but as a rule these rashes are very irregular in their distribution and polymorphic in character. The characteristic glandular enlargement and slight catarrh of rubella are absent.

Of skin diseases, erythema scarlatiniforme and pityriasis rosea are sometimes mistaken for rubella. The first named bears a greater resemblance to scarlet fever; unlike rubella, it avoids the face, does not give rise to swelling of the mastoid and occipital glands, and shows a great tendency to recur.

Pityriasis rosea, itself possibly an infective fever, is distinguished by a herald patch which precedes the general eruption, and the fact that the latter usually appears first on the upper part of the trunk. The rash often shows commingled macular and ringed lesions. The patches are slightly scaly and are decidedly larger and more persistent than the papules of rubella. There is no catarrh and no conspicuous glandular enlargement about the head. The patches desquamate in a characteristic manner from their centres, which are fawn coloured, towards the margins, which are slightly elevated and darker.

Secondary syphilides bear a superficial resemblance to the rash of rubella, but are distinguished by the presence of a primary sore, the characteristic throat and the conspicuous increase in size, and shottiness of the glands in the vicinity of the chancre. The Wassermann reaction is of value.

The Paul-Bunnell reaction will distinguish glandular fever.

Prognosis.—Recovery is the rule; second attacks are known, but not common, and relapse is very rare.

Treatment.—Prophylactic.—As the incubation period is long a quaran-

tine of 3 weeks is theoretically necessary for contacts, but is rarely imposed. They may be watched or isolated from the tenth to the twenty-first day from exposure to infection. Early warning of the imminence of attack may be gained by carefully watching the mastoid and occipital glands.

CURATIVE.—The patient should be isolated and kept in bed until all symptoms have subsided. In 7 days all infectivity has ceased, provided there is no persistence of faucial, nasal, respiratory or other symptoms.

SMALL-POX

Synonym.—Variola.

Definition.—An acute, specific, highly infectious fever, characterised by a definite incubation period and a distinctively distributed, deep-seated eruption which passes through the stages of papule, vesicle, pustule and crust. The fever shows two phases—a remission at the outbreak of the rash being followed by a reaccession on the onset of the pustular stage.

Ætiology.—All races, both sexes, and persons of every age are susceptible if unprotected by a previous attack, or by efficient vaccination. This general liability is most evident when the disease is introduced for the first time into a new community; under such conditions it may decimate the population. Its present-day incidence on adults is accounted for by vaccination in infancy; in endemic centres it was, prior to the introduction of vaccination, a disease of early childhood. Small-pox has at times been epidemic in every civilised country, following trade routes and the channels of communication. It is more severe in hot climates. Coloured races are said to take it badly. Unlike scarlet fever and measles, it frequently attacks infants at the breast. When small-pox occurs during pregnancy, infection of the fœtus is common but not inevitable. Abortion or premature delivery is to be expected in all severe attacks. The fœtus contracts the disease in utero, usually during the pre-eruptive (septicæmic) stage in the mother, the incubation period being shorter than the usual 14 days for contact infection via the respiratory tract, in some instances fœtal infection is acquired at the time of separation of the placenta. Few of the children born in these circumstances survive, sometimes they actually show the rash or its scars at birth.

In England and temperate climes most outbreaks occur during the winter and spring, and tend to die out with the commencement of summer. Small-pox protects against itself, and second attacks are rare. Vaccination gives complete immunity for some years and partial immunity usually persists afterwards. Complete natural immunity is very rare, but is reported. Inoculated small-pox affords more complete immunity than vaccination.

Infection with small-pox is, almost certainly, through the respiratory tract, and may be direct or indirect, *i.e.* by contact, which need not be very close, with a patient suffering from the disease or through the medium of objects infected by the sick person. Intermediaries may carry the contagium in their clothing or in their hair. The greater incidence in the neighbourhood of small-pox hospitals suggests the possibility of aerial convection of the virus for considerable distances, perhaps exceeding a mile, but the influence of human carriers in these cases is hard to eliminate. Bedding, clothing and rags may retain their infectivity for considerable periods of

time, especially when stored. Transmission by flies and domestic animals is regarded as a possibility. The infectivity of small-pox is slight at the time of the symptoms of onset, and is much greater when the eruption appears. It continues until all the scabs have separated. The virus is very resistant and long persists in the dry scales and crusts shed from the body. Corpses of those recently dead from small-pox can transmit the disease. Tramps are often responsible for the conveyance of infection from one locality to another.

There can be no doubt that small-pox is due to a living virus. Minute, but characteristic, intracellular bodies are found in the epithelial cells of the pocks of small-pox and vaccinia, and also in the cornea of the rabbit, after scarification with the virus of these diseases. They are known as *Guarnieri bodies* and some apparently contain the "elementary bodies" of Paschen. The elementary bodies of small-pox and of variola minor are agglutinated by the sera of patients convalescent from either form of the disease.

Pathology.—The cutaneous lesion of small-pox lies in the deeper layers of the epidermis. Vesiculation is due to serous exudation between the cells. Loculation is caused by vertical strands of degenerated epithelial cells which radiate from the base of the pock. The tenseness of the vesicle and tethering of the covering by this reticulum cause the pock to be umbilicated. In malignant attacks, where the pocks are flaccid, and in the old and debilitated where a similar condition may obtain, umbilication is often absent. With pustulation the fibres of the reticulum are ruptured and the pock becomes dome-shaped. The suppuration is attributed to secondary infection with extraneous organisms, particularly with streptococci. On mucous membranes the vesicles rupture almost as soon as formed and are rapidly converted into shallow ulcers. The chief blood change is an initial leucopenia, followed after the first week by a leucocytosis in which mononuclear cells preponderate. A secondary anæmia may become pronounced. The post-mortem appearances are those usually found in acute infective processes. The rash persists, the liver is often much enlarged, the spleen swollen, and the lungs broncho-pneumonic. Particular attention has been drawn to the presence of local necroses in the liver, testicles and bone marrow. These are often infiltrated with mononuclear basophil cells. In hæmorrhagic small-pox, petechial and purpuric hæmorrhages are found in the skin, mucous membranes, lungs and other viscera, sometimes also in the retro-peritoneal tissues and the roots of the mesenteries.

Symptoms.—*Unmodified small-pox; Variola major.*

Period of incubation.—Taking the first symptoms of invasion, this is from 10 to 14 days. The average period is 12, or counting to the appearance of the rash, 14 days. Extremes of 5 to 23 days are mentioned but are rare. In inoculated small-pox the generalised eruption appears on the eighth to the eleventh day.

Period of invasion.—In a typical attack the invasive symptoms are sudden and of great intensity. The most prominent are severe chills or rigors, marked pyrexia, severe frontal headache and intense pain across the loins. The temperature quickly reaches a maximum of 103° to 104° F., and is accompanied by severe prostration. Giddiness and nausea are present and vomiting may occur, particularly in children. Delirium, mental symptoms and even suicidal tendencies may accompany the invasive stage. With these

severe symptoms are coupled more ordinary febrile manifestations, such as anorexia, thirst, coated tongue and disturbed sleep. The breath is offensive, the skin usually hot and dry but sometimes perspiring, and the bowels constipated. There are, however, mild attacks in which the symptoms of invasion are much less severe, and even in more severe attacks pain across the loins is not always present. Mild invasive symptoms usually presage a mild eruption; with a severe invasion the attack is generally, although not invariably, grave.

Prodromal rashes.—These may precede the proper eruption for 1 or 2 days. They are not always present. There are two types, one purely erythematous, the other petechial or hæmorrhagic with or without accompanying erythema. The pure erythemas are of a bright red or dusky purplish colour and may appear on the trunk, where they are often patchy, or be limited to the bony prominences and extensor surfaces of the limbs. They may suggest the rash of scarlet fever or bear a superficial resemblance to that of measles. The hæmorrhagic or petechial rash, which often has at first a dusky erythematous background, is more characteristic. It appears in the flexures of the groins, which are stippled with small petechiæ; it invades the thigh for an inch or two and extends in an ill-defined manner on to the abdomen. Sometimes it extends towards the axilla and may be found on the back of the neck and flexures of the knees. The petechial rashes are persistent and indicate a severe attack. The erythemas are fugitive and of good prognostic import; the only exception is a very brilliant universal erythema of face, trunk and limbs which sometimes ushers in hæmorrhagic small-pox.

The eruption.—On the third day the symptoms of invasion are at their maximum and the eruption appears, showing first on the forehead and temples near the edge of the hairy scalp and also on the wrists. It extends rapidly over the body, but always affects most the parts usually uncovered and those most exposed to pressure, friction or other irritation. It is least profuse on the abdomen and in the groins, somewhat more marked on the chest, still more marked on the back, especially across the shoulders, thicker still on the arms, choosing their distal portions, and most profuse of all on the face, especially its upper part. It reaches the lower extremities within 24 hours of its first appearance. Meantime the lesions multiply on the parts already affected, the eruption becoming thick on the face, and perhaps in the scalp, whilst still scanty on the parts invaded later. In 3 days it will have attained its full density, but the earlier lesions will be in a slightly more advanced stage of development than those which appeared later.

In a characteristic way it avoids depressions, flexures and protected flexor surfaces, such as the armpits, flanks, groins, orbital hollows and supraclavicular fossæ. The escape of the axillæ and scantiness of rash on the flanks are marked. Abnormal irritation by clothing, irritants or scratching may determine a profuse eruption in areas on which, ordinarily, pocks are scanty. The pocks are aggregated over prominent bones and outstanding tendons, but the clavicles and malleoli are exceptions to this rule. The rash is more or less symmetrical; one arm will not escape when the other is involved.

On the *first* day of efflorescence the rash consists of small dull-red *macules*. Within 24 hours these are becoming obvious *papules* which feel shotty when pinched up between the finger and thumb, the hardness being best

marked on the face, hands and forearms. On the *third* day of eruption many of the papules have become converted into *vesicles*, but the commencement of vesiculation may be recognised on the summits of the papules at an even earlier stage. By the fourth or fifth day the eruption is completely vesicular and the early toxæmic symptoms and fever may have entirely subsided. The vesicles, which are circular in outline, slowly increase in size and become surrounded by an inflammatory areola. They are now about the size of split peas, greyish in colour, and set in the skin rather than on its surface. Umbilication is evident and loculation is proved by their failure to collapse when transfixed by a sterile needle. The contents of the vesicles remain clear for 24 hours only; they then gradually become purulent, so that by the *fifth* day *pustules* are in evidence on the face and by the eighth day are universal. With pustulation, the pocks soften, become flat-topped and lose their areolæ. Reaccession of fever with constitutional symptoms and often delirium, the *secondary suppurative fever*, accompanies the process of suppuration or maturation. Where the pustules are plentiful a marked inflammatory œdema of the skin may now appear, causing the features to become much swollen and impeding the movements of the hands and fingers. Much tenderness accompanies this œdema, and the patient may also be tormented by itching. Suppuration destroys the loculation of the vesicles and also obliterates umbilication. Adjacent lesions, particularly on the face and hands, may run together in the vesicular and pustular stage—a process which produces the *confluent rash*, and is a sign of severe infection. On the *ninth* and *tenth* day of eruption the pustules begin to *desiccate* and *scab*, some first rupture or are torn by scratching, and collapse. Brown or black crusts result which separate by the end of the thirteenth or fourteenth day, but where the skin is very thick, as on the palms and soles, the dried-up unruptured pustules may form deep-seated "seeds" which may take weeks to work their way to the surface.

To summarise: the rash is papular on the first to the third day; vesicular from the third to the fifth; pustular from the fifth to the ninth, and desiccating from the ninth to the seventeenth.

The cutaneous eruption is accompanied by an outcrop on the mucous membranes of the mouth, nose and pharynx. In severe cases the larynx, bronchi, gullet and even the stomach may also be affected. On the mucous membranes vesicles are soon transformed into shallow grey ulcers. Vesiculation may be observed on the palate, whilst the lesions are still indeterminate on the skin. In consequence of the eruption the fauces and tongue become sore, the nose is obstructed and deglutition is painful. Implication of the larynx will cause hoarseness or aphonia and even dangerous œdema. The mucous membranes of the vulva, vagina and rectum may also be involved.

The fever (Fig. 4) of invasion reaches its acme with the appearance of the rash, then it falls, but not immediately. It is generally normal by the fifth day of the eruption, often before this. It is at this stage, in the milder attacks with scanty rash, the patient may attempt to resume his ordinary occupation, and, in modified cases, very little further febrile disturbance may ensue. Ordinarily, however, the secondary suppurative fever now sets in and reaches its acme about the ninth or tenth day of the eruption. Its duration in the more severe cases is from 10 days to a fortnight. In severe and confluent

cases, the remission of temperature in the vesicular stage may be ill-marked or absent. The pulse and respirations are quickened proportionally to the degree of fever present, but in grave cases the respirations become shallow and irregular, and the pulse accelerated and feeble.

The urine is febrile in character. Some albumin may be present, and a diazo-reaction may be obtained.

Owing to the depth of the lesions in the skin, depressed scars are left, the amount of pitting depending on the degree of suppuration. The pits show a reddish staining which may persist for months. Some desquamation may accompany the separation of the crusts, particularly on the feet and hands. The hair often falls out freely. Convalescence is, in favourable cases, rapid and complete.

Small-pox may assume severe, modified or benign forms :

Severe types of small-pox.—These comprise the confluent and hæmorrhagic

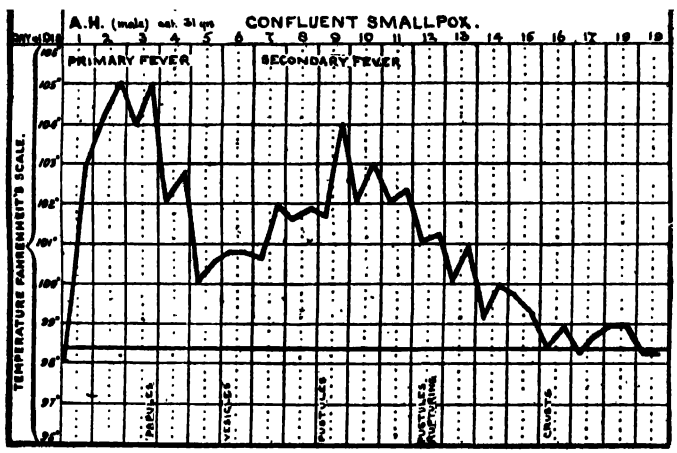


FIG. 4.—Confluent small-pox in an unvaccinated adult.

varieties. *Confluent small-pox* is characterised by fusion of the lesions, particularly on the face and hands. The rash may fuse whilst still papular, but more commonly does so in the vesicular and pustular stages. In such cases the toxæmia is severe and the remission of symptoms before the stage of pustulation may be absent or ill-marked. Delirium is common, and the secondary fever high. Inflammatory œdema is very marked, the features may become quite unrecognisable and the confluent pocks may form a continuous sheet of pus. Severe conjunctivitis, nasal obstruction, salivation, cough, aphonia and diarrhœa are common. Some patients pass into a typhoid condition. An offensive odour emanates from the skin, circulatory failure is progressive, and death may occur towards the end of the second week.

Hæmorrhagic small-pox.—In the most malignant variety, purpuric flecks and patches may appear in the skin before the development of the eruption, and are accompanied by subconjunctival hæmorrhages and bleeding from the mucous membranes. Initial symptoms, in particular backache, are

severe, and prodromal rashes common. The respiration is hurried and the breath fœtid, but the temperature not necessarily very high. Death may occur before the outbreak of the proper eruption gives a clue to the nature of the infection, but often towards the end careful inspection may show a few papular elements struggling to appear.

In other cases the bleeding first manifests itself about the time of the eruption, occurring in the form of petechiæ or of circular spots between the lesions and also infiltrating the bases of the vesicles and staining their contents. The vesicles are often badly developed, confluent and of a violaceous hue. Bruises form easily in the skin, and hæmaturia, epistaxis, hæmatemesis or uterine hæmorrhage may appear. The breath has a sickly odour.

The mere presence of blood-stained contents in the vesicles, especially those on the legs, without hæmorrhages into the bases of the pocks, in the skin and elsewhere, is not of bad prognostic importance.

Modified small-pox or varioloid.—Small-pox of a very mild type may occur in vaccinated subjects. In such cases initial symptoms may be slight, and the eruption, although typical, is scanty; sometimes it fails to appear. More commonly, the initial symptoms are severe, and the rash appears early, but it is generally sparse and discrete, tends to evolve quickly, and many of its elements fail to progress beyond the papular or vesicular stage, the suppurative fever being slight or absent. The lesions, which are often small, are superficial and may be unilocular, sometimes they appear fleshy and wart-like. The modification is most evident on the face. In such cases the arrest of development leading to the juxtaposition of papules, vesicles and small pustules may cause a resemblance to chicken-pox, but the distribution remains characteristic.

Variola minor.—From time to time a benign type of small-pox has prevailed in many parts of the world. The names alastrim, amaas, varioloid varicella and para-variola also designate this disease. It differs from ordinary small-pox in its mild course, low mortality (0·5 to 2 per cent.), lesser infectivity, the usual absence of secondary fever, the occurrence of residual pigmentation rather than pitting, and incidence on adults rather than on children.

The incubation period is 10 to 15 days, or longer. Invasion is abrupt, and may be accompanied by muscular pains, backache, vomiting and sometimes high fever, but many cases are ambulatory. The rash never appears before the third day, more commonly on the fourth or fifth. It is seen first on the face, then on the forearms and trunk, and within 12 hours on the lower limbs. The eruption may be scanty or moderately profuse. It rarely comes out in crops, but in any case the initial lesions are more advanced than those which follow. Maturation is more rapid than in variola major, papular and vesicular stages each lasting 2 days, pustulation beginning on the fifth day, and scabbing on the face being evident within a week. There is, as a rule, no secondary fever.

The distribution of the eruption is classical, the rash favouring the face and extremities rather than the trunk. On the limbs, the distal parts, and on the trunk the upper part of the back, rather than the abdomen and chest, are involved. Much weight is attributed to the detection of a few deep-seated lesions in the skin of the thenar and hypothenar eminences.

The lesions are more superficial than in variola major, but not so superficial as the blebs of chicken-pox. They are not always spherical, and are

often unilocular and not umbilicated. Mature vesicles have an opalescent appearance, and the crusts are of a deep amber colour. It is easy to understand why the disease is so often mistaken for chicken-pox. The distribution of the rash is the important diagnostic criterion. Although vaccination protects against v. minor the converse is not invariably true. As a rule, vaccination in the eruptive stage fails, but may take in modified form later.

Although serological tests fail to differentiate variola minor from variola major, histological examination shows that the inclusion bodies of v. minor show differences in numbers, size, staining reactions and localisation in the vesicles when compared with v. major.

Complications.—During the later stages of small-pox and in convalescence, boils and superficial abscesses often cause trouble. Septic rashes, erysipelatous or impetiginous infections may spread from the pocks. The cervical and axillary glands may become enlarged or even suppurate. In the more severe cases, bed-sores may rapidly form over pressure points. Rarely death is due to septicæmia arising from these cutaneous infections.

Ocular complications are important. Conjunctivitis is common. Pustules may form on the palpebral or ocular conjunctiva. The eyelids often become inflamed and œdematous. A rapidly spreading keratitis may lead to sloughing of the cornea, but corneal ulcers are more common and sometimes lead to perforation and panophthalmitis. Iritis is rare. Retinal hæmorrhages sometimes cause blindness. The scars of the corneal ulcers may much impair the sight. Otitis media is comparatively common.

Laryngeal inflammation may be so severe as to necessitate tracheotomy, and may lead to perichondritis and necrosis. Bronchitis and bronchopneumonia are frequent and often accelerate death. Lobar pneumonia and purulent pleurisy are rare. Endocarditis and pericarditis are exceptional, but degenerative changes in the myocardium are not infrequent. Occasionally a destructive arthritis supervenes; it is said to be more common in childhood. Although albuminuria is often found, a true nephritis is uncommon.

Parotitis is looked upon as a secondary duct infection from the mouth. Orchitis sometimes occurs during the acute stage.

As in other fevers encephalo-myelitis and neuritis may occur. On recovery from the toxæmic stage speech may be completely lost, but it returns. Less favourable are bulbar or limb paralysis, with or without derangement of sphincter control.

Disfigurement of the face, permanent blindness, deafness and sometimes alopecia may be the legacies of a severe attack.

Diagnosis.—The whole body should be stripped and examined in a good light. In some cases a preliminary bath is needful. Attention should first be focused on the distribution rather than on the characters of the rash. The individual lesions should be dotted on an outline diagram of the body, and a numerical comparison made of those on the abdomen, chest, back, upper arms, forearms, face, thighs and legs. Too great reliance should not be placed on shottiness or umbilication. The condition as to vaccination should be ascertained and the nature of any prevailing epidemic borne in mind.

The initial fever may itself lead to difficulty in diagnosis; the symptoms of onset are somewhat similar to those met with in other acute diseases, particularly influenza, acute rheumatism, pneumonia and cerebro-spinal fever.

Severe prostration and backache, when present, are suggestive. Often the diagnosis is not certain until the true eruption appears on the third day and the fever subsides, but the appearance of a petechial prodromal rash in the groins may enable earlier recognition. As regards influenza, it is more common for small-pox to be at first mistaken for this disease than for the converse to occur. Lumbar puncture is available in cerebro-spinal fever. In pneumonia sooner or later lung signs appear. Precipitate certification of a supposed case of small-pox, even in a contact, is unwise; it is better to await the appearance of the rash, remembering this should appear first on the forehead, near the roots of the hair, the cheek bones, sides of the nose, wrists, hands and forearms. The interior of the mouth should also be inspected and any parts of the skin which have been subjected to special irritation.

The prodromal rashes, if purpuric, may be confused with different varieties of purpura; if erythematous, with scarlet fever, measles, rubella, urticaria or other forms of erythema.

The characteristic groin incidence of the purpuric rash of small-pox should be remembered, and is of great assistance in diagnosis. More widespread purpuric rashes, however, are at times misdiagnosed as febrile purpura until the occurrence of small-pox in contacts reveals their true nature. Conversely, febrile purpura and purpuric rashes occurring in ulcerative endocarditis, cerebro-spinal fever and other conditions may be mistakenly thought to indicate small-pox. The distribution of the rash and the character of accompanying symptoms should be noted. Physical examination of the organs may reveal signs which help to clear up the diagnosis, which may be very difficult.

A scarlatiniform prodromal rash is distinguished from scarlet fever by the absence of tonsillitis and of punctate redness of the soft palate. The rash on the skin is not definitely punctate and the area of circumoral pallor is wanting. The tongue is not typical nor are the tonsillar lymph glands enlarged. The Schultz-Charlton test is negative.

Morbilliform prodromal rashes bear only a very superficial resemblance to measles. The diagnosis is discussed later. Nor should rubella be confused if its characters be borne in mind. The initial erythemas may resemble those induced by antitoxic serum, by soap enemas and by drugs. The characters of these rashes are given in the article on scarlet fever.

The *true eruption of small-pox* may be confused with measles, chicken-pox, perhaps typhoid or typhus, also with various forms of papular erythema, urticaria, acne, papular and pustular syphilides, and glanders. Sometimes drug rashes, particularly those due to iodides, lead to mistakes. Measles on the face may bear a close resemblance to the papular eruption of small-pox. It is distinguished by the catarrhal symptoms, Koplik's spots, the distribution of the rash on the body, and the fact the temperature tends to rise as the eruption increases instead of falling as it does in small-pox.

The differentiation of some cases of chicken-pox is a difficulty. Chicken-pox is a disease of childhood whilst small-pox chiefly affects adults (although with neglect of vaccination its incidence in childhood may again increase), but cases of chicken-pox in the adult are not infrequent, and in them prodromal symptoms may be sharp and the rash not appear until the second or third day. Chicken-pox presents the following distinctive characters:

1. The rash of chicken-pox appears first on the trunk, and is thickest on

the trunk, face, upper arms and thighs. It avoids the extremities of the limbs. It does not so markedly select irritated areas, nor does it avoid the axilla and groin. The presence of many lesions on the palms and soles is greatly against chicken-pox.

2. The eruption comes out in distinct crops over 3 to 5 days or more.

3. The vesicles develop much more rapidly and are mature in 24 hours. Vesicles are not seen at this period in small-pox.

4. The lesions are superficial and unilocular, rarely umbilicated. Their bases are not indurated. Near flexures they may assume an oval outline, sometimes they are irregular or crenated.

5. Pocks of all stages of development may be present at the same time on a given area of skin.

6. The lesions are smaller. Pustules and scabs half an inch across are almost certainly due to small-pox.

7. Successful vaccination within 5 years or revaccination within 10 years is evidence against the disease being small-pox. Chicken-pox does not protect against successful vaccination in an unprotected individual. If the disease is small-pox, vaccination will prove unsuccessful. This rule, however, is not absolute. Vaccination may prove successful in anomalous forms of small-pox, and has been alleged to take in ordinary small-pox on rare occasions.

Confusion with typhoid and typhus is uncommon, and should be eliminated by taking into consideration the distribution of the rash and character of the other symptoms. In distinguishing other skin eruptions it should be remembered erythemas are often polymorphic. They may show occasional vesiculation which is quite superficial and are sometimes febrile. Acne affects the face, shoulders, back and chest; it is chronic, afebrile, and often associated with comedones and scars. The lesions may be pustular but are never vesicular. The lesions are not found on the forearms or hands.

If syphilis is borne in mind its eruptions are not likely to be mistaken. Reliance must be placed upon their distribution, polymorphic character, other signs of syphilis, the history and the Wassermann reaction. A patient with syphilis may also have small-pox. Glanders is rare, but when the nodules on the face suppurate and are accompanied by fever, small-pox may be suggested. There is usually a nasal discharge and a history of association with horses. Bacteriological examination will show the *Bacillus mallei*.

Certain laboratory tests have been elaborated for the detection of small-pox. Of these, Paul's test is of value. It is carried out as follows. A rabbit's eyes are cocainised. One is scarified with the contents of a suspected pock, the other is simply scarified as a control. At the end of 48 hours the rabbit is killed and the eyes are examined in a sublimate alcohol bath. In the case of small-pox or vaccinia, but not of chicken-pox or other vesicular eruption, the inoculated cornea shows opaque white elevations on a milky background. The other cornea is evenly opaque without epithelial plaques. Guarnieri bodies are present in the plaques.

A more certain test and one more easy to apply and appraise is intradermal inoculation of the rabbit with material from a small-pox vesicle. After a short incubation period a characteristic inflammatory reaction ensues. This reaction remains in abeyance when serum from a rabbit hyperimmunised with vaccinia virus is mixed with the small-pox material before injection

into the dermis (Ledingham, Defries and M'Kinnon). There is also a "flocculation test" based on the fact that an extract of small-pox crusts is flocculated when mixed with the serum of a vaccinated rabbit.

Prognosis.—Natural small-pox has a mortality which varies from 25 to even 40 per cent. The prognosis may be considered under the following heads: (1) The vaccinal condition of the patient; (2) the age; (3) the nature of the attack; and (4) the character of the prevailing epidemic.

1. When a vaccinated person takes small-pox the nature of the attack usually indicates some residual immunity, the severity of the disease being less and the mortality much lower than in the unvaccinated. The presence of large, well-foveated vaccination scars renders the prognosis very favourable. After the age of 15 the protective influence of infantile vaccination will to a large extent have disappeared, but revaccination at puberty, properly performed, confers a high degree of immunity for the rest of life.

2. The death-rate in the first 5 years of life is very high and may exceed 40 per cent. After that there is a fall, at first gradual, then considerable, up to the age of 15 or 20, which is the most favourable period. Subsequently the mortality rises steadily and may even exceed the figures given for the first quinquennium. In the vaccinated, however, the younger the patient the more certain is recovery. If revaccination has not been performed, as age increases the mortality does so also, and may reach 15 per cent. in persons over 30 years of age.

3. The nature of the symptoms is important. Mild invasion presages a mild attack. Severe invasive symptoms usually, but not invariably, mean a severe infection, but they may precede mild attacks in the vaccinated and sometimes in others. Prodromal rashes of a vivid lobster hue, especially if petechiæ be present, are the heralds of grave, often hæmorrhagic infections. Very intense backache is also an ominous invasive symptom. The more profuse the pustular rash the worse the prognosis, but the intensity of the suppurative stage is much modified by previous vaccination. Confluent eruptions mean a bad outlook, whilst patients in whom the rash remains discrete usually recover. Hæmorrhagic small-pox is always fatal.

Other unfavourable symptoms are incomplete remission between the primary and secondary fever, sleeplessness, active delirium, especially in drinkers, considerable implication of the larynx and broncho-pneumonia. The influence of pregnancy in inducing abortion and miscarriage has already been mentioned.

4. Epidemics vary much in their severity and mortality. In some the disease is so slight and the mortality so low, that doubts arise whether the epidemic is really small-pox.

Treatment.—PROPHYLACTIC.—Efficient vaccination and revaccination are the most powerful safeguards. The chief measures to be taken when the disease is recognised are the following: (1) Prompt removal of the patient to an isolation hospital. (2) Thorough disinfection of infected rooms and clothing. (3) Immediate vaccination or revaccination of all other members of the household and of contacts. Four or even more days after exposure vaccination may prove effectual in preventing the disease, at all events will modify it. (4) Quarantining of contacts for 16 days, or a daily inspection so that initial symptoms may be detected at once. (5) Notification of schools or institutions attended by inmates of the same house.

Inoculation with small-pox, which prior to vaccination was a method of prophylaxis, is said in some instances to have a mortality of 2 or 3 per cent.; but even this compares favourably with a mortality of 50 per cent. as seen in some epidemics of ordinary small-pox. Inoculation, however, was found to spread the disease, and so has, in England, been made a penal offence.

CURATIVE.—This is purely symptomatic. Abundance of fresh air, cool surroundings, and not too great a weight of bedclothes, fluid diet, regulation of the bowels, and tepid sponging night and morning form the regular routine. The mouth should be cleansed regularly with peroxide of hydrogen, alkaline carbolic lotion, or some other mild antiseptic, and the nose gently douched or liquid paraffin instilled. A water pillow may be necessary in some cases. Severe pain in the head and back during the invasive stage may be mitigated by the application of an ice-bag to the scalp and use of fomentations to the back; at the same time aspirin, phenacetin, or chloral and bromide may give relief; but the drug most generally useful, both in this stage and in the sleeplessness, delirium and discomfort of the secondary fever, is opium in the form of 10 grains of Dover's powder. Sometimes paraldehyde is effectual. Delirious patients should never be left alone. The intractable vomiting of the early stage is allayed by citrating or peptonising the milk or substituting ice and champagne. Liquor iodi mitis in 5-minim doses is also useful. When fever continues high and is accompanied by toxæmia and delirium, tepid sponging may be replaced by hot or cold packs with advantage. Many methods have been tried of aborting the eruption and preventing the subsequent pitting. None is effectual, but there is hope that sulphonamides may prove of use. Evacuation of the contents of the pocks as soon as fluid appeared in them used to be recommended. Some advocate painting the face with liquor iodi mitis, diluted if painful, twice a day for the first 8 or 10 days, and then applying soft paraffin; or, better, commencing in the papular stage, a saturated (5 per cent.) solution of potassium permanganate may be painted over the whole body three times a day until scabbing begins, and afterwards less frequently. The application of a lint mask soaked in glycerin is useful, and glycerin may also be applied to the hands, or a dilute carbolic compress substituted. When the eruption is thick in the scalp it may be necessary to cut the hair short. The administration of salol in 10-grain doses every 4 hours is believed to modify the pustular stage. An attempt to combat the amount of suppuration by exposing the patient to red light, whereby actinic rays are cut off, is recommended by Finsen, but is said to prove too depressing. To mitigate the offensive odour which emanates from the skin, dilute carbolic lotions may be used (they also relieve the itching), or creosote may be vaporised in the sick-room. Starch poultices and alkaline washes are used for the removal of refractory crusts and zinc ointment applied. The eyes require special attention; they should be bathed with boric acid lotion at frequent intervals, and dilute nitrate of mercury ointment smeared on the edges of the lids. Should keratitis threaten, an ointment of atropine with yellow oxide of mercury should be applied.

Laryngitis calls for a steam tent and inhalations of benzoin or lysol. Circulatory failure is combated by the usual methods, and strychnine is useful as a nervous and respiratory stimulant. During decrusting and convalescence frequent warm baths are grateful, and quinine is a useful tonic.

Patients are to be regarded as infectious until the scabs are all separated and the skin quite healed.

VACCINIA

Vaccinia or cow-pox, a disease at one time very prevalent among cows, but now rare, is characterised by a vesicular eruption on the udders and teats. The vesicles, which are surrounded by an inflammatory areola, may by rupture form extensive ulcers. Abrasions on the hands of milkers may be accidentally inoculated from these lesions and they, in turn, may inoculate other cows in the herd. The hands of the infected milker show vesicles with surrounding induration, the axillary glands become swollen and there is some fever. Individuals thus inoculated are protected from small-pox, and Edward Jenner made practical use of this fact by inculcating the practice of deliberate vaccination and transference of the virus from arm to arm. In addition he demonstrated that those thus inoculated were refractory to subsequent inoculation with the virus from small-pox lesions, and milkers who had had small-pox did not catch vaccinia from the cows. But it appears that although vaccinia protects against small-pox, an attack of small-pox does not always protect against vaccinia. Apparently vaccinia is the more powerful antigen.

After long dispute, the question of the identity of cow-pox and small-pox has been settled by animal experiment in favour of Jenner's view that the two diseases are one and the same, small-pox virus being so modified by its transmission through the cow that its inoculation results only in a local lesion, a lesion which, however, affords a high degree of protection against small-pox. Vaccinia differs from small-pox, whether the latter be natural or deliberately inoculated, in that it has lost its infective character, and so can be used for purposes of vaccination without risk of propagating small-pox.

The histology of the vaccine vesicle is similar to that of the lesion of small-pox. It goes through the stages of papule, vesicle and pustule ; and loculation is produced by persistence of the remnants of vacuolated epithelial cells in the form of septa.

Professor Paschen has described minute " elementary bodies " as constant accompaniments of vaccinal lesions, and Ledingham has shown that these " Paschen bodies " are agglutinated by the sera of rabbits which have recovered from vaccinia. It is believed that these bodies are the filtrable virus of the disease.

For the purpose of vaccination vaccine lymph is prepared by the inoculation of healthy calves, the contents of the vesicles being collected and freed from pyogenic and other extraneous organisms by admixture with glycerine. This process of glycerinisation kills most of the adventitious germs, but leaves the virus of vaccinia uninjured. The lymph thus prepared is stored in capillary tubes at low temperature, and will remain efficacious for at least 8 months. Its use is preferable to the direct inoculation from human vaccine vesicles.

The operation of vaccination is carried out as follows : An area of skin over the insertion of the left deltoid muscle or on the outer side of the thigh is carefully cleaned with soap and water, and afterwards with ether. The contents of a tube of lymph are then ejected on to the cleansed area in 2, 3

or 4 separate portions, according to the number of insertions proposed. A ¼ inch scratch is made through each drop of lymph with a sterile lancet or sterile needle, care being taken to avoid drawing blood, and the lymph gently rubbed over the scratches with the instrument used. The scarified spots should be at least an inch distant from each other to avoid confluence. The lymph is given a few minutes for absorption, and any excess is removed with sterile wool. The scarified area is covered with sterile gauze. The whole procedure must be carried out with strict regard to asepsis. "Cross-hatching" is avoided.

If the operation is successful, inflamed areas appear at the sites of inoculation, and by the third day become distinctly papular. By the fifth day, small clear vesicles have formed which slowly increase in size and become depressed at their centres. By the eighth day the vesicles are large, sharply defined, and their inflammatory areolæ are confluent. From this time the contents become increasingly cloudy. The vesicles attain their full size by the twelfth day and collapse. By the tenth or twelfth day a brownish scab is forming. This after a time separates, leaving a depressed and pitted or foveated scar which at first is livid, but in course of time becomes dull white in colour. A more recent method of vaccination is by subcutaneous or intracutaneous injection of diluted vaccine. At present it is difficult to appraise its value.

The virus is distributed by the blood throughout the body. Headache, malaise and fever accompany maturation of the vesicles at the beginning of the second week; the axillary glands may become enlarged and tender and the spleen palpable. Sometimes febrile disturbance is noticed as early as the fourth day.

In revaccination the events are similar, but both the local and constitutional disturbances are less pronounced: sometimes they fail to appear at all. The lesions may run a very rapid course, aborting at the papular or early vesicular stage. Sometimes a slight itching and glandular tenderness are all that is observed.

Natural insusceptibility to primary vaccination is excessively rare, and at least three successive attempts should be made before insusceptibility is assumed.

Although infants can be vaccinated successfully in the first few weeks of life, under ordinary circumstances the best period is from the second to the sixth month. Revaccination is advisable after the seventh year and when small-pox is epidemic.

The degree of protection afforded against small-pox is in some degree proportional to the extent of the vaccinal lesion, and the resulting scars should, together, cover an area of not less than half a square inch. Hence the advice always to make at least two insertions and preferably four. The test of a successful scar is its depression and foveation. The period of immunity may be regarded as not less than 7 years. When vaccinal encephalo-myelitis is prevalent, vaccination by one insertion has been recommended.

Risks of Vaccination.—Fugitive erythemata, which are sometimes scarlatiniform, measly or urticarial, may appear about a week after vaccination; they resemble serum rashes. Erysipelas, septic infection and cellulitis sometimes result from the use of contaminated lymph or the lack of proper cleanliness at the operation or after. Under modern methods of glycerinisa-

tion and asepsis, these should not occur. There is no doubt, too, that syphilis has on rare occasions been conveyed by arm-to-arm vaccination. In such cases, the chancre does not appear before the fifteenth day, and is usually later. The calf being insusceptible to syphilis, the use of calf lymph has abolished this danger. Tetanus is another infection which has occasionally resulted, especially in hot climates. Tuberculosis and leprosy have also been cited as possible sequels, but with little or no proof. The addition of glycerine to the lymph kills the tubercle bacilli. The appearance of eczema and impetigo has been attributed to vaccination, as also a somewhat persistent form of anæmia. A rare sequel, to which attention has been drawn recently, is a form of encephalo-myelitis. Its greatest incidence has been in Holland, Great Britain and Germany, and has varied from 1 in 5000 to 1 in 100,000 vaccinations. The characteristic lesion is a focal, perivascular demyelinisation of nerve fibres, often associated with perivascular cuffing. It very rarely follows vaccination during the first year of life. Its chief incidence is after primary vaccination of children of school age or of adolescents. It is very similar to the encephalo-myelitis of small-pox and of measles. It sets in 7 to 12 days after vaccination, with headache, vomiting and paresis. These symptoms become aggravated, and delirium may pass into coma and death. In other cases the symptoms are more suggestive of meningitis, tetanus or lethargic encephalitis, with ocular palsies. The mortality may reach 50 per cent., but complete recovery is possible. Human serum, from a healthy donor who has been successfully vaccinated recently, or anti-vaccinal horse-serum, is the best antidote. The serum is given intrathecally or intravenously. The dose is 8–30 c.c., repeated if necessary. Repeated lumbar puncture is a valuable adjuvant.

Quiescent infection may be brought into activity and prominence by vaccination; this is the case with congenital syphilis and tuberculosis. Hence the advisability of postponing vaccination should the infant show signs of ill-health. Acute specific fevers are no bar to vaccination if necessary.

Very rarely the course of vaccinia is characterised by the appearance of a generalised vesicular eruption, the lesions appearing in successive crops, and passing through the stages of papule, umbilicated vesicle and crust. *Generalised vaccinia* of this type is usually febrile and occurs from 7 to 11 days after vaccination.

Accidental vaccinia is the term applied to fortuitous inoculation from a vaccinal lesion. Mothers are sometimes thus inoculated from their infants. The condition should be borne in mind. When occurring on the face, there is much œdema with swelling of the lymph glands, so that anthrax has been suspected. The vaccinated baby may also, by scratching, inoculate its own nose, cheeks or other parts of its body.

Protection afforded by Vaccination.—The immunity to small-pox which vaccination confers is not necessarily permanent. A child vaccinated in infancy should be revaccinated at the age of 7 years and again in adult life. Whatever their vaccinal condition, with the possible exception of those vaccinated within 2 years, persons coming into contact with small-pox should be revaccinated at once.

Since vaccinia has a shorter incubation period than small-pox, a person successfully vaccinated or revaccinated within 3 days of exposure to the latter disease will, in all probability, escape it. Ricketts makes the following state-

ment: "The period of incubation of small-pox, counting to the outcrop of the rash, may be taken as 14 days. If this period be divided into three intervals comprising 7 days, 3 days and 4 days, it will be accurate, in the main, to say that a successful vaccination done in the first period will wholly prevent the attack, done in the second will have more or less effect in modifying the eruption, and done in the third will merely add to the patient's troubles."

For a discussion of the evidence in favour of the practice of vaccination in the prevention of small-pox, the student is referred to the larger treatises.

CHICKEN-POX

Synonyms.—Varicella; Glass-pock; Water-pock.

Definition.—An acute infective disease, characterised by a rash which tends to appear in successive crops, each lesion passing rapidly through a papular stage to one of superficial vesiculation and subsequent partial pustulation. The lesions then desiccate and scab.

Ætiology.—Chicken-pox is universally prevalent and highly infectious. One attack usually affords complete protection, second attacks being extremely rare. It is mainly an affection of middle childhood, being uncommon after 10 years of age, but adults may contract it, and infants are not completely immune. Season and climate are not known to exert any influence on its incidence. It affects both sexes. Infection is in most cases direct by droplet spray, but articles of clothing may remain infectious for a considerable time, and the disease is sometimes carried by a healthy intermediary. The dried scabs can communicate the disease, probably by ingestion or inhalation. Like small-pox, chicken-pox is inoculable from the vesicles—but not easily. Convalescents from acute diseases, particularly from measles, diphtheria and scarlet fever, are believed to be peculiarly susceptible to chicken-pox. The disease occurs sporadically or in the form of limited outbreaks. The infective agent is unknown, but the association with herpes zoster lends support to the view that it may be a filtrable virus, identical with the neurotropic virus of that disease.

Pathology.—Micro-organisms occur in the pocks, and particulate bodies have been described similar to those seen in vaccinia and small-pox. Pure suspensions of these particulate or elementary bodies are agglutinated by the serum of convalescents from varicella or herpes zoster. The inflammatory lesions are more superficially situated in the skin than those of small-pox; but the process of vesiculation is similar. Loculation is indistinct, and umbilication exceptional. When the clear vesicles become clouded, but rarely before this, polynuclear and mononuclear cells are found in their contents.

Symptoms.—*Incubation period.*—This is usually a fortnight or a little more; but extremes of 11 to 23 days are mentioned.

In childhood the appearance of the eruption usually constitutes the first sign, and is taken to indicate the first day of the disease. In adults slight pyrexia and sometimes headache, shivering, and even pain in the back may precede the eruption for 48 hours. In exceptional cases, mostly in children, vomiting and convulsions have occurred.

Prodromal rashes are not very uncommon. An erythema, either patchy

or uniform, which may be punctate, sometimes precedes the eruption for some hours, and may be mistaken for scarlet fever; it avoids the face, does not blanch by the Schultz-Charlton test, and does not desquamate. The incipient papules of chicken-pox can sometimes be recognised in the erythema. Less frequently the prodromal rashes are measly or urticarial.

The eruption of chicken-pox appears first on the trunk, but soon spreads to the face, the scalp and the proximal parts of the limbs. Sometimes it is on the face that it is first noticed. Occasionally, and sometimes primarily, the eruption invades the mucous membranes, especially the fauces, soft palate and the pharynx. The spread of the rash does not conform to the orderly progress of small-pox, it appears in several crops on successive days; these may come out for 2 or 3 days in mild cases, for a week or more in those which are severe. The total number of lesions may be anything from a few to some hundreds. They are thickest on the trunk, especially on the back, and next to this on the face and in the scalp. They tend to invade the limbs from above downwards, being sparse and often small on the distal portions; a few vesicles are occasionally seen on the palms and soles. The axilla does not escape as in small-pox, and it is unusual for the rash to show an especial incidence over ridges or pressure points. Various forms of skin irritation may determine a local profusion of the rash.

The lesions are in turn macular, papular, vesicular and mildly pustular. The macules are very transitory, soon becoming rounded or ovoid papules of a pinkish colour and slightly salient, something like the rose spots of typhoid, or larger. Vesiculation rapidly ensues, and is complete in 24 hours or a little more. The vesicles seldom exceed a third of an inch in diameter. They look like translucent droplets, lying on rather than in the skin. An areola may or may not be present. On the scalp, forearms, hands and feet they may appear deeper, and show some hardness. Some assume oval or irregular outlines, especially when lying near creases or folds of the skin. On maturity the vesicles take on a pearly hue. When punctured, most of them collapse entirely, and umbilication is rare. Confluence of adjacent vesicles hardly ever occurs. Owing to its itchiness, the rash is often infected by scratching or rubbing, and then the lesions become larger and more inflamed. Otherwise the vesicles dry up into superficial brown scabs in a day or two, which on separating leave slight pink stains, but no appreciable pitting.

The appearance of the eruption in successive crops leads to the presence at the same time on a given area of skin of lesions in all stages of development, *i.e.* papules, vesicles, small pustules and scabs. On mucous membranes the vesicles soon rupture and leave shallow grey ulcers, often with red areolæ.

Slight pyrexia usually accompanies the appearance of the rash. Some cases are apyrexial throughout. Rarely the temperature rises as high as 103° or 104° F. Successive crops of spots may be accompanied by successive exacerbations of fever. Constitutional symptoms as a rule are absent.

Varieties.—Chicken-pox varies much in intensity. It may be so mild that only one or two pocks are recognised. As mentioned above, sharp invasive symptoms may mark its advent in the adult. There are three special varieties of the severe disease: (1) *Varicella bullosa*; (2) *Varicella gangrenosa*; and (3) *Varicella hæmorrhagica*. In *V. bullosa* the vesicles rapidly form large blebs, which on rupture leave painful raw surfaces. *V. gangrenosa*

is seen in debilitated children and those recovering from scarlet fever; large dark crusts form, and on separation reveal ulcers which may spread on the surface and in depth with great rapidity. Constitutional disturbance is severe, and pulmonary complications often supervene. Infection of the lesions with hæmolytic streptococci or virulent strains of the diphtheria bacillus should be suspected. *V. hæmorrhagica* is rare; hæmorrhages occur into the vesicles and intervening skin, and bleeding sets in from the mucous membranes. It is very fatal. Bleeding confined to the vesicles is not so serious.

Complications.—Laryngitis or slight bronchitis is present in some cases. Pocks on the conjunctivæ, vulva or prepuce may give rise to troublesome symptoms. Accidental septic rashes sometimes appear in the eruptive stage. Acute nephritis and arthritis are exceptional.

Nervous complications are very rare and usually benign. They are attributed to encephalo-myelitis, and chiefly affect children, usually occurring during the second week of the infection. Rarely they precede the eruption. The onset is acute and febrile; it may be accompanied by vomiting, vertigo and convulsion. Ataxia and tremor are more common than motor paralysis. With spinal lesions the picture may be that of a transverse myelitis. Optic neuritis, ophthalmoplegia and, very rarely, peripheral neuritis have also been recorded. In most cases recovery has ensued.

Herpes zoster is closely akin to chicken-pox. The zoster eruption may be preceded, accompanied, or followed by a vesicular rash indistinguishable from chicken-pox. Herpes zoster may also give rise in contacts, mostly children, to typical chicken-pox after an incubation period of from 12 to 21 days, and chicken-pox may follow inoculations from zoster vesicles. Conversely, for chicken-pox to give rise to herpes zoster, is a much less common event, which usually occurs in adults.

Diagnosis.—A mild or modified case of small-pox may erroneously be supposed to be chicken-pox, or chicken-pox with a profuse eruption and constitutional, or the rare hæmorrhagic, symptoms may be supposed to be small-pox. The differential diagnosis, in which the distribution of the rash is of primary importance, is considered in the article on small-pox. Here it may be stated that in a patient under 10 years of age, with well-foveated vaccination scars, a profuse eruption is generally chicken-pox, whilst a scanty eruption with well-marked invasive symptoms is more likely in these circumstances to be modified small-pox.

The erythematous prodromal rash may simulate scarlet fever; but other signs of this disease are wanting, and the chicken-pox eruption appears within 24 hours.

Certain skin diseases characterised by vesicles or bullæ may be mistaken for chicken-pox. These include insect bites, scabies, acne, impetigo, papular urticaria, pemphigus and erythema multiforme. Differential criteria are prolonged duration, recurrences, distribution, absence of fever, and of lesions in the mouth.

A varicella-like type of syphilide is known. It usually affects the trunk, is much more persistent, and is accompanied by other evidence of its nature.

Prognosis.—Death is very rare. The gangrenous form may prove fatal to debilitated children, and the rare hæmorrhagic form is said by most authorities to have a very bad prognosis.

Treatment.—Although most infectious in the pre-eruptive and early eruptive stages, patients should be isolated until every scab has separated—usually a period of 2 or 3 weeks. They should be confined to bed during the eruptive period. Skin irritation may be allayed by mild dusting powders, and it is sometimes advisable to fix the arms in light splints. It is rarely necessary to cut off the hair. Inflamed pocks may need fomentation with boric acid. Crusts which re-form may be removed by starch poultices and zinc or mercurial ointment applied. Gangrenous varicella may be treated by the use of scarlatinal and diphtheria anti-toxin, and drugs of the sulphonamide group.

When discharging patients particular attention should be paid to the scalp, as scabs may remain entangled in the hair. It is doubtful if lesions which have crusted several times are still infectious. The quarantine period for contacts is 3 weeks.

MUMPS

Synonyms.—Epidemic Parotitis; Infectious Parotitis.

Definition.—An acute infectious disease, characterised by swelling of the parotid, and sometimes of the other salivary glands, accompanied by constitutional disturbance which is usually mild. With the exception of orchitis, complications are infrequent, and a fatal termination is exceedingly rare.

Ætiology.—Mumps is endemic in most large centres of population throughout the civilised world. No climate is adverse and no race is immune. Children and young adults of both sexes are those usually attacked; but no age is entirely exempt, although the disease is rare in infants and in the aged. The mother has transmitted the disease to the fœtus *in utero*.

The malady usually appears during the winter or spring months. Outbreaks are generally localised, and often limited to particular schools, business houses or barracks. Infection is direct from patient to patient; but is sometimes conveyed by an apparently healthy intermediary, or by fomites. Epidemics of mumps may follow outbreaks of measles.

Pathology.—Mumps is attributed to infection by a neurotropic filterable virus. Invasion of the nervous system is thought by some to occur prior to invasion of the salivary glands. An alternative view is that a primary septicæmia is followed by localisation of the virus in susceptible organs. The disease can be passed to cats and monkeys by bacteria-free filtrates of saliva or puncture fluid from the swollen glands, and has been re-transferred from monkey to man. Older views were that certain diplococci or spirochætes were the infecting agents.

An interstitial inflammation is said to occur in the affected salivary glands, but parenchymatous inflammation is described in the case of the pancreas and the testicle.

Symptoms.—The incubation period is 3 weeks; but extremes of 14 and 35 days, or even 37 days, are admitted. A swelling of the parotid gland is usually the first indication of the malady, but this may be preceded for a day or two by pain and stiffness in the region of the masseter muscle, or by such prodromal symptoms as feverishness, shivering, and sore throat. Sometimes a meningeal reaction marks the onset (*Cerebral Mumps*).

The parotid swelling is at first unilateral, and commonly appears on the left side. It may increase for 2 or 3 days, forming an ill-defined, elastic swelling, which obliterates the sulcus between the mandible and the mastoid process, lifts the auricle away from the head in a characteristic manner, and extends forwards on the surface of the masseter. Only rarely is the skin over the gland either reddened or œdematous. The swelling subsides after a few days, sometimes very quickly, but a distinctive and, when present, highly diagnostic feature is the occurrence, 24 or 36 hours after onset, of swelling in the other parotid region, sometimes with fresh febrile disturbance ; or the submandibular and sublingual glands may be attacked. The interval between the invasion of the two parotid glands may extend to 4 or 5 days, or even longer ; but sometimes they are attacked simultaneously. Sometimes, too, the submandibular glands become swollen first, in which case palpation with one finger in the mouth and another below the jaw will reveal the acorn-like swelling. The parotid may escape, or may swell in its turn. When multiple bilateral glandular swellings are present the features become much distorted.

Moderate pyrexia (101° or 102° F.) may accompany the onset and persist for a day or two ; but the attack is often afebrile and the pulse rate hardly quickened. On rare occasions constitutional disturbance is severe, the temperature rising to 104° or 105° F., with delirium and circulatory depression.

The inflamed parotid gland may cause great pain on attempts to separate the teeth, to chew or to swallow. The secretion of saliva is often defective, but in some excessive salivation is noticeable. Injection of the orifices of the salivary ducts, pharyngitis, faucial congestion and even tonsillitis are sometimes observed at the height of the attack. Enlargement of the cervical lymph glands rarely occurs. Mumps may appear in so mild a form as to be hardly noticeable. At times the only salivary gland affected is the submandibular (submaxillary mumps), and occasionally orchitis is the sole manifestation of the disease. Invasion of the lachrimal gland has occurred.

With rare exceptions the swellings caused by mumps neither suppurate nor persist, although, occasionally, the parotid is said to be several months in resolving. Relapse occasionally occurs.

During the period of glandular swelling the blood usually shows a moderate leucocytosis, a characteristic feature being a relative and absolute increase in the number of lymphocytes. The supervention of orchitis does not invariably alter the blood picture, although, according to some authorities, it may give rise to an increase in the number of polynuclear cells.

Complications.—*Orchitis* occurs in 15 to 30 per cent. of the males. It affects boys about the age of puberty and young adults ; in childhood it is rare. Sexual over-activity is held to be a definite predisposing factor. The seventh or eighth day of illness is the usual time of onset ; but it may appear 2 or 3 weeks later. In some instances orchitis precedes the inflammation of the salivary glands. The condition is really an epididymo-orchitis. Where surgical attempts have been made to relieve tension by decapsulation or incision, effusion has been found in the tunica vaginalis, the testis engorged, and the epididymis deep red. The onset is characterised by pain in the testis, which soon becomes swollen. Delirium, vomiting, collapse and considerable fever may accompany the testicular inflammation. The temperature may rise abruptly to 103° or 104° F. Fortunately the complication is usually one-

sided, but in 10 to 20 per cent. of cases the other testicle is attacked in turn. Orchitis may be accompanied by œdema of the scrotum, swelling of the spermatic cord and enlargement of the inguinal glands. Exceptionally a urethritis accompanies the testicular swelling. Subsidence of orchitis within a week is the rule, the temperature falling rather abruptly. Suppuration is very rare; but relapse sometimes occurs. When bilateral orchitis occurs before puberty the development of the individual is usually checked; rarely feminism has been reported. In the adult, even when both testes appear atrophic, spermatogenesis may return after many months.

In the female, corresponding complications are ovaritis, shown by ovarian pain and tenderness, inflammation and œdema of the vulva and mastitis. The latter has also occurred in the male.

Pancreatitis is a much less common complication than orchitis. It should be suspected when acute abdominal pain, fever, vomiting and epigastric tenderness, occur as sequels to the parotid swelling, which under these circumstances may show a rapid subsidence. Sometimes the swollen pancreas may be felt, but often its presence is masked by abdominal rigidity. The bowels are constipated, the stools may be fatty, or even contain blood. The urinary diastase is increased, and glycosuria may occur. The blood sugar may be raised. Jaundice is rare. The onset may be accompanied by alarming collapse. Fortunately recovery has occurred in most cases. Diabetes as a sequel to mumps is very exceptional. It should be noted that in mumps a raised diastatic index may occur without clinical evidence of pancreatitis, and is attributed to infection of salivary glands.

As regards the *nervous system*, symptoms of meningo-encephalitis may occur towards the end of the first or during the second week, and have even been known to precede the appearance of the glandular swellings. Sometimes on recovery such disabilities as aphasia, hemiplegia, monoplegia or ataxia persist. Rarely a general paralysis of the limbs with loss of deep reflexes, attributed to peripheral neuritis, occurs. Weakness of the muscles supplied by one facial nerve rarely accompanies the parotid swelling.

Acute mania and other forms of insanity are rare sequels.

An excess of lymphocytes may be found in the cerebro-spinal fluid, and is not uncommon during the first fifteen days of mumps, even in the absence of definite meningeal symptoms.

Certain affections of the *organs of special sense*, although uncommon, deserve mention on account of their importance. Quite apart from deafness, due to the occasional occurrence of otitis media, true nerve deafness may occur unaccompanied by signs of middle ear disease. The deafness is of sudden onset, and when accompanied by nausea, vomiting, tinnitus and inco-ordination it is attributed to hæmorrhage or exudation within the labyrinth; but it may occur without any labyrinthine symptoms. Fortunately the deafness is usually unilateral, for it is incurable.

Papillœdema and optic atrophy with loss of vision are other important sequels. Iridocyclitis, paralysis of certain extra-ocular muscles and loss of power of accommodation may also at times ensue; these mainly terminate in recovery after a variable time.

Among other possible complications may be mentioned epistaxis, bronchitis, pneumonia, pericarditis and arthritis. Albuminuria is not uncommon and nephritis sometimes occurs as late as 4 or 5 weeks after the salivary

swellings; uræmia has been responsible for death in rare instances. Gangrenous appendicitis has also been noted.

Suppuration in the parotid gland, gangrene of the gland, cellulitis of the neck and floor of the mouth, œdema of the glottis, and suppuration of the cervical lymph glands are very rare occurrences, which are generally attributed to superadded septic infection. Relapses, characterised by a recurrence of the glandular swelling after a distinct interval, are not very uncommon. Although one attack of mumps usually protects the individual for life, second attacks are not unknown.

Diagnosis.—In the presence of an epidemic this presents little or no difficulty; but the true nature of the infection may be overlooked when the parotid swelling is insignificant, or when the disease primarily affects the submandibular or sublingual glands, or again when orchitis or even pancreatitis constitutes the first, and perhaps the only, manifestation.

Parotitis, usually unilateral, and attributed to ascending duct infection, is a well-known complication of certain fevers, and of some abdominal diseases; but it also may be primary and assume a recurrent form. This is distinguished from mumps by the circumstances under which it occurs, and by the fact that it is not contagious. It generally ends in suppuration, and is accompanied by a polynuclear leucocytosis. Swelling of the salivary glands may follow the administration of certain drugs, such as iodide of potassium and pilocarpine.

A painless enlargement of the parotid and lachrymal glands, of great chronicity, occurs in Mikulicz's disease. In uveo-parotid fever irido-cyclitis accompanies the parotid swelling.

Inflammatory swelling of the higher cervical glands, especially when accompanied by peri-adenitis and œdema, may be mistaken for mumps. Swelling of this character occurs in certain cases of diphtheria, and also in scarlet fever. Careful attention to the history, proper examination of the fauces, and search for rashes should eliminate this error. Enlargement of the pre-auricular lymph gland due to lesions about the nostrils and angle of the mouth, and the swelling caused by periostitis of the lower jaw, or otitic infection of a zygomatic air-cell, may superficially resemble inflammation of the parotid.

When the submandibular and sublingual glands alone are swollen the distinction from lymphadenitis may be difficult. In such cases extension to the opposite side indicates mumps, as also does the transitory character of the swelling.

In glandular fever, which is an acute infective adenitis of the cervical and other lymphatic glands, the salivary glands are not involved.

Prognosis.—The mortality from mumps is remarkably low. The majority of deaths occur in children under 5, especially in infants, usually from some complication. Cases of mumps in pregnancy may also prove fatal.

Treatment.—Mumps is infectious for 2 or 3 days before the swelling appears, and isolation for not less than 2 weeks from the onset is advisable, provided that one clear week has elapsed since the subsidence of the glandular enlargement. Contacts should be removed from exposure and either isolated for 28 days or supervised from the fourteenth to the twenty-eighth day, unless they have already had the disease. Thirty c.c. of whole blood or 15 c.c. of serum of convalescents, if given on first exposure, seems to prevent infection.

Attenuated attacks are difficult to produce, but see also remarks under measles (p. 141). On account of the liability to orchitis, it is better to have mumps before puberty than after.

The patient should be isolated and confined to bed. The incidence and severity of orchitis are said to be less in those who are not allowed to get up until the time at which this complication usually appears is past. Foods which need no mastication are indicated during the acute stage. The mouth should be kept clean. Pain may be relieved by local applications and acetyl-salicylic acid. The inflamed testicle should be enveloped in cotton-wool and suspended or supported by a small pillow. If pancreatitis be suspected, fomentations may be applied to the abdomen, small doses of opium administered, and the diet strictly restricted to fluids. Delirium and pyrexia are met by sponging, wet-packs or the ice-cap. Repeated lumbar puncture is beneficial in meningo-encephalitis.

CHARLES R. BOX.

INFLUENZA

Definition.—An acute infectious disease of short duration, existing in pandemic and epidemic form, with sporadic outbreaks. It is characterised by sudden onset, pyrexia, headache, pains in the back and limbs, and a tendency to inflammatory complications in the respiratory system.

Ætiology.—Are the protean features of disease which are at present included in our conception of influenza all manifestations of the same *materies morbi*? Are there influenzas rather than influenza? What causative factors determine the pandemics of the disease during which the case-incidence rises so rapidly and so enormously? What is the association between benign influenzal catarrhs of endemic and sporadic occurrence and the pandemics which decimate whole races of mankind? These are questions which have baffled epidemiologists and bacteriologists for many years, nor did the exceptional opportunities for observation and research afforded by the pandemic of 1918–19 serve entirely to answer them.

We are ignorant of the reasons why a state of relative quiescence in regard to the incidence of the disease—scattered sporadic cases and mild epidemics—suddenly blazes up into a devastating pandemic. We know that when this conflagration arrives the disease becomes very highly infectious in character, that its virulence is enormously increased and that the usual close association with catarrhs and seasons and latitudes and lowered general resistance is no longer observed. Age gives no security at such times; witness both the high case-incidence and high case-mortality in young adults during the pandemic of 1918–19.

A previous attack of the disease gives little or no protection; according to some authorities the reverse is the case.

In the matter of its relation to other catarrhal states the absence of definite criteria makes it impossible to be precise in diagnosis. It is only in the presence of a severe and widespread outbreak that the guide of probability is of assistance in this respect.

Andrewes and his co-workers at the National Institute for Medical Research in 1933 isolated from the nasopharyngeal discharge of influenza patients a

virus which is capable of infecting ferrets. When human influenzal garglings are dropped into the noses of ferrets they become ill in 48 hours and the disease has been transferred from the experimental animals to the experimenter. Further, they have shown that patients who have had influenza recently develop antibodies in their blood which kill, or inactivate, the virus. Neutralisation tests with antisera prepared from human strains prove that different serological varieties of the virus exist. Pfeiffer's bacillus is to be regarded as the commonest secondary invader of the infected tissues. Next to Pfeiffer's bacillus, the micro-organisms most commonly found in association with the disease are streptococci of the hæmolytic kind, pneumococci, *M. catarrhalis* and *Staphylococcus aureus*. It seems certain that many of the most serious and fatal cases owe their lethal character to virulent streptococci. Pfeiffer's bacillus occurs in cases of disease quite other than clinical influenza—septic endocarditis, sinusitis and meningitis. The bacillus is of very small size, is Gram-negative in staining reaction, grows with difficulty on ordinary media and has low vitality outside the human body. A special feature seen in regard to it is the fact that, when present in acute cases of influenza, it usually occurs in enormous numbers in the infected tissues and their secretions.

Symptoms.—So far as can be judged the incubation period is, with considerable constancy, something from 24 to 48 hours. A marked feature of the disease is the abruptness of the onset. So abrupt is it at times that the victim is striken down, as it were, in the street, and, from being quite well he is, within a few hours, prostrated and already suffering the maximum discomforts of the disease. The temperature rises rapidly; there is often a rigor. The chief symptoms are racking headache, intolerable aching pains in the loins and limbs, dryness and irritable redness of the mouth and fauces, and a distressing dry cough. An erythematous rash is not uncommon.

Although the symptoms are protean, it is customary to describe certain types of case that are frequently met with, dependent largely upon the particular tissues and functions which suffer the chief results of the infection. It is to be noted that different outbreaks of the disease are prone to be characterised by different clinical types, as also by differing degrees of severity.

1. *The febrile type.*—In this variety of the disease the chief features are pyrexia, with associated malaise, headache, pains in the back and limbs and a moderate degree of catarrh of the upper air-passages. In many cases this type differs only from the "common cold" in its more abrupt onset, its higher degree of pyrexia, its disproportionately severe prostration and its relatively "dry" form of catarrh. The eyeballs are often painful, with some conjunctivitis, and the fauces are often red and slightly œdematous. Cough is often present, with few or no associated pulmonary signs. The pyrexia lasts for a variable time, usually 4 to 6 days; the temperature chart may show two peaks in the 24 hours. It is unusual to see the fever prolonged past the eighth day without some focal complication, generally pulmonary. Defervescence is quite frequently by crisis, but this is by no means the rule.

2. *The respiratory type.*—This is the form of the disease which is most prevalent in pandemics, and, when severe, it is the form to which the mortality is chiefly due. Somewhere about the fourth day of the disease it becomes obvious that the catarrhal process is growing troublesome, with more definite

involvement of the larynx, trachea and bronchial tract. A dry catarrh of the larynx and trachea, with pain and distressing cough, may constitute the main feature of the disease. In many cases the temperature falls about the third or fourth day, to rise again concurrently with a definite exacerbation and extension of the catarrh. The respiratory involvement does not tend to remain localised as a bronchitis, but involves the lung tissue, leading to a bronchiolitis and, in many cases, an alveolitis also. Then ensue the signs of acute pulmonary congestion which are so characteristic of the disease, and cause so much anxiety for fear of untoward developments. The respiratory manifestations of influenza infection extend from laryngitis and tracheitis through bronchitis to lobular and lobar pneumonia and pleurisy, both "dry" and with serous or purulent effusion. But the dominant feature, rarely absent in any really severe case, is a condition of capillary bronchitis with intense pulmonary congestion. This may be unilateral or bilateral, is more often basal than apical, but is not seldom universal. The physical signs are copious fine râles (crepitation), with impaired vesicular sound, and, less often, impaired percussion tone. This condition may well be termed the essential lesion of the disease, for even when actual consolidation of the lung is present, this is quite often an incident by comparison, and if the patient dies, he dies with the consolidation rather than of it.

Cough is usually a very troublesome symptom in this type of the disease, and is often quite independent of the need to expectorate. The sputa vary considerably. They may be quite absent, even in cases where there is widespread lung congestion. When present they are generally of a kind that corresponds with the nature of the chief lesion, whether tracheitis, bronchitis or pneumonia. Two special kinds of sputa are very typical of influenza, and they are seen frequently during epidemics. (*a*) Bright, pink, frothy mucus, sometimes produced in large amount, it may be as much as a pint in 24 hours. This rose-red mucus results from acute inflammatory œdema of the lung. It may be expelled involuntarily during cough and sometimes it spurts from the nostrils. (*b*) Tenacious mucus, less viscid than in lobar pneumonia, and more copious, differing also in colour which is of several hues—red, brown, saffron and various shades of green, all of these being occasionally present at the same time. Seen in a white earthenware vessel these sputa are very striking and in a high degree diagnostic.

3. *The malignant type.*—This severe and very fatal form is almost confined to pandemic or to epidemic periods. The patient is gravely ill from the onset, or soon after, with intensely toxic symptoms, cyanosis of a peculiar character ("heliotrope cyanosis") and rapid development of heart failure before focal manifestations have time to show themselves—unless it be the presence of copious fine râles of the kind referred to in (2). The duration of this type of case varies from 48 hours up to a week, and no measures of treatment, however prompt, serve to avert the almost certain issue. It is asserted by reliable observers that death may occur even within the first 24 hours from the onset.

4. *The gastro-intestinal type.*—More strictly, perhaps, gastric and intestinal types. These types are less common in pandemics and epidemics than in small endemics and in sporadic cases. The gastric cases are quite common, and some of the milder endemics seem to "breed true" to a remark-

able degree in this respect, leading to a very constant clinical picture of an illness with acute, even abrupt, onset, vomiting, marked anorexia, epigastric and umbilical tenderness, and general prostration. Considerable difficulty often arises in diagnosis (see p. 171), even when there are several cases of a similar kind prevalent.

Jaundice of the catarrhal kind is not very uncommon as a complication. Some of the intestinal cases give no less difficulty, and when severe the likeness to typhoid fever is sometimes very close indeed. Tympanites, diarrhœa and enterorrhagia, associated with continued high fever and a leucopenia, may deceive the very elect.

5. *A nervous type* has been described, but it is perhaps more correct to say that a variety of nerve symptoms may arise both during and after the acute infection, rather than that a recognisable clinical picture is produced (see p. 171).

Complications and Sequelæ.—These are both numerous and important. Indeed, if we except the malignant cases and the very severe respiratory cases occurring during pan- and epi-demic periods, it may be said that the importance of the disease lies more in its complications, and perhaps still more in its sequels, than in the stage of infection proper. For convenience these disabilities may be grouped as follows:

1. *Respiratory.*—The main extensions of the catarrhal process have been already referred to, as also has the occurrence of pleurisy. Sinusitis may be mentioned here; it is both common and troublesome. Otitis media also occurs. Asthma sometimes appears for the first time in a patient's life after influenza, and the age of the sufferer may be much more advanced than is usual with asthma generally. Pulmonary tuberculosis not seldom shows itself also for the first time in the same association. The most frequent sequel of all, however, is the maintenance of a state of chronic congestion or bronchiolitis at one base or both bases of the lung. This condition, which may persist for years, ebbing and flowing with the seasons and with the occurrence of intercurrent catarrhal infections, may prove the starting point of bronchiectasis.

2. *Circulatory.*—Perhaps the most serious complication and sequel is referable to the heart. Some degree of dilatation is very common during a severe attack of the respiratory type, and this condition is apt to prolong convalescence in a very tedious fashion. In some cases a bradycardia due to heart block has been observed: the prognosis in this condition is good. But a much more common form of heart disability is that which arises insidiously after the patient begins to resume his usual routine of life. He is the subject of palpitation, præcordial distress and a sense of undue fatigue with slight effort. In women this state of things is complicated often by nervous symptoms, and attacks of breathlessness and a sense of impending collapse are quite common. As there is frequently in addition a considerable degree of true nervous prostration with mental depression it becomes exceedingly difficult to decide to what extent the heart is really affected. Physical signs in these cases are wholly inadequate; quite often they are absent altogether. Although, with care and encouragement, many of these cases get quite well after a time, a large number unfortunately become more or less permanent "heart invalids." It is not clear what is the exact pathology of the "influenzal heart," but it is perhaps near the truth to consider it in

the main a toxic myocarditis; though to what degree it is the nervous mechanism, and to what degree the heart muscle, that suffers we cannot say.

Vasomotor troubles are not uncommon and often complicate the heart condition. Phlebitis may occur.

3. *Nervous.*—The most common complication is the intense depression from which the patients so frequently suffer. In a few cases this leads to actual mental instability and, in fewer still, to suicide. The depression may continue for a long time after the acute illness is over. So common a symptom is it that patients themselves often consider the nature of a recent febrile illness to be definitely established as influenza because of this resultant depression. And they are probably in most cases correct. The headache, which is another very constant accompaniment of the illness, may be so severe as to raise the question of meningitis; it quite commonly leads to some delirium in patients whose nervous system is, in health, none too stable.

A true meningitis occurs now and again with *H. pfeiffer* in the cerebro-spinal fluid and a clinical picture that is unequivocal. Encephalitis and myelitis are described, but here, again, the diagnosis—from epidemic encephalitis—must always be a difficult matter.

Many other nerve conditions are described by authors. Perhaps neuritis, of both single and multiple types, is the most common. One of us (H) has seen a condition indistinguishable from paralysis agitans follow a severe attack, which ended in complete recovery after several months.

Diagnosis.—During pan- and epi-demics the diagnosis is, as a rule, not difficult, especially when the case if very severe. "Filming" the sputa in a case of the respiratory type is a valuable aid to diagnosis. If the highly characteristic condition of bronchiolitis with copious fine râles referred to on pp. 168–169 be present in a febrile illness with nerve prostration and general toxæmia, the diagnosis is fairly certain.

The gastric and intestinal cases, and especially the latter, present more difficulty than do the respiratory cases. The gastric cases resemble food-poisoning not a little, and appendicitis may require careful consideration in patients with abdominal tenderness, pain and vomiting, of acute onset. From typhoid fever a severe intestinal case with hæmorrhage and enlarged spleen can only be distinguished by absence of agglutination and negative blood culture. A leucopenia is present in both diseases.

The diagnosis of milder cases of influenza, if occurring in sporadic fashion, is frequently a frank admission that it is well to give the patient and his friends a label to his disease. There are so many causes of an acute febrile illness with malaise and slight catarrh that exact diagnosis may not be possible.

A word of warning is perhaps necessary in respect of diseases known to be prevalent coincidentally with outbreaks of influenza. Thus, true pneumococcus pneumonia, whether lobular or lobar, is not infrequently called influenzal when this latter disease is epidemic. Of greater importance is the fact that waves of incidence of influenza and poliomyelitis and encephalitis sometimes concur. If the practitioner's attention is bent only upon the former disease he is apt to put down to it certain serious nerve lesions that really belong to the latter.

Treatment.—PROPHYLACTIC.—As we do not know the factors leading to

the production of influenza epidemics we do not know how to prevent them. When they arrive we can, to some extent, control them by efficient quarantine, by early diagnosis and notification and by a proper system of hospitalisation, adequate to the peculiar features presented by the disease. In regard to individual prophylaxis it was formerly held that to keep generally "fit" was a good protection against infection. But recent experience does not confirm this view: influenza attacked the strong as well as the weak; indeed, the robust young adult fell a victim by preference, though this may have been partly because he was more open to infection by virtue of the conditions of his life. The age-mortality as well as the age-morbidity during the 1918-19 pandemic seemed to make it clear that some method of specific immunisation is essential before we can hope to protect against infection. The available vaccines for protective inoculation aim at raising resistance against the secondary infections. Regarded in this light they are rational. So far the virus is not available for specific prophylaxis.

CURATIVE.—1. *General Measures.*—With the onset of symptoms the patient is put to bed and is kept there until the temperature has reached normal and has remained there for 48 hours. He is only allowed up if examination of the heart and lungs, and a review of his general condition, reveal nothing abnormal. If the attack has been severe, the patient should be induced to remain in bed for a week after the temperature is normal, because relapses are common, and are often more dangerous than the original attack. This rule of practice should certainly have no exception in the case of patients over 50 years of age.

The largest available room is chosen, and the bed is placed well away from the walls. Blinds, curtains and screens are dispensed with, and the windows are kept open day and night. The room temperature is kept as near to 60° F. as possible. If the ideal of free ventilation with warmth cannot be secured in the room, then warmth must be sacrificed rather than ventilation. Neglect of fresh air not only seriously prejudices recovery in the event of pulmonary complications, it undoubtedly tends much to induce them. It is probably the most important point in the general treatment.

The diet is confined to warm fluids, given frequently, but easily digested solids are allowed if the stomach tolerates them; efforts at "feeding up" the patient are to be deprecated. Unless the patient is elderly, alcohol is not needed in the early stages of the disease when there are no complications. The bowels are made to act thoroughly by a double dose of the patient's customary aperient. If he has none, he is given ¼-grain doses of calomel every hour for 4 doses, and this is followed by a saline draught. The patient is sponged all over with warm water twice daily.

2. *Drugs.*—There is no drug which acts as a specific. Aspirin and Dover's powder in 10-grain doses may be given together as early as possible and may be repeated once or twice every 6 or 8 hours. This may be followed by a simple diaphoretic mixture. The sulphonamides are only of service when secondary infections are present, and especially when these are of a pulmonary nature.

3. *Treatment of Symptoms.*—If the headache is severe, phenacetin gr. 10 with caffeine gr. 2 may be given 4-hourly for 4 doses. If the stomach gives trouble, and the tongue is foul, sod. bicarb. and sod. sulphocarb., of each gr. 10, with glyc. acid. carbol. min. 10, may be given 6-hourly with the

feeds, well diluted. For vomiting, all feeds are reduced to a minimum, or omitted entirely for 48 hours, giving sips of hot water only, with minim doses of liq. iodi mitis in 60 min. of water hourly for 6 or 8 doses, and one pint of normal saline is introduced into the bowel two or three times during the period of starvation.

Distressing and persistent cough is often the most difficult problem. Local applications to the chest are often of service. If the origin of the cough is irritability of the upper-air passages inhalations of tinct. benzoini co. 4 parts, with menthol or eucalyptus 1 part, are useful. Failing this a spray containing chlorbutol (chloretone) and menthol, 2 per cent. of each in liquid paraffin, may be used to the nose and throat. In the "essential cough" of the disease, syr. cocillanæ co., syr. codeinæ and tinct. terp-heroin. co. are of some value. In intractable cases relief may follow syr. chloral min. 30, ammon. brom. grs. 10, with ext. glycyrrhiz. liq. min. 20, etc., in 4-hourly doses for 4 doses.

Insomnia calls for a general review of the whole programme—ventilation, control of pyrexia, posture, food, stimulants, etc. Failing attention to these things, a sedative draught of ammon. brom. grs. 20 and tinct. valern. min. 20 may be tried; if not successful, min. 120 doses of paraldehyde, with tinct. quillaiæ and tinct. aurantii to cover its unpleasant taste. Failing this, again, chloral and bromide may be given, since drugs of the barbitone group are better avoided.

4. *Treatment of more Severe Cases and of Complications.*—(*a*) *Intensely toxic cases, with hyperpyrexia.*—Attention to good ventilation should be redoubled. The thermometer and not the patient's sensations must be the guide to the amount of bedclothes. "Cradling" is often very useful, as also is tepid or spirit sponging. In cases in which the temperature is even then resistant, the cold pack should be used and repeated if necessary. Febrifuge drugs are to be avoided in such cases. Stimulants are now advisable to counteract circulatory failure.

(*b*) *Pulmonary cases.*—Linseed and mustard poultices are of service here, or kaolin poultice, applying these to the most "congested" parts. Volatile stimulants, sedative expectorants and diaphoretics are the most useful drugs: sp. ætheris co., the iodides in small amounts, bromide and chloride of ammonium, tinct. senegæ, tinct. belladonnæ and liq. ammon. acetatis. Ammon. carb. should only be used where sputa are present, and large doses are of doubtful value at any time. Oxygen delivered through a nasal catheter is useful in all severe cases with cyanosis.

(*c*) *Heart failure*, to be estimated more by the general state of the patient (facies, cyanosis, dyspnœa, delirium, posture) than by pulse-frequency or physical signs, is met by alcohol, strychnine injections, nikethamide (coramine) subcutaneously, and, as a measure supplementary to these, strophanthin $\frac{1}{500}$ grain in 20 minims of sterile saline solution, injected slowly into a vein of the arm and repeated, if indications are still present, in 8 or 12 hours.

(*d*) The *post-febrile stage*, often a stage of cardiac and nervous exhaustion in severe cases, requires some caution. Strict recumbency should be enjoined, with careful feeding, stimulants and tonics.

FOOT-AND-MOUTH DISEASE

Synonyms.—Aphtha Epizootica ; Epidemic Stomatitis.

Definition.—A contagious disease, due to a virus, communicated from animals to man, characterised by mild pyrexia, swelling and vesiculation of the tonue and buccal mucosa, accompanied, sometimes, by a vesicular eruption on the hands and fingers.

Ætiology.—Man is relatively insusceptible to infection which, however, is of almost world-wide distribution amongst cattle, pigs and sheep. Up to 1872 there were but few reported cases of supposed foot-and-mouth disease in man. In that year a more virulent form appeared in cattle, and human cases were more frequently described. Bussenius and Siegel in 1897 analysed the reports of more than 1500 cases ; the majority are sporadic or occur in small groups.

Three types of virus have been recognised by immunological tests: antiserum of types O and A (Vallée and Carré) and C (Waldman) has no protective influence against infection by either of the other two types. In cattle the virus enters through the mucosa of the alimentary tract, a septicæmia ensues during which all the secretions and excretions of the body become infective, with subsequent localisation in the specific lesions. The virus can remain active on hair or in soil for a month.

Foot-and-mouth disease is communicated to man: (1) By the consumption of unboiled milk from a cow suffering from the disease. (2) By direct inoculation: from (*a*) the saliva if infected animals, or (*b*) milking cows suffering from the specific eruption on the teats or udders. Those affected are for the most part either children, milkers, or cowmen.

Symptoms and Course.—The incubation period of foot-and-mouth disease in man appears to be the same as in cattle, namely, 2 to 5 days. Whatever the route of infection the disease sets in with slight headache, a mild grade pyrexia and dryness of the mouth. This state continues for a few days, and is then succeeded by a period of salivation and the development of the characteristic lesions—vesicles upon the lips and tongue, which contain yellowish-white turbid fluid. In 48 hours or so the vesicles rupture with the formation of superficial ulcers having a smooth purplish base. There may be considerable swelling of the tongue and mouth, which, with the pain, renders mastication and swallowing difficult. At the same time a crop of small vesicles may appear around the nails and on the hands ; they increase rapidly in size, become pustules and then scabs, which fall off early in the second week. In adults the disease runs a mild course with recovery in from 7 to 10 days. In young children, fed on infected unboiled milk, the condition is prone to be more severe because of the liability to anorexia, gastro-enteritis and diarrhœa.

Treatment.—This is entirely dietetic and symptomatic. A weak solution of permanganate of potash is perhaps the best local application ; strong antiseptics, whether to the mouth or to the hands, must not be employed.

HORDER.
A. E. GOW.

PSITTACOSIS

Definition.—An acute infective disease derived from parrots, resembling typhoid fever in its mode of onset and general features, but presenting also signs of an atypical pneumonia.

Ætiology.—The disease is derived from parrots (hence its name), the green Amazonian parrot being usually the source. Grey parrots, however, are not exempt, and love-birds also suffer from it. Infection is usually conveyed direct from a sick parrot to a human being who has been in close contact with the bird, but a parrot dead of the disease is also infectious. It is probable that a healthy parrot can act as a carrier. Infection from one human being to another, although it seems to occur occasionally, is very rare. In 1892, Nocard isolated a bacillus from the bone-marrow of an infected parrot, and named it the *Bacillus psittacosis*; it was afterwards shown, however, that this was identical with the *B. œrtrycke*. In none of the cases in recent outbreaks, however, has there been any evidence of the presence of this bacillus, and it is now proved by the work of Bedson that the infecting organism is a filtrable virus.

Pathology.—The post-mortem appearances are those of a severe septicæmia, with characteristic changes in the lungs. The latter do not present the picture of classical lobar pneumonia or broncho-pneumonia, but of a "peculiar hæmorrhagic vesicular pneumonia, complicated by pulmonary thrombosis and free from bacteria" (Turnbull). In addition, areas of mucopurulent bronchitis and broncho-pneumonia may occur from secondary infection. The gastro-intestinal tract is usually free from severe inflammation.

Symptoms.—The disease usually sets in rather suddenly after an incubation period of probably about 10 days. The rise of temperature is commonly abrupt, and headache is pronounced. Epistaxis sometimes occurs. The patient is generally dull and apathetic, and passes into a condition suggesting a typhoid infection. The abdomen may be slightly distended, and there may be a little sickness and diarrhœa at the outset. The spleen is not palpable, but in some cases a few rose-spots have been observed which are of a smaller size than the spots in typhoid fever. Pulmonary symptoms may be present from the outset, or appear after the disease has lasted some days. Cough is often frequent and troublesome, but, as a rule, there is little expectoration. Respiration may be rapid, but the pulse-rate remains low. The signs in the lung range from those of a bronchial catarrh up to massive, sometimes very dense, consolidation. Pleuritic signs are very rare. The disease usually lasts from 2 to 3 weeks, and the temperature may fall abruptly. Temporary rises of temperature during convalescence are often observed, and there may even be a complete relapse.

Diagnosis.—Clinically the disease can be suspected on circumstantial evidence. If one has a patient who presents a general resemblance to a case of typhoid or paratyphoid fever, but whose blood does not give the agglutination reactions, who presents also pulmonary symptoms and signs of an atypical sort, and who has also been brought into close contact with a sick parrot or love-bird, then the diagnosis is justified. A deceptive feature in the diagnosis from typhoid, however, is that sometimes the agglutination reaction to the *B. typhosus* is positive. Indeed, a positive agglutination to

one strain of typhoid organism occurring early in the disease and in a high degree of dilution is rather suggestive of psittacosis than otherwise. The blood cultures, however, are negative. It may be impossible at the outset to distinguish psittacosis from influenza, but the supervention of pulmonary complications *within the first few days* is in favour of the latter. Bacteriologically the existence of the disease is proved by the presence of a positive complement fixation reaction in the patient's serum.

Prognosis.—The mortality varies considerably in different epidemics, but may perhaps be put at about 1 in 6. Young people usually recover. Severe involvement of the lungs and failure to maintain a relatively slow pulse are unfavourable factors.

Treatment.—There is no specific treatment, and the use of convalescent serum has proved disappointing. Patients should be nursed with the usual precautions adopted in a typhoid case, but need not be further isolated. Special signs and symptoms must be treated as they arise.

PROPHYLAXIS consists in forbidding the importation of infected birds; cages should be kept clean, and the birds should not be fondled. A bird which falls sick should be immediately isolated or destroyed.

ROBERT HUTCHISON.

YELLOW FEVER

Synonyms.—Febris Flava; Typhus Icteroides; Yellow Jack; Black Vomit; Kendal's Fever; Fièvre Jaune; Fièbre Amarilla.

Definition.—An acute infectious disease of sudden onset, endemic in parts of tropical America and West Africa, characterised typically by pyrexia, vomiting, a slow pulse relative to the temperature, early albuminuria, and a tendency to hæmorrhages and jaundice. It is caused by a filtrable virus and, with the exception of jungle yellow fever, is transmitted to man by the common domestic mosquito, *Aëdes ægypti* (*Stegomyia fasciata*).

Ætiology.—The endemic haunts of yellow fever have been curtailed in recent years by the destruction of its intermediary host. A circle with its centre in the Isthmus of Panama, and embracing the northern parts of South America, the West Indian Islands and the southern parts of North America includes most of the area of its late prevalence in the Western Hemisphere. Recent work has shown unsuspected reservoirs of infection in the Amazon basin and in parts of Columbia, Venezuela and Brazil. The disease is widely endemic in West Africa, while cases occur far in the interior from the coast of Senegal eastward for over 3000 miles, and northward to the Sahara desert. Stokes, Noguchi and Young all died when investigating it there. Probably infection was acquired by direct contact with infective blood rather than by the mosquito vector, *Aëdes ægypti*, which Carroll in 1900 showed would transmit the disease after a period of 12 days, provided it was fed on the blood of a yellow-fever patient during the first 3 days of fever. Reed and Carroll also found that the injection of 0·1 c.c. of blood from a yellow-fever patient collected during the first 3 or 4 days of fever produced the disease, and that the serum after filtration remained infective. *Aëdes ægypti* bites in the day time, and is most aggressive in the early morning. Its domestic habits make it an efficient vector, as the larval stages develop

mainly in artificial containers in or near human habitations. Males and females are equally susceptible, and infection in childhood is common. This type of urban and rural yellow fever differs from jungle yellow fever, which is found in or near tropical forests in Brazil, where *Aëdes ægypti* is absent. Adult males who work in the jungle are mainly infected. Wild jungle mosquitoes have been found to harbour the virus, but the common vector is not yet known. Monkeys and probably other animals play an important rôle as reservoir hosts. In 1927 the West African Yellow Fever Commission found that the Rhesus monkey (*Macaca mulatta*) was susceptible, only 1 out of 30 monkeys surviving. One attack confers lifelong immunity and 0·1 c.c. of convalescent human serum protects monkeys. The virus, if dried, will keep for months; it penetrates the intact skin of both man and monkeys, but is no longer demonstrable in the blood and viscera after the fourth day.

The diameter of the virus as determined by filtration through collodion membranes lies between 17–28 millimicrons. It possesses two qualities, viscerotropism and neurotropism; when both are present it is known as "pantropic" virus. In 1930 Theiler found that if pantropic virus was inoculated intracerebrally into susceptible mice they developed encephalitis, unless immune serum was simultaneously injected. After repeated passage through the brain of mice the virus lost its viscerotropism or capacity to attack the abdominal and thoracic organs, and was converted into a neurotropic virus with fixed characters. Injection of this virus or of pantropic virus attenuated by tissue culture immunises against yellow fever and is the basis of prophylactic immunisation.

The fact that immune bodies are demonstrable in the blood of yellow fever cases shortly after infection, and persist permanently in recovered cases has been utilised to determine the endemic incidence of the disease. Mice are employed for the purpose. The protection test, as developed by Sawyer and Lloyd, consists of an intracerebral inoculation of starch solution, followed by the intraperitoneal injection of virus and the serum to be tested. In the absence of immune bodies in the serum the virus produces encephalitis and death within a fortnight; if immune bodies are present the animal remains unaffected. This test has been of great value in affording an index to past epidemics, and in accurately determining the past and present geographical distribution of the disease. Examination of liver specimens obtained by means of the viscerotome from persons dying of illness of not over 10 days' duration have also lead to the detection of unsuspected reservoirs of infection.

Pathology.—Death generally occurs between the fifth and ninth day of the disease. Rigor mortis comes on early. The skin may show ecchymoses and is an intense yellow colour, which becomes accentuated after death. The liver is of approximately normal size, reddish yellow, brownish yellow or "chamois leather" colour, and may show hæmorrhages. Microscopically a midzonal fatty degeneration is characteristic on the fourth or fifth day, but later all zones undergo necrosis, and the nuclei may contain acidophile inclusion bodies. The gall-bladder contains tenacious, dark bile. The kidneys are congested, and show cloudy swelling and fatty degeneration. Petechial hæmorrhages, casts and degeneration of the convoluted tubules are seen on section. The adrenals may show cortical fatty degeneration. The left ventricle is often dilated, and its muscle pale and flabby. Brady-

cardia is due to damage to the auriculo-ventricular bundle, and fatty degeneration of muscle cell-elements are common. Erosions and petechial hæmorrhage in the stomach and proximal duodenum occur, hence the coffee-ground vomit and the tarry blood in the entero-colon. The spleen is almost normal in size and appearance. The pleura and meninges may show hæmorrhages, the brain is congested, and the lungs congested and apt to show hæmorrhages.

Clinical pathology.—The outstanding pathological features are cloudy swelling and necrosis of the parenchymatous cells, especially of the liver and kidneys, and degeneration of the capillary endothelium, resulting in hæmorrhages. Jaundice and albuminuria with casts are thus produced. Hypoglycæmia related to liver inefficiency may occur from the fourth day onwards, while the van den Bergh may show a biphasic direct positive reaction and a positive indirect reaction of from 2 to 20 units. In the later stages the blood urea may be increased, and in monkeys Findlay found an increase in guanidine bodies. Though the leucocytes may vary from 5,000 to 15,000 per c.mm., leucopenia being the rule, the lowest counts occur about the fifth to sixth day; the neutrophiles are increased, the lymphocytes decreased and the eosinophiles tend to disappear. The clotting time is markedly increased. The cerebro-spinal fluid is under increased pressure and contains increased quantities of albumin and chlorides.

Symptoms.—The incubation period is from 3 to 5 days, but may be 10. Clinically, the disease is divided into: (1) Larval and mild forms; (2) Severe; (3) Malignant. In well-established severe cases the clinical features vary according as the liver, kidneys or heart bear the brunt of the attack, acute hepatitis and cholæmia, uræmia and anuria, and cardiac insufficiency being respectively manifest. Most cases show evidence of both renal and hepatic involvement.

1. *The larval and mild types.*—During epidemics, as well as where the disease is endemic, aberrant and irregular types are not infrequent; transient fever of 1 to 4 days duration, perhaps associated with albuminuria, occurs with rapid return to health. Where the pyrexia persists over 48 hours, headache, vomiting, eye pain and mild jaundice may ensue. Diagnosis in the larval forms is dependent on showing that convalescent serum is protective.

2. *Severe or ordinary types.*—The typical case presents three stages: (*a*) the sthenic; (*b*) the stage of remission on the third or fourth day; (*c*) the asthenic stage. In the *sthenic stage* the onset, which often occurs at night, is sudden with chilly sensations or a rigor, the temperature rapidly rising to 102° F. or 104° F. There is severe pain in the back and limbs, frontal headache with flushed face, injected conjunctivæ (ferrety eye) and photophobia. Prostration is severe, often disproportionally so to the temperature (Carter). The tongue is pointed and red; anorexia, nausea and vomiting, which may be bilious, appear. Epigastric discomfort and tenderness are characteristic, and insomnia is frequent. Albuminuria generally occurs on the second day and steadily increases. The pulse is at first rapid (90 to 110 per minute) and of high tension with raised blood pressure, but later slows until by the third day it may be 60 to 70 per minute despite the fact that the temperature remains elevated. This is known as Faget's sign, the pulse actually falling away from the temperature. It also remains slow when the temperature rises again in the relapse. Constipation is the rule.

Stage of remission.—About the third or fourth day the temperature may

fall to 100° F. or lower with amelioration of symptoms. Recovery may result or fever be re-established. Frequently this stage is absent altogether.

The asthenic stage.—The temperature rises again if it has remitted, turgidity of the face decreases, and jaundice now appears; it is first seen in the conjunctivæ and is not obvious in the skin until the fourth day of fever as a rule; sometimes, however, it is demonstrable on the third day. The gums are swollen and bleed on pressure, while the tongue is coated and later dry and brown. The liver is tender and only slightly, if at all, enlarged, while the spleen is not palpable. Hiccough may be very distressing, and black or "coffee ground" vomit, tarry stools and skin petechiæ may occur. Bradycardia is marked (40 to 60 per minute) and the blood pressure low. The urine is acid and decreased in quantity; it contains urobilin and much albumin, granular casts and possibly bile salts, bile pigments, bile-stained epithelial cells, and red blood corpuscles. Anuria is frequent in fatal cases. After the intermission the fever does not last as a rule more than 3 days.

Malignant forms.—In this type the temperature may reach 106° F. and profuse hæmorrhages, melæna, black vomit, epistaxis, hæmaturia, purpura, jaundice and anuria may develop by the third day. Symptoms referable to the nervous system such as hiccough, tremor, subsultus tendinum and delirium are also encountered, death from overwhelming toxæmia rapidly ensuing.

Complications.—Complications are uncommon, but boils, abscesses and troublesome jaundice, appearing for the first time in convalescence, may occur.

Course.—If the patient survives, the acute disease rarely lasts longer than 10 days, and convalescence generally progresses slowly but surely once a normal temperature is established. Relapses are rare and generally fatal.

Diagnosis.—Difficulties in diagnosis are mainly encountered in atypical cases, especially early in an epidemic. In the average case fever associated with undue prostration and early and increasing albuminuria should at once arouse suspicion, while later, the tender liver, absence of splenic enlargement, Faget's sign, hæmorrhages and jaundice appearing about the fourth day will be confirmatory. In blackwater fever, jaundice appears in the first 24 hours; in bilious remittent fever on or about the second day; while in Weil's disease it is generally found on the fourth or fifth day. Dengue, malignant tertian malaria, and relapsing fever also occasionally give rise to difficulty in diagnosis. Malaria, bilious remittent fever, and relapsing fever are generally associated with an enlarged spleen, while blood smears should reveal malaria parasites or spirochætes. Special laboratory investigations may be necessary to differentiate Weil's disease. In the larval forms of yellow fever intracerebral inoculation of susceptible mice with 0·03 c.c. of blood collected during the first 3 days of fever may reveal the virus. More frequently it will be necessary to take two specimens of blood at a fortnight's interval and establish a rise in the titre of protective antibody by the mouse protection test in order to establish the diagnosis.

Prognosis.—The prognosis differs in various epidemics, the mortality rate varying from 10–70 per cent., the average being 20–30 per cent. Anuria deep jaundice, black vomit, hæmorrhages and severe nervous disturbances are of grave significance.

Treatment.—PROPHYLACTIC.—The segregation of infected individuals in mosquito-protected wards, and the destruction of the adult and larval

stages of mosquitoes (Aëdes) have done much to stamp out the disease. Rubber gloves must be worn in collecting blood from all pyrexial cases in endemic areas. Convalescent serum affords temporary protection. All persons visiting or living in a yellow fever area should be vaccinated with virus modified by tissue culture. A single subcutaneous injection of 0·5–1·0 c.c. produces protective antibodies and confers an immunity which probably lasts several years. No local reaction follows inoculation, but fever with headache and general aching may develop on the sixth or seventh day.

CURATIVE.—Careful nursing of the patient in the recumbent position is essential, and as much fluid as can be taken is given during the acute illness, but food is contra-indicated. The juice of citrus fruits and dextrose and lactose are given in water; citrates should be added to the drinks to combat acidosis and alkalinize the urine. Only when the temperature has been normal after the second paroxysm can a gradual increase in food be permitted—rice water, chicken soup, Benger's, custard, etc.—and even in convalescence it is only gradually increased. In severe cases with vomiting 1 to 2 pints of 5 per cent. dextrose, given intravenously every 24 hours, may be helpful; also tap water may be administered by proctolysis. Calcium lactate, grs. 60 daily, is advocated to prevent hæmorrhage. Unfortunately, though protective to monkeys, convalescent serum does not affect the course of the disease once symptoms have appeared. Symptomatic treatment includes the use of an ice bag locally for headache, a mustard plaster to the epigastrium for hiccough, hot fomentations and catheterisation for retention and sedatives for insomnia. Champagne may help the vomiting. On admission a mild purgative is administered and constipation is subsequently treated by a daily enema. A cold sponge is indicated when the temperature exceeds 103° F.

PHLEBOTOMUS FEVER

Synonyms.—Papataci Fever; Three-day Fever; Sand-fly Fever; Simple Continued Fever; Pym's Fever.

Definition.—An acute specific fever lasting about 3 days due to a filtrable virus and spread by *Phlebotomus papatasii*.

Ætiology.—The disease occurs in parts of Africa, Asia, Northern Argentina and is common in the Mediterranean basin, in India, Mesopotamia, Persia, etc., where it affects especially white races, though natives also suffer. The virus is present in the peripheral blood for the first 24 hours, and sand-flies sucking up such blood become infective 7 or 8 days later and remain so for life. Experimentally, blood taken on the first and second days may produce the disease on inoculation, and volunteers bitten by infective flies develop fever in 2 to 7 days. One attack generally confers immunity.

Pathology.—This has been inadequately studied, as the disease is not fatal.

Symptoms.—Prodromata like malaise, vague pains, headache and weariness may usher in the disease, the onset of which is sudden, with chilly feelings or shivering, frontal headaches and lumbar pains. The temperature rises rapidly to 104° F. or 105° F. The face is flushed, the eyes injected, the throat and mouth congested, and the skin dry, though sometimes there

is sweating. Diarrhœa, joint pains and cramps may occur. Bradycardia is present, also a leucopenia of 4,000 to 5,000 leucocytes per c.mm. After 36 to 48 hours the temperature falls slowly to normal, accompanied perhaps by epistaxis or sweating. Convalescence is generally rapid, but depression and asthenia may persist for some days or even weeks. Afebrile and abortive forms are described.

Diagnosis.—The diagnosis lies between influenza, malaria and especially dengue, which it closely resembles, but secondary rises in temperature, secondary rashes and glandular enlargement rarely occur.

Treatment.—Destruction of sand-flies, the employment of a fine mesh net, and spraying bedrooms with 1 per cent. formalin are helpful. Medically, cases are treated by rest in bed during the fever, with cold sponging and a mixture of aspirin, phenacetin and caffeine citrate.

DENGUE

Synonyms.—Dandy Fever; Break-Bone Fever.

Definition.—A specific fever, generally lasting 6 to 7 days, due to a filtrable virus transmitted by *Aëdes ægypti*. A saddle-back temperature chart, severe joint pains and backache, leucopenia and a skin eruption about the third to the fourth day are characteristic.

Ætiology.—The disease occurs universally throughout the tropics and sub-tropics, and is often epidemic. All ages and sexes are liable. The virus exists in the blood for the first 3 days of fever and for 18 hours previously, and is communicable to man by direct inoculation during this period or by mosquitoes after feeding. The mosquito takes 11 days before becoming infective, and remains so for life.

Pathology.—Nothing definite is known of this, as the disease is so rarely fatal.

Symptoms.—Prodromata include general malaise and pains in the limbs, but generally the onset is absolutely sudden, with a rapidly rising temperature of 102° F. to 105° F., headache and aching eyeballs more marked on movement. The skin, especially of the face, is congested and shows a general flushing—the so-called primary rash. Backache is very severe, and much pain occurs at the muscular insertion about the joints. Insomnia, initial depression, anorexia, vomiting and constipation are not infrequent. The pulse, at first rapid, now begins to slow, and after 3 to 4 days the temperature falls by crisis, diarrhœa, sweating and epistaxis often synchronising with it. Symptoms now improve, but after 12 hours to 3 days the temperature rises again, giving rise to the saddle-back chart. Pains and depression recur, and a measly, roseolar rash fading on pressure appears, best seen on the dorsal surface of the hands and feet and spreading to the forearms and legs. Desquamation with itching may follow. Glandular enlargements are described in some epidemics, and a leucopenia with lymphocytosis is characteristic. After 2 or 3 days' fever the temperature falls and convalescence begins. Some cases present a one-phase fever in which no secondary rise occurs, while others show a continuous fever of 6 to 7 days with a terminal rise.

Complications and Sequelæ.—One attack may confer immunity, but

two and even three have been recorded. General debility combined with insomnia and mental depression may persist well into convalescence, and intractable muscular pains may lead to considerable crippling.

Diagnosis.—Influenza, measles, German measles, scarlet fever, rheumatic fever, secondary syphilis and malaria may be confused with dengue. Yellow fever is readily distinguished by the marked albuminuria and jaundice.

Prognosis.—Different epidemics vary in virulence, but the death-rate is very small.

Treatment.—Destruction of the vector, *Aëdes ægypti*, will prevent the disease. The patient should be kept in bed for 10 days on a light fluid diet. Liniments, a mixture of aspirin, phenacetin, and caffeine citrate, and even morphine may be required to allay the pains in the joints. In convalescence gentle massage, tonic treatment and a change of air should be advised.

RIFT VALLEY FEVER

Synonym.—Enzootic Hepatitis.

Definition.—A specific fever due to a filtrable virus causing fatal epidemics amongst sheep and cattle in British East Africa, and producing in man a three-day fever.

Ætiology.—This disease was first described by Daubney, Hudson and Graham in Kenya Colony as an epidemic amongst lambs, sheep and cattle. Possibly it occurs in other parts of the tropics. Man may be infected directly from contact with animals or from virus in the laboratory. The blood is infective, the virus passing through Berkefeld N. V. and W. filters. Experimentally, rats and mice are susceptible and die of the disease. The transmitting agent may possibly be a mosquito.

Pathology.—Pathological changes include fatty infiltration and a focal or generalised necrosis of the parenchyma of the liver in experimentally infected animals. The intestines may show congestion, and hæmorrhages may occur in different organs.

Symptoms.—The incubation period is 3 to 6 days. A dengue-like fever lasting 1 to 3 days is produced in man, characterised clinically by fever, rigors, headache, muscular pains and possibly epistaxis. There is a primary polymorphonuclear leucocytosis followed by a leucopenia (Findlay), and protective and complement fixation antibodies appear in the blood of man after infection. Three cases of laboratory infection have recently occurred in England.

Diagnosis.—The presence of a transient fever in natives herding sheep and cattle, or in laboratory workers handling the virus, should arouse suspicion; mouse inoculation would confirm the diagnosis.

LYMPHOPATHIA VENEREUM

Synonyms.—Climatic Bubo; Tropical Bubo; Lymphogranuloma Inguinale; Poradenitis.

Definition.—A venereal disease due to a filterable virus characterised by a herpetiform chancre on the genitalia or peri-anal region, inflammation of the corresponding regional lymphatic glands, and fever. In males the inguino-cruro-iliac glands and in females the pararectal and pelvic glands are chiefly involved. Chronic ulceration and elephantiasis of the pudenda are not uncommon in females, and inflammatory stricture of the rectum may occur in both sexes.

Ætiology.—The disease has a world-wide distribution, but is especially common in China, Japan, Malaya, East and West Africa, and in North and South America. Though more common amongst coloured races, especially negroes, it is being recognised with increasing frequency in Europe. The disease occurs mainly in adults, is essentially venereal in origin, and is commonly acquired in the tropics and sub-tropics following coitus with native women. Sailors often acquire the disease in Eastern ports. The virus particle has a diameter of 0·125 to 0·175 μ, is filtrable, and was first successfully transmitted to monkeys by intracerebral inoculation of bubo pus by Hellerström and Wassén. Mice are similarly susceptible. In guinea-pigs large buboes may follow the subcutaneous injection of sterile bubo pus. Surgeons have developed axillary buboes from lesions on the fingers when operating on infected patients, and children have acquired infection from simple contact.

Pathology.—The extirpated glands show marked periadenitis, and form conglomerated masses. The cut section often presents a reddish or violet tinge. Foci of purulent softening may occur, and sometimes pus cavities, containing thick muco-pus of a grey to light green colour, are produced by their coalescence. Microscopical sections of the bubo reveals granulomatous tissue, epithelioid cells, fibroblasts, occasional giant cells, and polymorphonuclear leucocytes; epithelioid cells with palisade arrangement are very characteristic. Chromatin staining inclusion bodies, known as Gamna bodies, are found within lymphocytes and plasmocytes in the infected glands.

Symptoms.—In males, the primary lesion is as a rule overlooked. It occurs as a small herpetiform ulcer, generally situated in the coronal sulcus on the penis, and appears a few days to 3 weeks after coitus. Swelling of the median group of inguinal glands draining the ano-genital region follows in about 2 or 3 weeks, the limits being 1 to 6 weeks. Bilateral glandular involvement occurs in 35 per cent. of the cases. The onset is generally insidious, with slight stiffness or tenderness in the groin, and fever. Often pain is absent; rarely it may be severe. The skin is at first red, but as swelling of the glands with periadenitis and hard brawny infiltration proceeds, it changes to a bluish-violet tint. The conglomerated glands are hard to the touch, generally only slightly tender, and show no fluctuation unless suppuration is advanced. Fistulæ form in about half the cases. Though the iliac glands are frequently enlarged and palpable, they never present clinical evidence of suppuration. Healing with scarring may occur within 2 months or be delayed 1½ years. The general symptoms include fever, anorexia, weakness and loss of weight. Although the fever is usually remittent in type no characteristic temperature chart is present, and not infrequently the temperature becomes normal in 7 to 10 days, but sometimes it is prolonged and a typhoid-like state supervenes. Recurrent fever is occasionally associated with extension of the adenitis. Rheumatic and allergic skin manifestations are not

uncommon, and include painful red swollen joints, erythema nodosum, erythema multiforme, scarlatiniform and urticarial eruptions.

In females, primary lesions may occur on the genitalia or peri-anal region, and the para-rectal glands are commonly involved; these glands often suppurate and form fistulæ which may open into the vagina, the rectum, or the skin near the anus. The disease runs a chronic course; fibrous stricture of the urethra, vagina and rectum may develop, or elephantiasis of the vulva (esthiomène) follow lymphatic obstruction. Polypoid swellings may occur about the anus, while the lower portion of the rectum may ulcerate and become converted into a narrow indurated ulcerated tube, with widespread fistulæ below the stricture. According to Stannus this is generally situated some 3 to 8 cm. above the anus. Rectal stricture is more common in females —especially in prostitutes—and is associated with the passage of blood, mucus and pus from the bowel, and increasing constipation.

Diagnosis.—Climatic bubo has been called the sixth venereal disease, and the history and clinical features are most important in making a correct diagnosis. Where periadenitis and induration are extreme, actinomycosis may be simulated. Herpes genitalis, filarial adenitis, septic and tuberculous adenitis, venereal bubo the result of chancroid, gonorrhœa and syphilis, as well as other buboes, such as result from plague, rat-bite fever and tularæmia, may need differentiation. Histological section of material obtained at biopsy and Frei's intradermal test, using a 1 in 10 dilution of virus-containing pus sterilised at 60° C., may be of assistance; 0·1 c.c. of this antigen is injected intradermally, readings being made at the end of 48 hours. A positive reaction is characterised by the appearance of a reddish, infiltrated papule, measuring from 7·5 to 20 mm. in diameter. It is regarded as a manifestation of cutaneous allergy, and is said to be specific for climatic bubo. Animal inoculation and the mouse protection test may be resorted to in doubtful cases.

Lesions in the ano-genital region must be differentiated from filarial elephantiasis and ulcerative granuloma pudenda. Polypoid swellings should be distinguished from piles, simple polyposis and bilharzia polyps. Rectal stricture which is not due to surgical or other trauma or new growth is almost certainly caused by this virus; in the past it has generally been erroneously attributed to gonorrhœa, chancroid, syphilis, or tuberculosis.

Prognosis.—The disease runs a different course in different individuals. In males, unless the rectum be involved, the outlook is good though the disease may last many months. In females, with extensive ano-genital manifestations, such as fibrous strictures and multiple fistulæ, permanent invalidism may result.

Treatment.—The patient should be put to bed, have a nutritious high vitamin diet, and given a course of sulphapyridine (M. and B. 693). If the glands are small and have not suppurated they are best left alone, but after the acute stage has subsided they may be painted with linimentum iodi. If suppuration has taken place, aseptic aspiration may be undertaken. Excision at this stage may result in secondary infection, and should not be attempted. When operative intervention is practised in early cases, it should be remembered that too extensive removal of the groin glands may result in elephantiasi and the femoral chain must be left intact.

G. Carmichael Low.
N Hamilton Fairley.

HERPES SIMPLEX (see p. 1467).

HERPES PREPUTIALIS (see p. 1468).

VERRUCA VULGARIS (see p. 1482).

MOLLUSCUM CONTAGIOSUM (see p. 1483).

ACUTE ANTERIOR POLIOMYELITIS (see 1568).

LETHARGIC ENCEPHALITIS (see p. 1576).

HERPES ZOSTER (see p. 1583).

RABIES (see p. 1585).

C. THE MYCOSES

Numerous fungi are pathogenic to man, and the lesions caused thereby are conveniently described as the mycoses.

Some of the diseases, for example the ringworms, are described in other sections. Six of them will be described here—actinomycosis, mycetoma, sporotrichosis, aspergillosis and blastomycosis, the lesions of which are of the nature of infective granulomata.

ACTINOMYCOSIS

Synonym.—Ray-fungus Disease.

Definition.—A local infection, tending to become general, due to the *Streptothrix actinomyces*, producing granulomatous lesions chiefly in the jaw, skin, lung and digestive tract.

Ætiology.—*Actinomyces bovis* was first described by Böllinger in 1877 as the micro-organism producing large, hard, sarcomatous-like masses occurring about the jawbones of cattle, and in the following year Wolff and Israël found the same organism in human cases.

The characteristic of the disease is a suppurative lesion, the pus from which contains visible granules which, examined microscopically, are seen to have a centre of a closely meshed filamentous network, with a border of radially arranged striations, often ending in club-shaped bodies. Formerly these club-shaped bodies were thought to be spores, but they are now regarded as hyaline thickenings of the sheaths of the threads. The clubs are only found in preparations made from pus from active lesions, or in cultures on media in which serum or blood is employed.

It is essential in examining suspected pus to isolate a granule. If granules be not readily detected in the wound or in the pus, Colebrook has pointed out that if pus be vigorously shaken in a tube of water the granules, not being emulsified, will sink to the bottom and may be removed by a pipette. Microscopical examination is very much facilitated by crushing the granules between two slides. The mycelial filaments retain Gram's stain, while the clubs lose it and take the counter-stain. Culture is in any case difficult, depending to a large extent on the amount of secondary infection. To

eliminate this as far as possible the granules should be well shaken in a sterile saline solution, and then after crushing between sterile slides should be sown on to glucose agar plates which are incubated anaerobically, or crushed granules may be shaken up into melted glucose agar which is aspirated into long sterile tubes according to the method of Vignal. Numerous subcultures may be necessary to complete the isolation of the organism.

Mode of invasion.—Till recently the view has been held that actinomycosis was conveyed to cattle and man from vegetable sources. Colebrook, in a review of 28 cases coming under his observation, brings forward strong reasons for believing that the fungus may be present under normal conditions in the alimentary tract. He quotes Lord as finding similar organisms in carious teeth and tonsillar crypts, and himself found not dissimilar filamentous organisms in each of six carious teeth examined. He also has shown that the serum of heavily infected patients causes agglutination of suspensions of actinomyces, as also does the serum of inoculated rabbits. The same observer supports the observation of Klinger as to the frequent association with actinomyces bovis in actinomycotic lesions of a minute Gram-negative cocco-bacillus, to which Klinger gave the name of *Bacillus actinomycelium comitans*. The significance of the association is not known.

Symptoms.—These depend upon the anatomical distribution of the granulomata.

1. The Jaw and adjacent Structures.—When the infection occurs in these parts the patient presents a swelling very like a sarcoma, generally about the angle or ramus of the mandible. The swelling may, however, affect the submandibular tissues and lymph glands rather more than the jaw itself, and one of the writers has recently seen a case in which the lesion was confined to the glands. The swelling is tender, somewhat painful, and not generally so hard as in sarcoma. It may show one or more spots of softer consistency than the rest of the lump. In most cases there is no obvious source of infection inside the mouth; the assumption is—in the light of observations quoted above—that the avenue of invasion is a carious tooth, or the gums and periodontal membrane.

2. The Intestines; Appendicitis.—The favourite site of infection is the cæcum and appendix region. The disease manifests itself either as an attack of appendicitis, most often acute, in which case the diagnosis is made only at the time of laparotomy; or as a slowly growing lump in the right iliac fossa, with some pain, tenderness, and constitutional disturbance, in which case suspicion may be aroused as to its nature, if it be remembered that this region is a site of election for the ray fungus. There is a tendency for the infection to spread from the ileo-cæcal region—(*a*) to the adjacent *peritoneum*; (*b*) to the *abdominal wall*; (*c*) to the *liver*. For this reason it is rare to find the lesion confined to the appendix by the time operation takes place. For this reason, too, the first evidence of cæcal infection may be the involvement of the parietes in the lower right quadrant of the abdomen, in which case there is always a probability that the infection has spread from the bowel. The *liver* is sometimes involved alone, that is, without obvious intestinal infection. The disease is only to be distinguished from abscess by puncture or by free incision.

3. The Pleura and Lung.—Actinomycosis in these tissues is by no means rare (see section on Respiratory System, pp. 1216, 1269), and the

disease should constantly be borne in mind by the practitioner when faced with an obscure case in which indefinite physical signs appear at one base, with cough, fever and (not seldom) hæmoptysis. In some cases a fairly frank pleuritic effusion appears, and the bacteriological examination of the exudate reveals the nature of the disease. In other cases the clinical picture resembles a basal tuberculosis. As the disease progresses the differential diagnosis lies between ray fungus, bronchiectasis and new growth. Hæmoptysis which recurs in the absence of any evidence of tuberculosis in an obscure case of pulmonary disease, is highly suggestive of actinomycosis of the lung. The later stages of the disease still resemble pulmonary tuberculosis; wasting, intermittent fever, purulent expectoration, cough and physical signs of progressive lung infiltration with destruction.

4. The Skin.—Granulomata sometimes appear in the skin and subcutaneous tissues (*a*) alone, or (*b*) complicating the disease in deeper structures.

(*a*) The neck and scalp are the parts most often affected. The initial lesion is a rounded swelling, not very acute, and therefore resembling a tuberculoma rather than the result of a pyogenic infection, but usually firmer in texture and larger than the lesion seen in tuberculosis of the skin. It has therefore to be distinguished from sarcoma and from gumma. As the lesion progresses it involves the subcutaneous tissue and tends to ulcerate, after the appearance of one or more soft and dusky-red areas on it. When ulceration occurs at these points, pus escapes, and this contains the tell-tale granules characteristic of the infection. At this stage the appearance is not unlike that of a chronic carbuncle or a suppurating gumma. Ultimately the skin "breaks down" over a considerable area of the swelling, and a chronic ulcer forms, which discharges freely.

(*b*) Similar skin lesions appear not seldom in association with primary infections of deeper structures, these superficial deposits having the significance of metastatic pyæmic deposits.

5. The Brain.—The brain, like the skin, may be infected by direct spread from an adjacent lesion, or it may suffer by way of a general pyæmic process. In a case under the observation of C. Ernest West and Horder a chronic otitis media was complicated by granulomata in the scalp, from which the streptothrix was demonstrated in films and grown in tubes of blood-broth. Cerebral symptoms developed, and the patient died comatose. At the post-mortem examination a large abscess was found in the centrum ovale of one hemisphere, and the mycelial threads were found in the pus in considerable numbers.

Diagnosis.—Hints have been given in the preceding account relative to the differential diagnosis from tuberculoma, sarcoma, pyogenic infection and gumma. *The chief reason why actinomycosis goes unrecognised is that the possibility of its existence is overlooked.* All materials from a suspected case (pus, pleural exudate, sputa, material from liver puncture, excised lymph glands, etc.) should be carefully examined for mycelium, and the bacteriologist should have his attention drawn to the possibility of its presence. Sputa from a case of recurring hæmoptysis, in which a negative report in respect of tubercle bacilli has been returned on several occasions, have been found to contain threads of actinomyces when the necessary investigation has been specially asked for.

Course and Prognosis.—Although these vary much, there is, as may

be inferred from remarks already made, a tendency for ray-fungus infection to become pyæmic in character. It is this feature which gives the serious note to prognosis in all cases. In lesions about the jaw and in skin infections, that are primary and not associated with visceral infection, the outlook is not nearly so bad as when the lungs, liver or intestinal tract are involved and when the skin lesions are multiple and secondary. Early diagnosis, if possible before secondary infection (usually staphylococcus) has taken place, adds greatly to the chance of recovery. One of the most important points in connection with prognosis is the uncertainty as to the complete extirpation of the fungus after treatment has been apparently successful. Relapses are common, and must be allowed for in any thorough programme of treatment.

Treatment.—So soon as the diagnosis is made, the question should be raised whether or not radical surgical measures are practicable. If they are they should be pursued without delay; any abscess or infected area should be drained, or incised and freely curetted; infected lymph glands should be excised; doubtful teeth should be sacrificed. The exhibition of potassium iodide in full doses should follow these surgical measures, or should take their place in all cases in which they are for some reason impracticable. In some cases it is reasonable to try the patient's response to iodine before planning operative measures. The drug should be given freely diluted with water, and it should be gradually increased from an initial dose of 30 grains in the day to 60 grains, or even to 120 grains if this amount can be tolerated. If recovery takes place the iodine treatment should be renewed for certain periods now and again to guard against relapses.

Vaccine therapy is of help when combined with adequate surgical measures. The preparation of an autogenous vaccine presents few practical difficulties, and stock vaccines are available, containing 25 million mycelial fragments per cubic centimetre. If staphylococci be also present the appropriate vaccine may be combined with the mycelial one.

Treatment by X-rays has also been advocated as a supplementary measure.

SPOROTRICHOSIS

In this disease, which is much less common than actinomycosis, lesions (granulomata) appear in the skin, and rarely in the muscles and bones.

Ætiology.—The causative microbe was first described by Schenk in 1898. Two varieties, *Sporotrichum schenki* and *S. beurmanni*, were originally described, but are now generally regarded as identical. The organisms occur in pus as oval or fusiform spores, and grow in culture as a colourless branching septate mycelium, with clusters of brown fusiform spores on the ends of the filaments. Occasionally the spores are arranged round the filaments. They stain well with the aniline dyes, but irregularly with Gram's stain. Growth occurs under aerobic conditions only, and on ordinary laboratory media. Cultures are best made from closed lesions, which should be punctured with a wide-bore needle, and the material aspirated should be thickly sown on glucose agar plates, which should be kept at laboratory temperature. The colonies, which appear in from 4 to 10 days, are very

characteristic. At first white, thick and leathery, they later become convoluted and coffee-coloured, and still later may become black. Laboratory animals, especially mice and rats, are susceptible, the lesions resembling those in man; but the disease is seldom fatal. The serum of infected individuals agglutinates the spores of the organism, and specific immune bodies can be demonstrated by complement-fixation tests.

Symptoms and Diagnosis.—See p. 1467.

Treatment is on the same lines described for Actinomycosis.

ASPERGILLOSIS

Infections with aspergillus, usually *A. fumigatus*, have been observed in the middle ear, on abraded corneæ and in the lung. The organism is of the group of Ascomycetes; it grows on ordinary laboratory media, and frequently occurs as a contamination.

Cases of lung infection are not very rare (see p. 1217). They resemble cases of chronic pulmonary tuberculosis very closely; indeed, they are generally mistaken for this disease until investigation of the sputa reveals their true character.

HORDER.
A. E. GOW.
JOHN MATTHEWS.

MYCETOMA

Synonyms.—Madura Foot; Fungus Foot; Pseudo-actinomycosis.

Definition.—A chronic granulomatous condition affecting especially the feet, characterised by marked swelling and the appearance of external nodules connected with deeper sinuses which exude oily, purulent fluid containing various coloured fungoid granules.

Ætiology.—The disease is endemic in certain parts of India, especially in the Madras Presidency (Madura), but it also occurs in Ceylon, Madagascar, parts of Northern Africa such as Egypt, the Sudan and Algiers, as well as in Cochin-China, Senegambia, the United States, West Indies, and South America. It is found in country districts, and generally attacks those who go barefooted, the mycetoma fungus probably gaining access through thorn punctures, small cuts or abrasions. Males are more commonly affected than females, and the disease is especially prevalent in the third and fourth decades of life, being generally confined to natives. Many different fungi which have the capacity in animal tissues to produce grains composed of hyphæ have been described as causing mycetoma. Laveran divides them into two groups: (1) the Actinomycoses, caused by fungi of the genus Actinomyces (Discomyces, Nocardia, etc.); (2) the Maduramycoses, caused by true fungi, the most important of which is the genus Madurella. White, red and black varieties of mycetoma occur clinically.

Pathology.—On section through the softened, jelly-like tissue, sinuses and cystic dilatations communicate with external nodules and internal granulomatous infiltrations which ultimately implicate muscle, fascia and

bones, forming a honeycombed cheesy mass. Both the cysts and sinuses are filled with whitish-yellow, red or black granules like fish's roe, which microscopically show narrow, nucleated threads and peripheral, club-like swellings. Section shows fungoid granules surrounded by mononuclear and leucocytic infiltrations and by fibrous-tissue cells.

Symptoms.—The incubation period is not definitely known, but in about 50 per cent. of cases there is a history of trauma ; many weeks or months may elapse before local lesions develop. The first signs are the presence of one or more hard, painless, subcutaneous nodules which are about 0·5 to 1·0 cm. in diameter and generally involve the sole of the foot, and more rarely the hands, face and limbs. Unlike actinomycosis the glands and viscera are never affected, adenitis, if present, being due to secondary bacterial infection. After several months swelling increases, the nodules break down and ulcerate, sinuses are formed and discharge their characteristic contents. Finally, the parts become riddled with sinuses, exuding foul-smelling, semi-purulent fluid. The foot becomes more and more swollen and distorted, but it shows little tendency to pain or hæmorrhage. In the early stages the general health is not adversely affected, but later anæmia and cachexia develop if secondary bacterial infection supervenes.

Diagnosis.—This is readily made by finding the characteristic fungi in the pus, but the identification of the actual species of mycetoma requires detailed laboratory investigation.

Prognosis.—There is no tendency to natural cure, and if untreated the prognosis is bad, the patient generally dying from intercurrent disease or secondary infection within fifteen years of onset.

Treatment.—PROPHYLACTIC.—Protection of exposed parts, like the feet, from thorns and spikes of barley would probably prevent the disease, and walking barefooted is to be avoided.

CURATIVE.—Surgery is the only satisfactory treatment. In the early stages curettage, or local excision of the nodules with the electric cautery may prove successful. In sinus-riddled feet amputation is the only cure. Potassium iodide in large doses is worth a trial.

BLASTOMYCOSIS

Synonyms.—Gilchrist's Disease ; Chicago Disease.

Definition.—A term applied to certain chronic granulomatous lesions of the skin or viscera, caused by yeast-like blastomyces.

Ætiology.—People of any age are susceptible, but males in the industrial classes are most often affected. The disease was especially prevalent in Chicago, but is now known to occur in all parts of the world. Castellani holds that there are at least three different species of Blastomycoides—*B. immitis*, *B. dermatitidis* and *B. tularensis*.

Pathology.—Nodules, gummata, papillomata and ulcerations may be produced in the skin, and tumour-like granulomata and abscesses in the viscera. The pathological lesions resemble the tissue reactions induced by the tubercle bacillus, but the central necrosis is less, and yeast-like organisms are present.

Symptoms.—The clinical manifestations are very variable. Jacobson

divides the primary cutaneous manifestations into papulo-ulcerative, papillomatous and gummatous types: cutaneous lesions secondary to systemic blastomycosis consist of superficial ulcers with granulating bases which exude pus or form crusts. Local pain and discomfort are produced.

In systemic blastomycosis the clinical picture resembles a subacute or chronic pyæmia, and almost any organ may be involved; the lung (95 per cent.) and kidneys (30 per cent.) are most frequently implicated, producing localising features resembling pleurisy or pneumonia on the one hand and nephritis on the other. Osseous involvement and blastomycotic meningitis may also occur.

Diagnosis.—This depends on the demonstration of blastomyces in pus, sputum or cerebro-spinal fluid; moist specimens are prepared by mixing with a drop of sodium hydroxide (10 to 30 per cent.) and examined microscopically, when the round or oval, highly refractile bodies (5 to 20 μ) surrounded by a hyaline capsule, may be observed. They may also be cultured on glucose agar.

Prognosis.—Cases with localised cutaneous lesions as a rule ultimately recover if properly treated, but in systemic blastomycosis 90 per cent. of cases end fatally in a few weeks to 3 years (Jacobson). Cerebro-spinal cases invariably die.

Treatment.—Skin lesions should be radically treated by complete resection with the cautery, or curetted and cauterised. Radium and X-ray treatment combined with full doses of iodide, *i.e.* 20 to 60 grains three times a day, are sometimes successful. Systemic blastomycosis cases should receive large amounts of iodide, and autogenous vaccines are worth a trial.

COCCIDIOIDOSIS

Synonyms.—California Disease; Coccidioidal Granuloma.

Definition.—An acute, sub-acute or chronic disease, characterised by granuloma formation in the skin or viscera, caused by the hypho-mycetic fungus, *Coccidioides immitis*.

Ætiology.—The disease is endemic in certain parts of North America and affects persons of any age. Males of the working class are particularly prone. The causative agent is *C. immitis* which appears in the tissues or pus as a spherical, double-contoured body measuring 5 to 60 μ. The fungus is readily cultured and laboratory animals are susceptible.

Pathology.—The lesions are those of an infectious granuloma and the tissue changes include tubercles, caseation, necrosis, abscess formation, cavitation, fibrosis and even calcification.

Symptoms.—As in blastomycosis both cutaneous and systemic manifestations may be present, but the latter are more frequently observed. Acute, sub-acute and chronic types are described. Nodular lesions may involve the dermis, and flaccid tumours, gummatous-like ulcers, and abscesses containing thick mucoid pus may be found in the subcutaneous tissues. A scrofulodermic type of lesion involving the superficial lymph glands, especially of the neck, is also described. Systemic coccidioidosis frequently involves the lungs, when it resembles tuberculosis, though early hæmoptysis is rare. Meningitis and involvement of the bones of the foot, ribs and vertebral column may occur.

The disease is progressive in character, lasting a few weeks to several years.

Diagnosis.—Numerous diseases including tuberculosis, syphilis, blastomycosis, sporotrichosis, mycetoma and bacterial osteomyelitis may be simulated. Diagnosis essentially depends on isolating *C. immitis* from pathological exudates. X-rays may be of assistance where bone is implicated.

Prognosis.—The more chronic type of the disease responds if treated early, but once the viscera are involved recovery is doubtful. Acute cases die.

Treatment.—X-rays and iodides have proved disappointing. Jacobson recommends intramuscular injections of colloidal copper every 4 to 7 days, and coccidioidin (exotoxin and endotoxin) every 8 to 14 days, the interval being determined by the local and constitutional reaction. Carbon dioxide snow may be used for isolated local lesions. Where the lesions have been confined to one limb early amputation has resulted in cure.

TORULOSIS

Definition.—An infection produced by a yeast-like organism, *Torula histolytica*, possessing a special affinity for the cerebro-spinal system and lungs.

Ætiology.—The disease affects both men and women and has a widespread geographical distribution. Species of the genus Torula reproduce only by budding without mycelial or endospore formation and do not ferment sugar; in pus and cerebro-spinal fluid they appear as ovoid or spherical structures, measuring 3 to 15 μ, with definite cell walls (Jacobson).

Pathology.—Chronic leptomeningitis is present, while the brain shows tubercles and gelatinous cyst-like structures in which torulæ abound. Clear spaces containing gelatinous material are found round the parasites in the tissues, and this constant finding led Stoddard and Cutler to name the parasites *Torula histolytica*. Similar lesions may occur in the lung which may be honeycombed, the interstices being filled with gelatinous material.

Symptoms.—Occasionally localised torulosis involves the skin or mucous membranes, but much more commonly there is primary involvement of the cerebro-spinal system. The lungs are generally secondarily implicated, but we have observed one case in which the patient was treated for pulmonary tuberculosis many months before meningitis ensued; at autopsy the lungs showed extensive gelatinous infiltration.

Diagnosis.—Clinically, these cases simulate tuberculous meningitis, and unless cultures are made the torulæ may readily be mistaken for lymphocytes. The cerebro-spinal fluid is under increased pressure, and contains excess of globulin and lymphocytes, but the sugar reaction is negative.

Prognosis.—The course of the disease is sub-acute or chronic, lasting a few weeks to 2 years, with an average duration of 4½ months. In localised infections the outlook is fairly good, but systemic torulosis is practically always fatal.

Treatment.—Surgical resection with the cautery is the treatment for local lesions but no therapy is effective in generalised infections.

RHINOSPORIDIOSIS

Definition.—A chronic disease due to *Rhinosporidium seeberi* (Wernicke, 1903), which produces nasal polypi and papillomata of the cheek, conjunctiva and lachrymal sac.

Ætiology.—Until recently the organism was regarded as a protozoon, but Ashworth has now shown it to be a vegetable mould belonging to the order Phytomycetes. The younger forms are rounded bodies, some 6 microns in diameter, possessing a capsule, a single nucleus and cytoplasm containing food granules. Multiplication by fission occurs and sporangia or large cysts, 250–300 microns in diameter, with a cellulose coating result; later, numerous daughter cysts are discharged from a definite pore in the wall of the mother cyst. Infections have been recorded from India, Cochin-China, Ceylon, Argentine and North America. The mode of transmission is unknown, but a similar if not identical fungus, *Rhinosporidium equi*, affects the horse, and man may acquire the disease from this source.

Pathology.—The organisms develop in connective tissue cells, causing fibroblastic activity, round-cell infiltration and epithelial proliferation. Polypi result which may involve the nose, conjunctiva, lachrymal sac and ear, and papillomata of the penis and vulva have also been described.

Symptoms.—A history of nasal symptoms extending over years may be obtained. The polyps are soft, vascular, bleed easily and show a marked tendency to recur.

Treatment.—The polyps are removed surgically, a wire snare often being employed. Wright has observed tumours disappear after a course of tartar emetic intravenously.

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D. SPIROCHÆTAL INFECTIONS

SYPHILIS

A specific disease due to entry of a micro-organism (*Spirochæta pallida* or *Treponema pallidum*) into the tissues, either by inoculation into the skin, mucous membrane, or veins (acquired syphilis), or by transmission *in utero* (congenital syphilis).

In acquired syphilis, unless conveyed by transfusion, a primary sore commonly develops at each site of inoculation, and may be followed after a few weeks by a succession of lesions of the skin, mucous membranes, subcutaneous tissues, arteries, muscles, bones, viscera and central nervous system, which may recur again and again at varying intervals throughout the patient's life. After many years, degeneration of the parenchyma of the brain (general paresis) or of the spinal cord (tabes dorsalis) may develop. From an early stage changes in the blood serum can be detected by the Wassermann and various flocculation tests. Any or all manifestations, even the primary, may

be omitted. In congenital syphilis and in syphilis acquired by transfusion the systemic disease is the first manifestation.

Ætiology.—The specific micro-organism was discovered by Schaudinn in 1905 and named by him *Treponema pallidum*. Subsequently this was changed to *Spirochæta pallida*, but the original name is preferred by many workers. *S. pallida* is a minute organism which in fresh specimens under dark-ground illumination appears as a bluish white, very delicate corkscrew. Its length varies from 5 to 24 μ (average 8 to 10 μ); the distance between individual coils is 1 μ, and the depth of each coil is 1 μ. It is very active in its own ground but slow in moving from place to place. It alternately contracts and expands its coils, bends into loops or forms itself into a right angle. It has been demonstrated in every syphilitic lesion, including the brains of general paralytics. It has a life of only a few hours under natural conditions outside the body, and is killed at once by drying, by comparatively low degrees of heat, and by much feebler antiseptics than suffice to destroy ordinary pathogenic organisms.

The usual methods of transmission are by sexual intercourse and to the fœtus *in utero*. It does not seem necessary for a person transmitting the disease by intercourse to be suffering at the time from syphilitic lesions of the external genitals, and it is clear that often the semen contains the micro-organism. The period during which a person suffering from syphilis is liable to convey the disease by sexual intercourse varies; after the second year the chances diminish, and it is unusual for infection to be passed on in this manner after the fifth year. There is no doubt, however, that in the case of the fœtus, although the mother is most dangerous in the first five years of her infection, this may be transmitted up to a much later period, and there is, in fact, no limit to the length of time during which an infected mother may transmit the disease to her unborn child; infection occurs most often in the second half of pregnancy. Accidental infection usually results from contamination of any minute abrasion with secretion from a syphilitic lesion. The most dangerous from this point of view are the primary sore and the early secondaries of acquired syphilis and the early lesions in congenital syphilis, but although it is possible to infect an animal with secretion from later or tertiary syphilides, the chances of conveying the disease at this period by ordinary social intercourse are extremely slight. Even in the earlier stages, owing to the low resistance of the organism to external agencies, the risks of accidental infection by ordinary social intercourse appear to be very slight, judging by the great prevalence of syphilis and yet the very low proportion of extragenital chancres in countries where the standards of personal hygiene are equal to those in Western Europe. A number of instances of infection by transfusion of blood have been recorded, and they include cases in which the donor was still in the incubation stage; on the other hand, tertiary syphilitics have now been used as donors in cases of emergency in a number of instances without harm to the recipients, and it is clear that the older the infection the less likely is the micro-organism to be in the blood stream.

Pathology.—Kolle and Evers have shown that, after inoculation by scarification, the micro-organism has reached the nearest lymph glands of a rabbit in half an hour, and those of a guinea-pig in 5 minutes. The syphilitic lesion of every stage is histologically the same—a granuloma composed of a

collection of epithelioid cells, plasma cells, very numerous lymphocytes and some giant cells, with obliterative endarteritis of the vessels.

The pathology of syphilitic arteritis is discussed on p. 1031. Here it may suffice to sketch the main general effects of syphilis on the vessels. The changes in the vessel wall may lead to aneurysmal dilatation, as in the case of the aorta and other large arteries of the body, and in the cerebral vessels. The aortic valve may be involved in syphilitic mesaortitis, with resulting regurgitation. A common result of syphilitic arteritis of smaller vessels is thrombosis of the vessel, with important effects resulting from failure of the blood to reach the part supplied. In tertiary lesions the cutting off of nutritional supplies to the centre and the action of the toxin lead to necrosis and liquefaction, as seen in the clear-cut ulceration which often characterises tertiary syphilitic granulomata. If bone is involved in the tertiary gumma it may necrose throughout as in the flat bones, or only partially as in the long bones. Where necrosis does not occur, the granulomatous tissue of a syphilitic lesion tends to become fibrous, though at the same time natural forces work towards its removal. If the exudate is comparatively small, as in some primary and in practically all secondary lesions, the exuded cells may all be removed. If the exudate is a large one, a considerable proportion of it may reach the fibrous stage before the natural scavengers have had time to remove it. Thus many primary lesions are marked by hard scars for years afterwards, and gummata, their centres having liquefied, may be enclosed by dense connective tissue. Bone gummata are often ringed by heaped-up bone of ivory hardness.

Scarring from formation of fibrous tissue and its subsequent contraction may have important effects on viscera, interfering seriously with their functions.

It is well known that syphilis is a milder disease in females than in males, and experimental evidence suggests that the difference is due to female sex hormones.

The changes which occur when the parenchyma of the central nervous system is invaded are described elsewhere.

Incubation and early course.—The incubation period varies from a minimum of about 10 days to a maximum of about 90, with an average of 3 to 4 weeks. A small papule then appears at each site of inoculation, and quickly enlarges to a round or oval sore about the size of a threepenny bit, a sixpence, or larger; the centre usually becomes eroded, or perhaps more deeply ulcerated, and the broken surface is surrounded by a dull-red areola varying in width from half to 2 or 3 mm. Beyond the confines of the eroded area the tissues are infiltrated, feeling tougher than the corresponding tissues on the other side of the part. This induration becomes more and more pronounced until in the case of some primary sores, it feels as if there were a button embedded in the tissues. The sore does not bleed easily when scraped, but serum oozes freely from it, and this serum usually teems with syphilitic organisms. The sore is comparatively painless.

Individual features vary with the site. Thus the most indurated are those on the under-surface and mouth of the prepuce in males, and the labia, posterior commissure and *portio uteri* in females. In the case of a sore at the reflection of the prepuce on to the *corona glandis*, when the prepuce is retracted, the lesion flicks over like a plate turning on its edge. A sore at the

mouth of the prepuce often converts it to a fibrous ring. Induration is easy to elicit in sores affecting one wall of the *fossa navicularis*, which then feels as if a plate were embedded in it. In primary sores of the glans itself induration is difficult to elicit owing to tightness of the tissues, but the sore is easy to recognise by its dull-red areola, even contour, eroded centre, and indolent progress; rarely a primary sore has been reported deep in the urethra, the diagnosis being made by urethroscopic examination together with the discovery of *S. pallida* in the scanty urethral discharge. Primary sores of the skin are dark red, covered with a dark scab, and tough in consistency. Ulceration is usually more marked in sores affecting the mouth and undersurface of the prepuce, the skin at the peno-scrotal angle, the tissues around the nails, the lips and the tonsils. Almost all primary sores are comparatively painless, but when affecting the terminal phalanx of a finger or thumb they may be exquisitely painful, and thus may be mistaken for whitlow. The primary sore affecting the prepuce, the skin of the penis, or (especially) the female labia may be accompanied by a toughly indurated œdema of the affected parts, which become somewhat livid; the same condition may affect the uterine cervix.

The course of the primary sore varies greatly. In some cases the lesion is fleeting and its apparent triviality may lead to neglect of treatment; the history of a substantial proportion of cases of tabes and general paresis is that the initial lesion was either unnoticed or was very trivial. The ordinary sore which remains untreated lasts for a month or longer, and long after the erosion has healed over, a button of indurated tissue may remain to mark the site; syphilitic organisms have been found by histological examination in such scars many years later; weeks or months after it has healed the sore may break down again. When a sore is infected by secondary organisms, ulceration is a more prominent feature, and in rare instances it becomes phagedenic. In such cases the surrounding tissues very rapidly become black and necrotic, and the resulting loss of tissue may involve large portions of the external genitals.

Shortly after the appearance of the primary sore the nearest lymph glands often become painlessly enlarged, and in the case of the penis the lymphatics running from the sore can frequently be felt below the skin. The affected glands may reach a large size, bulging out the overlying skin; and this, with the fact that there is no reddening of the skin or other sign of acute inflammation, often gives the clue to the nature of the sore on which it depends. In females if the inguinal glands escape, owing to the internal situation of the sore, enlarged pelvic glands may often be found by palpation through the vagina against the ischiac bone. Syphilitic buboes do not usually suppurate, but may do so if the sore has become contaminated by secondary organisms, so that suppuration should not weigh heavily against a diagnosis of syphilis. A week or so after the local lymph glands have begun to enlarge there is universal adenitis, which can be appreciated by palpation, particularly of the epitrochlear, axillary and cervical glands.

About this time, or when the sore is about 15 days old, the blood serum often for the first time gives positive Wassermann and other serum reactions, such as the Kahn, Kline, Meinicke, Müller, Sachs-Georgi and Sigma. The last six depend on directly visible changes which occur in mixtures of syphilitic serum and diluted extract of heart muscle prepared by special methods.

The percentage of cases in which the Wassermann and other reactions are given increases with the age of the disease until the outbreak of the skin lesions which manifest the next or secondary stage. Practically 100 per cent. of patients in the secondary stage are positive.

Diagnosis of the Primary Stage.—It is axiomatic that every genital sore and every non-malignant sore elsewhere on the body which is not easily accounted for should be examined for *S. pallida*. This should be done before any antiseptics have been applied, as they kill the organisms in the superficial layers and prejudice the success of the examination. The sore should first be cleaned with a swab and its edge scraped, or a fairly deep puncture made in its margin with the point of a scalpel or a vaccination lancet. The sore should then be squeezed and the serum collected after it has oozed for a few minutes. When the necessary apparatus is at hand it is better to examine the specimen at once by dark-ground illumination; if it has to be sent away, the serum should be allowed to run into a capillary tube, only one end of which need be sealed. Alternatively a good method is to puncture the nearest enlarged gland and aspirate a little of the gland juice. A moderately stout hollow needle is run obliquely into the gland, and a few minims of sterile saline injected into it. The gland is massaged and aspiration applied by a syringe.

Spiral organisms other than *S. pallida* may be seen in a specimen obtained from the genitals or the mouth. They are largely eliminated by taking care to clean the surface of the lesion before collecting the specimen. All coarsely spiral organisms should be excluded at once, and only three others need cause difficulty.

A fairly fine spirochæte, with closely set spirals, often found in specimens from the genitals is about twice as thick as *S. pallida*, shines more brightly, has a slight rusty tinge, and spirals which are not so cleanly cut as those of *S. pallida*. Two spirochætes may be found in the mouth, both as fine as, or finer than, *S. pallida*. One is distinguished by the angularity of its turns, the other by its spirals being much more closely set, so that it looks like a piece of twisted silk.

Clinically, primary syphilitic sores are distinguished from others by the incubation period, colour, indolence, surrounding infiltration, comparative painlessness, slighter tendency to bleed, indolent enlargement of neighbouring glands, and the presence of *S. pallida*. The length of the incubation period is a guide only when the patient has not been exposed to infection for over 10 days.

A collection of *herpetic vesicles* on the penis is made up of minute, pinhead sized circles without induration, but usually irritable.

Chancroid has an incubation period of only a few days; the sore is more inflammatory and undermined, often with a more irregular edge which is merely tipped with red and has no areola; it is excavated, rather than worn down. Chancroid may be accompanied by a bubo which tends to suppurate. A syphilitic bubo may, however, suppurate, so that it would be a mistake to exclude syphilis on the sole ground of suppuration. If the glands, though distinctly enlarged, showed no sign of active inflammation, it would be strong evidence in favour of syphilis. Since there may be a double infection, microscopical examination should be repeated at intervals until the sore has healed, and the serum be tested for 3 months.

Scabietic runs on the glans and skin of the penis are mound-like and not eroded or indurated.

Syphilitic sores in parts of the body other than the genitals are often overlooked, mainly because syphilis is not thought of in those parts. A unilateral tonsillitis should arouse suspicion, especially if associated with painless enlargement of the submaxillary glands on one side. Similarly, the clue to the nature of a lip chancre may be given by the glands. Primary sores affecting the terminal phalanx of a thumb or finger often simulate whitlows; the syphilitic sore is more brawny, and remains so much longer after the sore has been lanced.

Secondary Stage.—Usually, but by no means always, a generalised rash appears three to six weeks after the sore. It generally starts on the sides of the trunk as pinkish spots, varying in size from a split-pea to a little-finger-nail, which deepen in colour with age to a dull-red or somewhat brownish tint. At first they may be difficult to see, but become more manifest after the patient has been stripped for a few minutes. Sometimes the spots are slightly raised and urticarial in appearance (roseola urticata). The eruption spreads gradually over the trunk and limbs, and fades in a few weeks, leaving little or no staining. It may recur at a later period, and the spots are then annular or ring-like.

After the fading of the first roseola, a peculiar change in the distribution of the pigment may occur, especially on the necks of brunettes. The neck becomes generally discoloured, or looks dappled (syphilitic leucodermia), as if the pigment had been washed out of a number of circular areas, each about the size of the end of a finger-tip, and had collected at the margins. An unusually high proportion of cases of syphilitic leucodermia have been found to have syphilitic changes in the cerebro-spinal fluid.

The *papular* eruption follows closely after the roseolar, and takes a number of different forms, the commonest and usually the earliest being dome-shaped, dull-red papules distributed over the trunk, limbs and face. Most are about the size of a lentil, but amongst the smaller papules may be many larger ones, sometimes even the size of a silver threepence. The papule feels tough and when squeezed between finger and thumb appears glistening white, while its surface cracks slightly. Variations of the ordinary papular eruption are the papulo-squamous, squamous, papulo-pustular and pustular. In the *papulo-squamous* a large proportion of the papules are covered at their centres by loose scales. The *squamous* syphilide is a papular eruption in which scaling is a still more prominent feature. In the *papulo-pustular* syphilide the centre of the papule necroses, and looks rather like an acne spot. When the whole papule breaks down a pustular syphilide results and this may resemble a varicellar or a variolous eruption. A more severe and malignant form is the ecthymatous type, in which the papule breaks down quickly, and the underlying tissues are eroded or ulcerated. As the destruction of tissue extends, the secretion dries to a crust. This may become heaped up by the deposit of successive layers, and the result is a blackish crust, shaped like a limpet (*rupia*).

Peculiar appearance of the papular syphilide in different situations.—Between the buttocks, on the lateral surfaces of the scrotum, on the labia, and on the upper and inner sides of the thighs, the papular syphilide often becomes very prominent and wart-like, with a greyish-white appearance;

these syphilides are called *broad condylomata*; the whole of the contiguous surfaces of the buttocks may be covered with them. On the scrotum this syphilide often looks like white slightly raised rings with brownish centres; it is best displayed by stretching the skin. Between the toes, under the pendulant mammæ, and in almost all moist situations, papules tend to run together, and a moist, pinkish-red surface, fringed with loosened epithelium, is left. Condylomata and moist papules generally exude serum freely, and the discharge is rich in *S. pallida*. On the palms and soles the papules appear as flat or slightly raised spots, varying in size from a split-pea to a sixpence. They scale easily, leaving collars of loosened epithelium surrounding the shining papules; sometimes the lesions run together into large plaques traversed by weeping fissures. The finger-nails may show characteristic changes, more especially in the recurrent secondary stages. The end of the finger becomes pinkish-red and bulbous, and at the reflection of the skin on the nail are weeping granulations. The nail becomes brittle and lustreless and is shed. The papular syphilide may be well marked on the forehead, following the margin of the hair (*corona veneris*), and it is often possible to find many papules in the hairy scalp. On other parts of the face, especially about the naso-labial fold and the chin, the papules are often set in rings. In some cases the facial lesions may be prominent, especially at a naso-labial junction, appearing like condylomata; on account of its similarity to yaws this condition is called a framboesiform syphilide.

The small follicular syphilide usually appears later than the lenticulo-papular. It occurs in small clusters of minute brownish papules, often thickly distributed on the back. The affected areas, which may be as small as 1 cm. across, have a goose-skin appearance and the part generally looks as if it had not been properly washed. The *lichenoid* syphilide, also a late secondary manifestation, occurs as small flat red elevations a few millimetres across, often polyhedral.

Recurrent papular eruptions.—Recurrences of the papular eruption tend to be much more limited in distribution. A common form, the corymbose syphilide, appears as one or only a few rather densely packed groups of papules from 1 to 3 inches or more in diameter. In some cases in the centre of the group is a large papule and around it, separated by a zone of healthy skin, a crowd of smaller papules. The chief sites are the extensor surfaces of the arms, the shoulders, back and abdominal wall. Sometimes the recurrence is a single papule as big as a shilling; it may occur on the genital area and be mistaken for a primary sore.

The *hair* is shed to a varying degree in the secondary stage. In most cases the thinning is not particularly noticeable; in others the fall is patchy, giving the back of the head a moth-eaten appearance; and in a few the patient may become temporarily bald. The beard and eyebrows may participate in these changes.

The syphilitic eruption in the mouth and throat.—Before the rash appears on the body the soft palate may become erythematous. Other lesions of the mouth usually make their first appearance at the time of the papular syphilide of the skin. On the mucous surface of the lips and the pillars of the fauces the early syphilide is a greyish-white patch, edged with a pinkish-red areola, which marks it off from the surrounding mucous surface. On the pillars of the fauces the appearance is that of a snail-track creeping up over the pillar

on to the soft palate. On the tonsil the lesion tends to ulcerate rather deeply. The mucous patch on the lip is usually round or oval and, if it crosses the angle of the mouth, is fissured. On the sides of the tongue fissuring and ulceration are more pronounced, but on the under-surface there may be condylomata, while on the dorsum are pink, bald spots, the pile of the tongue having been rubbed off at each papule. The discharge from these lesions teems with syphilitic organisms, and is very contagious. Papules can also be seen in the nose, on the septum and the floor. In the larynx, by suitable examination, they can be seen chiefly on the epiglottis and aryepiglottidean folds; they are apt to become eroded and ulcerated, causing the husky voice often heard in syphilitic patients. As these lesions of the mouth and throat are more apt to recur in uncured cases than are those of the skin, it is very important to examine the mouth thoroughly in a possible case of syphilis.

Other mucous membranes.—Mucous patches also occur on other mucous membranes such as those of the labia, just within the vagina, at the posterior commissure, the cervix, just within the anal canal, and on the glans penis and the mucous surface of the prepuce. Usually these are eroded and appear as sharply defined lesions against the background of normal-looking mucous membrane. On the genitalia, especially on the glans, they are quite often diagnosed as primary lesions, but this error can usually be avoided if it is remembered that not all sores on the genitalia are primary chancres.

Joints and bursæ are not often affected in secondary syphilis, but occasionally an *acute synovitis* occurs. It is fairly painful, and usually worse at night. A more indolent form of synovitis causes swelling without pain or great limitation of movement. The tendon-sheaths may be affected similarly, and the tendency to formation of adhesions may lead to permanent limitation of movement. Mild *periostitis* and osteocopic pains, worse at night, may occur in the secondary stage or even before any rash appears, but bone affections are commoner in the tertiary.

Thrombo-phlebitis, in the form of painless nodules in the superficial veins, particularly in the legs and resembling erythema nodosum, sometimes occurs.

From about the sixth month, or even earlier, the patient may develop symptoms pointing to syphilitic disease of the *central nervous system*, which are dealt with elsewhere. It is well to remember that in over 30 per cent. of cases in the secondary stage changes in the cerebro-spinal fluid indicate invasion of the central nervous system, though only a small proportion of these cases show clinical signs of nervous disease; this fact should be borne in mind when eventually tests of cure are being considered.

Constitutional symptoms.—Fever.—Even in the incubation period rigor followed by some degree of fever and pains in the limbs may occur. In some cases, towards the end of the primary stage, or on the outbreak of the rash, the patient's temperature may become irregular, the pyrexia being intermittent, continuous, or remittent, and accompanied by some constitutional disturbance. In rare cases the fever and constitutional symptoms may be more prolonged and pronounced, and if no rash appears, the symptom-complex may be very puzzling. Its association with generalised adenopathy should arouse suspicion. Sometimes, just before the outbreak of the eruption, and during the early part of the secondary stage, the limbs ache and there may be definite lightning pains, which lends support to the idea that all these symptoms may possibly be due to meningeal involvement and irritation.

In the early secondary stage also, headache may be severe, and may not improbably be due also to meningeal involvement.

Anæmia.—The red cell count may be slightly reduced, to between 4,000,000 and 5,000,000, and the colour index be as low as 70 per cent. In the early stages the white cells may reach 20,000 per c.mm. In early untreated cases the increase is due to polynuclear leucocytes, but under treatment these give way to lymphocytes, which may constitute 65 per cent. of the total; this lymphocytosis may persist for months. In rare cases the anæmia may be much more severe, Müller having reported one with a blood state resembling that found in pernicious anæmia.

Diagnosis of Secondary Eruptions.—The maculo-roseolar syphilide is fairly easy to distinguish by the history of a primary sore with indolent adenitis; by the subcuticular, deeply grounded appearance of the spots, which first appear on the flanks, very rarely itch, and are pinkish or dull-red, and by the coincidence of positive serum reactions. Other erythemata are brighter red and irritable, and often affect the backs of the hands. *Seborrhœa* is more superficial and is more scaly, the scales being greasy. *Pityriasis rosea* is often mistaken for syphilis, but the lesions are brighter in colour and more irritable; they tend to become annular, with their centres covered by branny scales. *Ringworm* is more superficial and irritable, and the fungus can be found in scrapings from its border. *Tinea cruris* or *dhobie's itch* affects a triangle at the upper and inner part of the thigh; it is brighter red, more irritable, and quite superficial. *Drug rashes* are more inflammatory and irritable; they appear more suddenly, and are associated with a history of the patient having taken such a drug as copaiba, cubebs, antipyrine, quinine or belladonna. The *eruptions of specific fevers* are usually accompanied by more pronounced constitutional symptoms.

The ordinary dome-shaped papular syphilide is usually easy to distinguish from a non-syphilitic eruption. The indurated feel of the papule, its shining appearance when pinched, its readiness to scale, and its dull or pinkish-red colour are valuable diagnostic signs, as is also the association with mouth and throat lesions. The different appearances which a papular syphilide presents in different parts of the body, such as dry papules on the trunk and most areas of the limbs, moist papules on the scrotum, between the toes and in other moist, warm parts, and wart-like condylomata on the scrotum, contrast strongly with non-syphilitic dermatoses, which are true to type, wherever situated. *The microscopic test should always be applied to the exudate from the lesion in any doubtful case,* and very rarely fails, even with the papulo-pustular or the pustular syphilide. *Acne spots* are more inflammatory, and affect the upper front of the chest and between the shoulders behind, rather than the flanks, loins and limbs. Pus can usually be expressed from blind acne pimples when they are pricked and squeezed. *Molluscum* spots are white and umbilicated, while caseous matter can be squeezed from their centres. *Lichen ruber planus* is characterised by flatter, smaller, polygonal spots of a violet tinge and waxy covering; it is more irritable. *Psoriasis* is usually less indurated, more superficial, bleeds at a number of points when slightly scraped, and affects the extensor rather than the flexor surfaces of the limbs; the scales are more silvery, and in moist situations the rash remains true to type, contrasting with the syphilide, which here becomes sodden with the secretion that freely oozes from it. *Varicellar spots* are

vesicular at one stage, more superficial and irritable. In *variola*, besides the febrile prodrome with backache, the spots are of uniform character and appear first on face and wrists. *Bromide* and *iodide* eruptions appear more suddenly, and are considerably more irritable. The deeper forms of pustular syphilide with considerable crusting, such as the superficial and deep ecthymatous, or the rupial, are distinguished from ordinary *impetigo* by the darker colour of the crusts, the circular rather than linear shape of the lesions, and the greater degree of tissue destruction below the crusts. *Scabies* is often mistaken for a crusted syphilide, and vice versa. The individual scabietic lesion is easy to recognise, but the tendency is to forget that scabies and syphilis often coexist.

Secondary syphilitic mouth lesions are easily diagnosed by the characters mentioned. *Vincent's angina* may cause confusion, but there is no pinkish areola, and the microscope easily settles the diagnosis.

Tertiary Lesions.—There is no sharply dividing line between the secondary stage and the tertiary, since the earliest tertiary lesion, the tubero-serpiginous, is merely a collection of large papules, which are more deeply embedded, and tend more to ulceration than the papules of what is called the early secondary stage.

The *tubero-serpiginous syphilide* occurs in one or more isolated areas of the skin as a collection of skin gummata, each about the size of a pea, often running into one another to form a more or less continuous, brownish-red ridge, often arranged in roughly concentric circles, or arcs of circles, or as a snake-like line of varying length. The affected area may be as small as a finger-nail or larger than a hand. The individual gummata may degenerate only so slightly as to produce some scaling, or may ulcerate more deeply and become crusted. The lesion extends centrifugally, and leaves in its wake a reddish-stained area in which are supple, papery scars, showing well the concentric distribution of the lesion. Sometimes the nodules do not resolve as the lesion extends, and a red nodular plaque of indurated tissue is formed. On the palms the lesion may be serpiginous as described above, or affect chiefly the folds, which become fissured. In some ulcerative cases extension is more rapid than healing, and a large patch of small skin ulcers may be left in the wake of the advancing arcs of new lesions. Very rarely, and then mostly when situated close to the angles of the mouth, or at a nasal orifice, the ulcer may become phagedenic, causing extensive destruction of tissue. The areas chiefly affected are those exposed to injury or constant friction.

Gummata of the subcutaneous tissues and muscles grow up as indiarubbery lumps which vary in size from a shrapnel bullet to an orange, or larger. They are painless, quietly expanding growths, which tend to break down in the centre, leaving clean-cut ulcers with tough, wash-leather sloughs occupying the bases. Sometimes the affected muscles are diffusely infiltrated, and much deformity results when the degenerated tissue is replaced by scar.

The *joints, bursæ and tendon-sheaths* are not often invaded in tertiary syphilis. The parts affected are, again, those most exposed to stress and strain, such as the knee-joint and the prepatellar bursa. The swelling is non-inflammatory, of soft rubbery consistence, and follows the lines of the affected joint, bursa or tendon sheath.

The *bones* are affected in tertiary syphilis in different ways, and in each of them the affection is commonly accompanied by boring or gnawing pains

worse at night (osteocopic pains). In the long bones the most usual manifestation in acquired syphilis is a localised gumma which either ossifies and remains as a boss on the bone or breaks down in the centre, leaving either a depression ringed with ivory-hard bone, or an ulcer. If the process begins deeper, the local swelling may not be so obvious and, eventually, with discharge of the necrotic contents, one or two fistulous openings lead to the interior of the bone. Diffuse osteitis and periostitis are not so common in acquired as in congenital syphilis. A sign of congenital syphilis in adolescents and adults is the sabre-scabbard tibia resulting from diffuse periostitis in earlier years; the bone is thickened from before backwards, and its anterior crest is curved with its convexity forwards, giving the bone the shape from which the condition derives its name. Of the long bones, the most commonly affected in acquired syphilis are the clavicle (sterno-clavicular joint), sternum, ribs, tibia and femur; but no bone is immune, and the process is particularly apt to affect those which have received a blow or other injury. Syphilitic dactylitis is very uncommon. Usually the proximal phalanx is affected, and a quiet, painless swelling results. Sometimes a sinus forms and the bone becomes rarefied. The whole bone may become permanently thickened, or absorption may result in shortening. The cranial bones tend especially to become carious under gummatous infiltration, and some of the worst mutilations result from syphilitic caries of the bones of the nose and palate. After a period of ozœna the bridge of the nose may fall in, or a large perforation suddenly appear in the hard palate. The process may spread to the skin and most disfiguring ulceration of the face ensue. Gummata of the cranial vault may start in the inner or the outer tables of the affected bones. In the latter case, unless the resulting swelling is absorbed under treatment, a circular or perhaps a horse-shoe- or trefoil-shaped ulcer is formed with an ivory-hard ridge. The skull may be perforated, but usually by then the cranial cavity has been shut off. If the inner table is first affected, irritative and pressure symptoms result. Vertebral gummata are rare; according to their situation they may cause retro-pharyngeal, lumbar, or iliac abscesses. Rarely they may cause pressure on the cord.

The *mouth and throat* often suffer severely in tertiary syphilis. Gumma of the tonsil is followed by ulceration. The soft palate may be strewn with a number of pea-like nodules which often ulcerate and result in all grades of deformity. Perforation, usually at the junction with the hard palate, is common, and sometimes the soft palate becomes adherent to the posterior pharyngeal wall. Perforation of the hard palate may result from gummata commencing on the mouth side.

In the *tongue* discrete gummata may eventually reach the surface and cause deeply punched-out ulcers. In a form analogous to the tubero-serpiginous syphilide a number of pea-like nodules affect a moderately large area of the tongue. This becomes swollen and tender, but, unlike the diffuse glossitis mentioned below, is very amenable to treatment. A much commoner manifestation of tertiary syphilis of the tongue is diffuse glossitis, which may be deep or superficial. The affected portions are swollen and the surface is smooth, hard, inelastic and usually covered by a bluish-white pellicle (*leucoplakia*). On retrogression, the tongue becomes cut up into numerous islands by fissures of varying depth. The tongue is tender, and intolerant of spices and hot food.

The insides of the cheeks opposite the gap between the upper and lower teeth often show leucoplakia as a white ridge cut up herringbone fashion, which is quite characteristic.

Tertiary syphilis of the *testicle* occurs in two forms, diffuse interstitial and nodular. In the former the testicle slowly enlarges and becomes heavy but remains quite smooth ; the testicular sensation is lost. In the nodular form, often engrafted on the diffuse, gummata project like bosses from the surface of the testis. The epididymis is usually not palpable, and commonly the cord is moderately thickened. There may be a hydrocele. The gummata may break down, giving rise to a form of *fungus testis*. Syphilitic epididymitis is rare, and syphilitic prostatitis more so. It is interesting that, although histological evidence of involvement of the body of the testicle can be found in almost every case, changes in the ovaries are very rare.

Fever occurs in some cases, and its dependence on syphilis has been shown by its response to anti-syphilitic treatment. It has been seen mostly in hepatic syphilis. As examples of the type of fever and the importance of an investigation with syphilis in view in cases of obscure pyrexia, the disease has been mistaken for rheumatic fever in those cases of the former in which there was periostitis in the vicinity of joints ; it has also been mistaken for tuberculosis.

Diagnosis of Tertiary Lesions.—An indolent swelling, or an ulcer preceded by a swelling, the lesion being obviously deeply embedded in the tissues or breaking down in the middle (which contains a characteristically gummy material) and sclerosing at the margin, with a circular, crescentic or evenly sinuous contour, and brownish-red in colour, should always arouse a suspicion of syphilis. Denial of primary sore, or of secondary lesions, is of no importance, as they may never have appeared or have long ago been forgotten. The positive serum reactions may mislead, since by no means all ulcers in an old syphilitic are themselves syphilitic. On the other hand, negative serum reactions are rather strong evidence against tertiary syphilis. *Epithelioma* is perhaps more likely to be confused with tertiary syphilis when the lesion is in the mouth, but epithelioma has a considerably harder margin, and the edge is rolled, not clean-cut. A positive serum reaction may be a trap, as epithelioma is often engrafted on an old syphilitic glossitis. Ulcers on the legs resulting from *varicose veins* or *impetigo* may arouse a suspicion of syphilis. They are usually much less regular in contour and associated with more inflammatory or congestive manifestations. Syphilitic orchitis is easily distinguished from other conditions by the evenly smooth hardness of the testicle, the weight and the absence of testicular feeling. Syphilis of the viscera and of the central nervous system is dealt with in other sections of this work.

Congenital Syphilis

An infected mother can transmit syphilis to her offspring long after she has ceased to be sexually contagious. Syphilis transmitted to the fœtus during the early months or years of the mother's disease is usually fatal, and a miscarriage results. In the classical case, in successive pregnancies miscarriages of viable fœtus are succeeded by still-births at term, by infants born alive but dying shortly afterwards, by infants which survive though

syphilitic, and eventually by healthy ones. This history of gradual attenuation of the infection is, however, not invariable; in some families a healthy infant may be sandwiched between diseased ones, and in the case of twins one only may be syphilitic. It is generally believed that transmission almost always occurs through infection of the mother, though a few workers consider that the ovum can be infected directly. The fœtus is commonly infected in the second half of pregnancy.

Symptoms.—A syphilitic infant born alive may show an eruption of bullæ or pustules resting on dark-red bases. The secretion contains *S. pallida* in large numbers. A commoner event is the maculo-roseolar eruption, coming on about 3 weeks or a month after birth. It selects chiefly the napkin area, the neighbourhood of the nose and mouth, and the palms and soles, but the whole trunk and limbs may be affected. The macules often run together into large patches which may be annular, as in the recurrent form of acquired syphilis. In moist areas, and where the rash is exposed to friction, the affected area becomes red and glazed, or crusted. Condylomata and moist papules occur and ulcerative fissures or rhagades may form at the angles of the mouth. These often leave radiating scars which remain as stigmata of the disease. The nails may become opaque and irregular, or there is infiltration and oozing of serum around the nail, which is loosened and shed. The hair is often shed extensively; on the other hand, syphilitic infants may grow an abundant crop of hair, which has been called the "syphilitic mop," though it occurs in other diseases. Mucous patches in the nose, mouth, throat and larynx cause the well-known "snuffles" and the hoarse, raucous cry of the syphilitic infant. Suppurative otitis media is often an early manifestation, and leads to hopeless deafness.

Tertiary lesions may appear very early, or not until the ages of 7, 14, 21, or even later. Thus diffuse interstitial orchitis may occur during the first 6 months. Skin gummata may appear in the first year or two as small infiltrates which break in the centre to discharge their mucoid contents. Tertiary lesions of the mouth and throat may appear at any time after the first year, and result in perforation of the palate and great deformity of the soft palate and faucial pillars. Destruction of the nasal support results in saddle-nose, and from the age of about 11 there is a liability to sudden deafness from gummatous changes of the internal ear. The affection usually starts in one ear, but quickly follows in the other, and the child becomes permanently deaf. Choroiditis and iritis may appear as early as the age of 5 months, and, unless properly treated, lead to blindness, or considerable impairment of sight. Interstitial keratitis may begin at any age from 6 to 30 or even later. Usually it starts in one eye, and the other follows suit in a few months, often in spite of treatment. The cornea of the affected eye gradually becomes opaque from the margin inwards, and this is followed by vascularisation, causing a pink patch (*salmon patch*); the cornea may gradually weaken and bulge before the intra-ocular pressure, or it may ulcerate. Gradually, after many months, the cornea may clear more or less completely, but the patient is often left with permanently damaged sight owing to concomitant iritis and choroiditis. The permanent teeth may show signs of congenital syphilis in the form of notching of certain teeth, which are narrowed at their cutting bases (*Hutchinson's teeth*). The two upper central incisors are much the most usually affected, but all the incisors may be notched. These

characteristics are usually lost after the age of 20. The first molars are often dome-shaped (*Moon's teeth*).

The long bones may be affected in various ways. Syphilitic epiphysitis (Wegner's "osteo-chondritis syphilitica") is a very constant effect of congenital syphilis, being detectable at birth by radiographic examination, which shows broadening and irregularity of the epiphyseodiaphyseal zone. This radiographic examination is very valuable for diagnosis during the first 6 months; afterwards the appearances may not be so characteristic. Epiphysitis may cause signs simulating paralysis (*syphilitic pseudo-paralysis*) owing to the rapid loss of movement which occurs. Movement of the limb causes severe pain, which explains the apparent paralysis. The epiphysis is swollen, and occasionally definite separation occurs. Arthritis may be associated with epiphysitis, and the joint may suppurate. Between 5 and 18 years of age chronic synovitis may appear, affecting chiefly the knees, with swelling of joints (Clutton's joints), but with slight pain or intererence with movement.

Dactylitis occurring in the second year causes fusiform swelling of the proximal phalanges of two or more fingers, or, more rarely, toes. At a later period in childhood, between the ages of 8 and 14, chronic periostitis of long bones is apt to cause characteristic deformities, best shown in the tibiæ, which becomes shaped like sabre-scabbards.

The visceral and nervous affections of congenital syphilis are dealt with in other sections, and here it must suffice to say that in infants and young children anæmia and marasmus, as also delayed development and proneness to death from intercurrent affections, are common consequences of congenital syphilis.

Diagnosis.—The serum reactions at birth and for some weeks afterwards are of no help in deciding whether or not it has been infected. It has been shown by Fildes, Whitridge Williams, Cruickshank, Dunham and others that an important proportion of those born with positive blood become negative later, and vice versa. In a non-syphilitic infant any positive reaction dies out rather quickly, and if there is reason to hope that, through treatment of the mother or the age of the infection, the infant has escaped, before accepting a positive reaction as diagnostic the test should be repeated quantitatively at weekly intervals; maintenance or strengthening of the reaction over some weeks would justify a diagnosis, and vice versa.

Syphilitic pemphigus occurs on the palms, is earlier than ordinary *pemphigus neonatorum*, and *S. pallida* can be found in the secretion. Ordinary *erythemata* are brighter red, and associated with friction and moisture such as from wet napkins, while the syphilide is not necessarily accounted for by friction, or by moisture, and is associated with such signs as "snuffles" and chronic laryngitis.

Syphilitic epiphysitis is distinguished from *true paralysis* by the pain on movement and contraction of the muscles when the skin is irritated. It occurs earlier than *scurvy* or *rickets*, appearing about the third week, and is associated with the skin and mucous-membrane lesions of syphilis. It is well to remember that syphilis has been found to be responsible for many of the nutritional and mental disorders of childhood, and that it is advisable to investigate every obscure case with syphilis in view.

Treatment.—PROPHYLACTIC.—For males a good condom is a safeguard

so far as the parts which it covers are concerned; it also protects the female. It should be removed with care to prevent contamination of the parts by the discharge on it. Whether or not a condom is used it is advisable to disinfect, by washing well with soap and water and then steeping the parts for some minutes in $\frac{1}{2000}$ mercuric potassium iodide solution, or $\frac{1}{2000}$ mercury oxycyanide lotion. After this the parts should be anointed with an ointment, such as Gauducheau's, viz., mercury cyanide, 0·10; thymol, 1·75; calomel, 25·00; lanolin, 50·00; liquid paraffin, 10·00; soft paraffin to 100·00. Some mercury oxycyanide lotion $\frac{1}{4000}$ may be injected into the urethra after urination; in urination the meatus should be alternately squeezed and released so that the urine first distends and then rushes forcibly from the urethra. In females the prior insertion of a suppository which foams on insertion into the vagina is most likely to prevent contact of the secretion with the mucous membrane of the vagina and cervix; it should be followed by an antiseptic douche. Washing of the external genitals, followed by their inunction with ointment as above, should be practised as in males. It is important to remember that in all cases disinfection should be prompt and thorough.

Prophylaxis by ingestion or injection of anti-syphilitic remedies is not recommended, because it may only mask the symptoms for many months.

As any prophylactic measure may prevent only the appearance of the chancre, it should be followed by blood tests for at least 3 months.

Accidental infection of fingers, lips and other extra-genital parts is best prevented by avoiding contamination with fresh secretions from persons in the earlier stages. These should be warned of the risk arising from sharing table utensils, crockery, and house linen with others. They should not kiss others or talk directly into people's faces, and articles which they have used should be dipped in very hot water. A further precaution is to keep open lesions smeared with an antiseptic ointment such as the cream mentioned above.

The prevention of transmission to offspring is primarily a matter of preventing infection of mothers. A man who has contracted syphilis should be advised to wait for at least five years before marrying; by that time the risk of transmission by sexual intercourse has usually gone, whatever the treatment. The period can be shortened by treatment, but this must be prolonged and thorough. A syphilitic woman is liable to convey the disease to her offspring throughout the child-bearing period, especially in the first five years of the infection, but efficient treatment commenced in the first half of pregnancy will usually protect the fœtus; if treatment is started later and the mother's infection is recent, it is usually safest to regard it as remédial and to continue treating the infant after birth.

CURATIVE.—The remedies most commonly employed for the treatment of syphilis are preparations of arsenic, mercury, bismuth and iodine. The first three destroy the parasites; the last stimulate the removal of granulomatous tissue.

Arsenical preparations.—These are organic compounds in which the arsenic is trivalent or pentavalent.

Trivalent arsenical remedies.—These are by far the most efficient of the arsenical remedies for the treatment of syphilis outside the central nervous system and, beginning with the famous "606" or the Ehrlich-Hata remedy introduced to the public in 1910, have revolutionised the treatment of

syphilis. There are now a large number of these compounds whose different trade names are apt to be confusing, but fortunately they are subject to Regulations under the Therapeutic Substances Act, and each, besides being required to satisfy certain tests for toxicity and therapeutic potency, must bear on its label an official name according to its chemical constitution. The following are the principal remedies in this class.

(i) Arsphenamine, or the dihydrochloride of dioxy-diamino-arsenobenzene, which is the original "606," or salvarsan; it is sold under the trade names, Arsenobillon, Diarsenol, Kharsivan and Salvarsan; and it must have an arsenical content not less than 30 per cent. and not more than 34 per cent. (ii) The disodium salt of (i), or sodium salvarsan; it contains about 20 per cent. As. (iii) Neoarsphenamine, or the sodium salt of dioxy-diamino-arsenobenzene-methylene-sulphoxylic acid, which is the original "914," or neosalvarsan; it is sold under the trade names, Neoarsphenamine-Evans, Neokharsivan, Neosalvarsan, Novarsan, Novarsenobillon and Novostab; it must contain not less than 18 per cent. and not more than 21 per cent. As. (iv) Sulpharsphenamine, or the sodium salt of dioxy-diamino-arsenobenzene-methylene-sulphurous acid; it is sold under the trade names, Kharsulphan, Metarsenobillon, Myosalvarsan, Sulfarsenol and Sulphostab; and its arsenical content is the same as that of neoarsphenamine. (v) Arsphenamine glucoside, or Stabilarsan; the arsenical content of the dose stated on the label equals that of the same dose of neoarsphenamine. (vi) Silver arsphenamine. (vii) Neosilver arsphenamine.

All the above compounds except the diglucoside are in powder form, sealed, in stated doses, in glass ampoules containing a neutral gas. All the powders except the silver preparations are yellow. All oxidise and become increasingly toxic on exposure to air and must consequently be made up and administered as soon as possible after the ampoule has been opened. Oxidation in the ampoule, through a flaw in the glass, makes the powder become darker and sticky. Stabilarsan is in solution and ready for use when drawn from the ampoule. It must be used before the expiry date stated on the label.

Arsphenamine is therapeutically the most active of these compounds, but is little used outside U.S.A. because of the complexity of its preparation for administration and of its greater tendency to cause serious reactions on the day of injection. Sodium salvarsan is not greatly used in English-speaking countries.

Neoarsphenamine is by far the most commonly used of all the arsenobenzene compounds. In equivalent dosage it is less active than arsphenamine, but is more easily prepared for administration and causes less general reaction. It causes too much pain to be given as routine by the subcutaneous or intramuscular route, but when it is administered in this way it is therapeutically more active. This is probably because the subcutaneous route favours more the retention of the remedy in the body, thus giving better opportunity for the formation of the derivative which is believed to be the spirochæticidal agent.

Sulpharsphenamine was introduced by Lehnhoff-Wyld under the name of Sulfarsenol for injection by the intramuscular or deep subcutaneous route. It causes comparatively little discomfort when administered in this way. Being relatively stable, its action is inferior to that of neoarsphenamine when

it is given intravenously, and even when administered subcutaneously its effect is barely equal to that of neoarsphenamine given intravenously. It is rather more apt than are the other arsenobenzene compounds to cause blood dyscrasias.

Arsphenamine diglucoside is a convenient preparation in being ready for use when drawn from the ampoule, but its immediate effect in causing disappearance of *S. pallida* from the juice of early lesions is not so great as that of neoarsphenamine in equivalent dosage. A dose of 0·45 g. of a good brand of neoarsphenamine will cause *S. pallida* to disappear from such lesions in 24 hours in over 75 per cent. of cases, but, in my experience, even 0·60 g. stabilarsan has failed in this respect in over 50 per cent. of cases. Whether or not this preparation makes up for its slower spirochæticidal action by greater persistence is uncertain. Silver arsphenamine and neosilver arsphenamine are emery-coloured powders. They are more active but also more toxic than the others and are given in approximately half the dosage of the latter. They are useful as a change from neoarsphenamine but are not now greatly used in Great Britain. A newcomer to the market, though originally tested by Ehrlich, is chemically *m*-amino-*p*-hydroxy-phenylarsine oxide and is sold as Mapharside ; it is not subject to the Therapeutic Substances Act. It is claimed for it that it is the same as the active derivative that is formed when any of the above-named preparations is injected into the body and that, being already oxidised, it is stable. Its dose is about one-tenth that of neoarsphenamine. It is still on trial.

Dosage of arsenobenzene preparations.—Doses of the different preparations named vary greatly with circumstances and can be discussed here only in general terms, but guidance for treatment of individual cases will be found below in the discussions on toxic effects, on contra-indications, and on schemes of treatment. A rational approach to the problem of determining an average dose for an adult male with no contra-indication is a consideration of the amount required to bring about disappearance, within 24 hours, of *S. pallida* from the juice of an early syphilitic lesion, such as a chancre, a condyloma or a mucous patch. It is 0·45 g. to 0·60 g. in the case of neoarsphenamine, and is approximately the same for sulpharsphenamine ; these doses correspond to 0·30 g. to 0·40 g. arsphenamine. In the case of arsphenamine diglucoside the dose required to produce the same effect is somewhat higher, but in that of silver-arsphenamine it is only 0·15 g.

In a case of active primary or secondary syphilis it is reasonable to aim to bring about rapid disappearance of *S. pallida* from the juice of external lesions, and when there is no contra-indication in an adult male I commence with 0·45 g. neoarsphenamine. If, in such a case, I have to begin with a lower dose, it is with no illusion as to the effect on the spirochætes. It is well, therefore, that readers should bear in mind that the official dose of neoarsphenamine or of sulpharsphenamine, the only preparations of this kind in the British Pharmacopœia, commences at a level (0·15 g.) which in the case of an adult would not damage the spirochæte. At the same time it should also be borne in mind that in certain circumstances, as in administration of these remedies to cases of cardio-vascular syphilis, this lower dose may be too high. These remarks may serve to illustrate the difficulty of stating a dosage categorically but, as mentioned, sufficient guidance for treatment of individual cases will be found below.

Administration of arsphenamine preparations

Intravenous route.—This is the most usual route. In the case of neo-arsphenamine the dose is dissolved in 2 to 10 c.c. distilled water. Silver-arsphenamines are dissolved in not less than 8 c.c., and stabilarsan is already in solution and requires no further dilution. The solution is drawn into a syringe, which is armed with a fairly fine needle, any of it contaminating the outside of the needle is washed off under the hot water tap, and the point of the needle is inserted into a median basilic or other convenient vein, which should be distended as tightly as possible by fixing an elastic band round the upper arm and getting the patient to grasp a roller bandage. In making the vein-puncture the operator should look along the vein, and steady it with the index finger of the other hand laid on the skin below the site; the eye of the needle should look away from the skin, and its shaft be almost parallel with it. A pull on the piston causes blood to flow back into the syringe when the needle is properly within the vein. The rubber band may then be released (I usually retain it, for reasons given later), and the piston is *slowly* pressed home. After it has been emptied, a little blood is aspirated into the syringe and again injected in order to clear the needle of any solution.

Deep subcutaneous and intramuscular routes. — As already mentioned, arsphenamine remedies have a greater therapeutic effect when administered subcutaneously or intramuscularly, but most cause too much pain, and practically the only one which can be employed for the purpose is sulph-arsphenamine. The dose may be dissolved in distilled water, or in one of the glucose solvents containing local sedatives which are sold for the purpose. In either case as little as 1 c.c. may be used, but 3 or 4 c.c. of the glucose solvent seems to be more effective in preventing local reaction. The technique of intramuscular injection is described on p. 216. Deep subcutaneous injection causes less muscle reaction, and is usually preferable; it is given as follows: In the upper and outer quadrant of the gluteal region the skin and fat are pulled away from the underlying fascia, by grasping them with the thumb and fingers of the left hand, and a 2-inch record needle is entered obliquely at the base of the pyramid thus produced. The needle is made to underrun the fat so that its point may scrape on the fascia overlying the gluteal muscles. The charged syringe is fitted to the needle and the injection given fairly slowly. The site is then massaged with a pad of lint.

Toxic effects of arsphenamine remedies.—Local.—An intravenous injection of any arsphenamine preparation may cause thrombosis of the injected vein; this is not serious, but precludes the use of the vein for subsequent injections. Escape of any of the solution around the vein causes agonising pain, and swelling and infiltration of the tissues, which may go on to sloughing. When it occurs nothing appears to mitigate it better than such local and general sedatives as are used in any local inflammation.

General.—All these compounds tend to damage capillary endothelium. In patients who have died as a result of arsphenamine injections, there have been found blockage of cerebral capillaries with small hæmorrhages around; hæmorrhagic nephritis; hæmorrhage into lung alveoli; submucous petechiæ and ecchymoses in the stomach and bowel; and, in a comparatively few cases, degeneration of liver cells amounting to a condition like that found in acute yellow atrophy.

Clinically, toxic effects are manifested by one or more of the symptoms enumerated below. The list is a comparatively long one, but most of the symptoms are so mild, infrequent, or preventable as not to preclude the routine use of these remedies. In roughly chronological order they are as follows:

1. *During or immediately after the injection.*—(1) Vasomotor disturbances, also known as anaphylactoid symptoms or minor nitritoid crises; (2) urticaria; (3) syncope; (4) pain in the gums and teeth.

2. *Following the injection usually in a few hours,* and occurring generally on the same day.—(5) Rigor, rise of temperature, and headache; (6) vomiting, diarrhœa, pain in the back and cramp in the legs; (7) herpes (labialis or zoster).

3. *At various times from a day or two to a month or longer* after a single injection or a course of injections.—(8) Albuminuria; (9) stomatitis; (10) chronic headache; lassitude; loss of appetite, weight and sleep; (11) erythema and dermatitis; (12) jaundice; (13) severe cerebral symptoms; (14) various blood dyscrasias; (15) polyneuritis; (16) increase of syphilitic signs and symptoms (Jarisch-Herxheimer reaction).

The *vasomotor symptoms* simulate those of anaphylaxis. The face becomes flushed, and the tongue and lips may swell; there may be respiratory distress, and the patient may become unconscious. Often a severe attack is followed by more or less generalised *urticaria*. As a rule the symptoms last for about half an hour, but in rare cases recovery is not complete for a number of hours. Some patients are peculiarly susceptible. In others the symptoms may be produced by imperfect preparation of the remedy for injection or too rapid administration, as they depend on the physical state of the solution on entering the circulation. For prevention, all these remedies should be injected slowly, and retention of the tourniquet during the injection, as recommended by Sicard, is very effective. The treatment usually employed is to inject 10 to 15 minims of solution of adrenaline hydrochloride (1 in 1000) hypodermically. A feeling of *faintness* during the injection, or immediately after it, may be merely a precursor of vomiting, or due to fear. Occasionally, however, it may be very severe, fatal cases having been reported. Usually syncopal symptoms yield to ordinary restoratives; in some very threatening cases immersion in a hot bath has been reported to have brought about rapid recovery. *Pain in the gums and teeth* is probably vasomotor. The *peculiar taste in the mouth*, of which some patients complain during the injection, is a very common symptom when concentrated solutions are given.

Rigor, rise of temperature and *headache* are commonest after the first injection. The temperature is only rarely over 101° F. and is of no importance unless it increases after each successive injection. *Diarrhœa* and *vomiting* are not frequent unless there has been an error in technique, or the patient has been indiscreet in his dietary. Usually these symptoms have all disappeared by the next day. They are prevented to some extent by taking care that the patient has fasted for 2 hours before the injection.

Albuminuria very rarely causes any anxiety. *Stomatitis* is not often attributed to arsphenamine remedies, but these undoubtedly seem to increase the tendency to this complication which is manifested by patients on mercurial, or bismuth treatment. *Chronic headache, lassitude,* etc., are symptoms

of intolerance displayed by a few patients, and indicate the necessity of a rest from treatment.

Various *skin affections* may occur besides the urticaria and herpes mentioned above, and may be very serious. The mildest is some slight itching which quickly passes off. Another form is Milian's erythema of the ninth day. It appears from the seventh to twelfth day after the commencement of the treatment and within ½ to 2 days of an injection. It is ushered in with a rapid rise of temperature, to 101° F. or higher, headache, backache, and sometimes vomiting and diarrhœa. The temperature is intermittent for a few days, and ends with a generalised scarlatiniform, rubeoliform, or polymorphic eruption, which fades in a few days with very slight or no desquamation. In its prodromal fever and the subsidence of a generalised rash without desquamation in a few days Milian's erythema differs generally from the more serious type described next. Although it is said that arsenical treatment can be resumed after subsidence of ninth-day erythema, it is well to be very cautious on this point. The most severe dermatosis is relatively uncommon. It starts as a punctiform erythema which quickly spreads over the body, is accompanied by most intense itching, and often then passes on to exfoliative dermatitis. The incidence of dermatitis depends largely on the intensity of the treatment. Generally speaking, a male adult of average build will tolerate 5 to 6 g. neoarsphenamine in doses of 0·45 to 0·75, or the equivalent of this in other arsphenamine remedies, spread out over a period of 57 days but if this period is shortened the percentage of dermatitis increases noticeably. A careful look-out for signs of skin irritation will often supply timely warning of the idiosyncrasy and, by preventing the administration of more arsenic, will save the patient from a severe attack. The treatment of exfoliative dermatitis following arsphenamine injections is often troublesome on account of the generalised exfoliation and the local pustulation and eczema. If the attack is at all severe, the patient should be in bed and well protected. The injection of calcium thiosulphate, or sodium thiosulphate, which is now sold for the purpose in ampoules containing the remedy already in solution, has proved to be very useful in aborting the toxic effects of arsenic, bismuth and mercury. The dosage for general use is 0·6 to 0·9 g., injected intravenously very slowly every other day. The injection of calcium thiosulphate often causes a generalised tingling and flushing of the skin, which alarms the patient but passes off very quickly. On intervening days an intravenous injection of 25 c.c. of a 40 per cent. solution of dextrose is valuable. The administration of liver, on the same principles as in anæmia, has been found very beneficial. The diet should be simple, containing large quantities of bland liquids, and should not include eggs and meat. Locally, calamine lotion and liniment are soothing, and an occasional bran bath is valuable, but careful precautions should be taken against chill, as these patients are very prone to pneumonia.

Jaundice following injections of arsphenamine preparations appears to have become more common in recent years, and a voluminous literature on its ætiology has accumulated in all countries without any definite consensus of opinion having been arrived at. In the very great majority of cases the type is mild, with clayey stools and highly coloured urine. Occasionally it is much more serious, with severe epigastric and hepatic pain, restlessness and delirium, followed by death. The changes found in these rare cases have

been extensive degeneration of liver cells with round-celled infiltration of the supporting connective tissue, multiple subserous hæmorrhages, and frequently hæmorrhages into lung alveoli. Either type may occur during a course of injections or be delayed for many months afterwards. In this delay in onset, as in some other features, the fatal type of jaundice strongly resembles trinitro-toluene poisoning. The exact part played by arsphenamine in the production of jaundice is uncertain, but the weight of evidence seems at present to favour a connection between the amount administered as routine in a given time and the proportional incidence of jaundice, the more concentrated the course the higher being the percentage of jaundice. A feature of the fatal type of jaundice which has been noted in this and other countries is its tendency to occur in limited outbreaks which bear no apparent relation to changes in technique or brand of the remedy employed. This feature lends some support to the theory, held by some, that besides arsphenamine an extraneous agency (bacterial infection ?) plays a part in the causation. This view is supported by evidence furnished by Ruge from the German Navy, in which it was found that the incidence of salvarsan jaundice was closely parallel to that of ordinary catarrhal jaundice in the general population.

For the *prevention* of jaundice, apart from the value of care in dosage, clinical evidence suggests that the well-fed patient is far less likely to suffer from this complication than is the starved one. Recent work by Messinger and Hawkins shows that, contrary to the finding of Craven, the best preventive is a protein diet and after this a carbohydrate. For treatment, besides reduction of the diet to slops, administration of liver and daily intravenous injections of 25 to 50 or more c.c. of a 40 per cent. solution of dextrose are useful.

Severe *cerebral symptoms*, with headache followed by mental confusion, epileptiform convulsions and coma, ending in death in a large proportion of cases, are now very rare, thanks to the moderate doses with which treatment is usually begun. One patient, whom I saw in the comatose condition, was restored within half an hour by phlebotomy to 20 ounces, the removal of 15 c.c. of cerebro-spinal fluid, and the injection of 1 c.c. of solution of adrenaline hydrochloride 1 in 1000. Other workers have since been equally successful by this means. The treatment should be applied at once, and the lumbar puncture should be repeated if the symptoms continue.

Blood dyscrasias.—Three main forms of blood dyscrasias have been described, all of them very rare. They have followed sulpharsphenamine treatment relatively much more often than treatment by other arsphenamine preparations. They are thrombocytopenia, granulocytopenia, and aplastic anæmia. When any occurs it is often associated with the dermatitis and stomatitis. Their symptoms and treatment are described elsewhere in this work.

Polyneuritis has been reported occasionally but must be extremely rare; I have seen only one case, a very mild one.

Jarisch-Herxheimer reaction.—A temporary effect of these, as of other antisyphilitic remedies, may be to increase the intensity of the syphilitic process. This may be important when an artery supplying some vital organ is already partly blocked; then the increase in severity of the process may result in a complete blockage which may be disastrous, as when a coronary

artery becomes obstructed, or the patient develops hemiplegia, or dies of obstruction of the basilar artery. Such cases are very rare.

Neuro-recurrences.—Though not strictly a direct effect of arsphenamine treatment, paralyses of various cranial nerves, especially the seventh and eighth, became more common shortly after its introduction. These phenomena have been proved to be syphilitic recurrences and due to the small amount of treatment given in the early days of "606." Since then they have become comparatively rare, at any rate, when bismuth or mercury is given concurrently with the arsphenamine preparation in all early cases.

Precautions recommended in treating patients with arsphenamine preparations.—In the case of sufferers from hepatic and advanced Addison's disease, bleeders, and those on the point of death from severe visceral disease of any kind, these remedies are contra-indicated.

In visceral disease of a less severe type than is mentioned above, in alcoholism, and when the patient is prone to such skin affections as eczema and severe seborrhœa, it is advisable to begin with a dose of 0·15 to 0·3 g. of neoarsphenamine, and to increase the doses with caution; often in such cases the injections of small doses may be given with advantage twice weekly. The same applies to patients suffering from syphilis of the brain, cord or viscera when there is reason to fear an exacerbation of the process. In diabetes mellitus it is necessary to be very cautious, as arsphenamine compounds increase the blood sugar, and the patient should be watched carefully by some one experienced in the administration of insulin. Every patient should be watched carefully through the course for signs of intolerance. This precaution may not absolutely prevent severe side-effects, but such as do develop will usually be much milder than when no notice is taken, for example, of an erythema, and the treatment is continued to the end of the course.

In all cases where intravenous injections are employed it is advisable for the patient to fast for 2 hours beforehand. Other methods of prevention of this and other toxic effects of arsphenamine consist in scrupulous care over technique.

Pentavalent arsenical remedies.—The principal remedies of this class used in the treatment of syphilis are (i) Sodium N-phenylglycineamide-*p*-arsonate (tryparsamide); (ii) 3-acetylamino-4-hydroxyphenyl-arsonic acid, or acetarsol (kharophen, orarsan, spirocid and stovarsol); (iii) the sodium salt of (ii); and (iv) the diethylamine compound of (ii) (acetylarsan).

Of these, tryparsamide is the most important because of its value in syphilis of the central nervous system. It is a white powder easily soluble in water, and the dose for an adult is from 2 to 4 g. (usually 3 g.) dissolved freshly in distilled water and injected intravenously once a week. A course lasts 10 to 12 weeks, and the interval between any two courses can be a month or six weeks. The main risk is of amblyopia, and for this reason the patient's eye-grounds should be passed by an ophthalmologist before treatment is started. If this is stopped on the first complaint of haziness of vision, permanent restriction of vision is very rare. Acetarsol was introduced in 1922 primarily as a prophylactic of syphilis for administration by mouth. Later it came into extensive use for the treatment of infants with congenital syphilis. Acetarsol-sodium and acetylarsan are given by injection; their effects are mainly like those of acetarsol. Toxic effects are usually mild. Acetarsol

can cause gastro-intestinal disturbance if taken too near a meal. Sometimes a mild erythema occurs and very rarely a severe dermatitis.

Mercurial preparations.

Mercury was formerly the sheet-anchor in the treatment of syphilis, but for routine work it has been largely superseded by bismuth, and it is now used mostly in cases where injections are undesirable, or impracticable, or by way of varying the attack on the disease. A great advantage of mercury, as of bismuth, is that it can be kept almost continuously in the circulation, so that the action is maintained after the arsphenamine has been excreted until it is safe to administer another such injection. To ensure the certain destruction of all the parasites, it seems to be necessary that an anti-syphilitic remedy should be present constantly in the body fluids for a long period.

Methods of administration of mercurial preparations.—The *oral method* is much favoured, but is apt to cause gastro-intestinal disturbance, and is exposed to the risk of failure through the patient's forgetfulness. I employ it only when the patient cannot take injections or inunctions and also when the patient cannot continue injections or remain under close observation. Favourite preparations are—(1) Hydrargyrum cum creta, grs. 1 to 2; (2) hydrargyri iodidum viride or flavum, gr. $\frac{1}{6}$ to $\frac{1}{4}$; (3) hydrargyri perchloridum, gr. $\frac{1}{8}$; (4) hydrargyri tannas, gr. 1 to 3; (5) pil. hydrargyri, grs. 1 to 3; (6) liq. hydrargyri perchloridi, min. 30 to 60, often prescribed in a mixture with potassium iodide. The first five of these are usually given in pill form, often combined with a little opium, *e.g.* pulv. ipecacuanhæ et opii grs. 1 to 2, or extractum opii gr. $\frac{1}{8}$, to counteract the irritant effect, but it is better to prescribe the sedative separately, and regulate its dosage as required. I prefer to start with the iodide. A good plan of administration is to give courses of 6 weeks, gradually increasing the daily intake of mercury until slight signs of stomatitis appear, and then reducing the dose. After the first and second courses rests of a week are given, and at the end of the third the interval is one month, after which the series of three courses is repeated. The length of time over which this treatment is prolonged depends greatly on the amount and character of the previous treatment.

Inunction.—This is a valuable method of administering mercury, but must be carried out by a skilled rubber, and has the inconvenience of soiling the skin and clothes. On successive days 5 to 10 g. of mercurial ointment (B.P.) are rubbed for twenty minutes into thighs, calves, arms, chest and back, a bath being taken on the sixth day and the cycle restarted on the seventh. The number of rubbings varies from 60 to 200 in a course, the length of a course depending on the patient's tolerance, which is judged by the state of the gums, the weight and the general well-being.

Intravenous injections are rapid in effect, but apt to cause toxic symptoms; they have the further disadvantage that the effect is not sustained, and must be administered daily or every other day. The usual preparations employed are the cyanide and the perchloride, in doses of 1 c.c. of the 1 per cent. solution daily or on alternate days to a total of twenty or thirty.

For *intramuscular injections* both soluble and insoluble preparations are employed. Among the *soluble* preparations are the biniodide (1 per cent. solution) in doses of 1 c.c., the bibromide, the benzoate and the perchloride. Their disadvantages are similar to those of intravenous injections.

The *insoluble* preparations most commonly employed are mercury in fine subdivision (inj. hydrargyri), calomel (inj. hydrarg. subchlor. and mercury salicylate. Suspensions of these remedies ready for use can be purchased. The doses usually employed are: mercury, 1 to 1½ grs.; calomel, ½ to ¾ gr.; salicylate, 1½ to 2 grs. Calomel causes more pain than the other two, but is far more active, and is probably the best for this purpose if it can be tolerated. Mercury salicylate is probably the least active of the three. The advantages of the insoluble preparations are that, on account of the slow absorption, enough mercury can be given in one injection to last a week and that the effect is sustained.

The technique of intramuscular injections is simple. The best site is the upper and outer quadrant of the gluteal region. A needle 1½ to 2 inches long is introduced, almost to its full length, perpendicularly to the skin surface. The base is examined to see that no blood is oozing from it, the syringe is applied, the piston pulled upon to see that the needle point is still not within a vein, and the piston is then pressed home. The needle, having been withdrawn, the site is well massaged with a ball of cotton-wool. Before an insoluble preparation is drawn into the syringe, the suspension should have been well mixed, either by stirring with a glass rod or by energetic shaking of the bottle.

Toxic effects of mercury.—These are stomatitis, nephritis, colitis, general malaise and dermatitis.

Stomatitis can usually be prevented by care. The patient's teeth should be set in order before starting the course, and he should brush his teeth night and morning; the tooth brush should be kept in an antiseptic solution, such as chloramine T., 0·5 to 1 per cent., or in an atmosphere of formalin. Potassium chlorate is useful, and may be incorporated in the dentifrice. If the gums become sore, the mercury must be stopped and more energetic treatment applied to the mouth. Lozenges of potassium chlorate to suck, and swabbing with peroxide of hydrogen followed by the application of a 10 per cent. solution of neoarsphenamine usually suffice to restore the gums to a healthy condition. An astringent mouth-wash should be employed and injections given of calcium or sodium thiosulphate. (See p. 212.)

Nephritis rarely results from the moderate doses of mercury now employed, but the irritant effect of mercury on the kidneys should be remembered in cases where these organs are already diseased.

Colitis is extremely uncommon as the result of the ordinary mercurial course of treatment. *General malaise* is apt to result from pushing mercury too freely, and it is always advisable to keep a close watch on the patient's weight and general condition. *Dermatitis* as a result of mercurial treatment alone is very rare.

Bismuth preparations.

These were introduced by Sazerac and Levaditi in 1921, and have now largely supplanted mercury wherever the intramuscular, or deep subcutaneous, route of administration is practicable. Bismuth is tolerated better than mercury, and in doses which can be administered with at least equal safety, a course of bismuth injections goes farther towards eradicating the disease than does a corresponding course of mercurial injections. Some workers assert that bismuth is equal in effect to the arsphenamine preparations, but

the majority opinion is that it should be used in conjunction with these, in substitution for mercury. The toxic effects of bismuth are somewhat similar to those of mercury. The first sign of saturation is a slaty-blue line at the margins of the gums, particularly at the incisor teeth. If the remedy is continued, the buccal mucous membrane may become stained, and aphthous stomatitis supervene; if it is pushed still farther, gangrenous stomatitis may result. The early bismuth blue line may persist for many weeks after suspension of the remedy. Albuminuria may result from overdosing, but disappears quickly if the remedy is suspended as soon as it is noted. Colitis is uncommon. Some may complain of depression and insomnia, which may easily be attributed to other causes than bismuth poisoning.

Bismuth is at present administered almost exclusively by injection, but recently a preparation for oral administration has been introduced by Hanzlik, Lehman and Richardson. It is sold under the name of sobisminol, and has been reported to give good results in doses of 6 capsules of 0·75 g. daily. So far it must be regarded as in the experimental stage and will not be dealt with further.

Injection of bismuth compounds is now almost invariably by the intramuscular or the deep subcutaneous route, and the number of preparations is legion. They are best classified on the basis of rapidity of absorption as follows: (*a*) watery solutions; (*b*) solutions in oil (lipo-soluble preparations); (*c*) suspensions of insoluble compounds in a watery medium; and (*d*) suspensions of insoluble compounds in an oily medium. The comparative rates at which these different classes of bismuth preparations are absorbed are in the above order.

Watery solutions are not greatly employed now, because they are more rapidly absorbed than is usually convenient; on account of rapid absorption, their toxic effects may approach those of preparations given intravenously, a route which is practically never used. Examples of water-soluble compounds are: potassium sodium bismuth tartrate, containing 35 to 40 per cent. Bi.; bismuth sodium tartrate, containing 73·8 per cent. Bi.; bismuth thioglycollate, sold as thiobismol, a solution which contains 0·075 g. Bi. per c.c.; and sodium bismuth citrate, containing 65·8 per cent. Bi. Because of the rapidity of their absorption, an effective concentration of bismuth in the tissues can be maintained with watery solutions of bismuth only by injecting them two or three times a week.

Oily solutions contain organic, lipo-soluble compounds dissolved in oil. In absorbability they are stated to be a useful medium between watery solutions on the one hand and insoluble suspensions on the other. The following are examples of these preparations of which it is unnecessary to state the chemical formulæ (the bismuth content per c.c. is stated in brackets after each): bivatol (0·035 g.); cardyl and neocardyl (0·05 g.); neo-olesal (0·03 g.); and stabismol (0·1 g.). Their rate of absorption makes it advisable to give the weekly dose (see below) in two injections at a 3- to 4-day interval.

Insoluble suspensions are the most commonly employed preparations of bismuth for anti-syphilitic treatment, and this class contains the only three recognised by the British Pharmacopœia, namely, inj. bismuthi, inj. bismuthi oxychloridi and inj. bismuthi salicylatis. A number of insoluble salts of bismuth are used, and they are sold under a large number of names, of which the following are examples arranged according to their chemical

construction. (*a*) Precipitated bismuth. Preparations: inj. bismuthi, B.P. (bismuth in a dextrose solution with cresol), and bisglucol; both contain 0·2 g. Bi. per c.c.; and bicreol (0·15 g. Bi. per c.c.); (*b*) Bismuth oxychloride. Preparations: inj. bismuthi oxychloridi, B.P. and bisoxyl, both of them watery suspensions containing 0·08 g. Bi. per c.c.; chlorostab, a watery suspension, two preparations with, respectively, 0·16 g. and 0·20 g. Bi. per c.c.; (*c*) Bismuth salicylate. Preparations: inj. bismuthi salicylatis, B.P., a 10 per cent. suspension of the compound in olive oil with camphor and phenol; bisantol; bismosan; bismogenol, all oily suspensions; all this class contain about 0·06 g. Bi. per c.c.; (*d*) Bismuth hydroxide. Preparations: casbis, muthanol, and spirillan, oily suspensions containing about 0·08 g. Bi. per c.c.; (*e*) Iodo-bismuthate of quinine. Preparations: biquinyl; bismosalvan; quinby; quinostab; rubyl; vijochin, all oily suspensions containing about 0·02 g. Bi. per c.c.

Choice of bismuth preparations.—In syphilis with active external manifestations and when there is no contra-indication in the nervous system, the heart, and great vessels or other internal organs, we aim at complete eradication of *S. pallida* by attacking it over a long period with two types of remedy, namely, arsphenamine and heavy metal, the latter being either mercury or bismuth, of which bismuth is now almost always preferred. In this combination the arsphenamine compound rapidly stops the activity of *S. pallida*, and each injection of it deals a heavy blow at all *accessible* spirochætes, but the attack is not maintained; the dose of the arsphenamine preparation is quickly excreted, and for a considerable portion of the interval between any two injections, and still more between any two courses of injections, the arsenical remedy is not in action. In these circumstances it is conceivable that spirochætes not hitherto destroyed by the arsphenamine remedy, perhaps because of their entrenchment behind barriers of fibrous tissue, would have an opportunity of recovering unless the attack was carried on by another agent. This is the rôle of the heavy metal, an effective concentration of which can be maintained in the tissues for long periods. It will be understood from the above that, if an arsphenamine preparation is being employed in the treatment of the types of syphilis mentioned, one does not look to the bismuth for speed, but for persistence of action, and a preparation is needed which is absorbed slowly but steadily throughout the intervals between injections; this requirement is met by the use of a suitable insoluble compound. In the choice of such a compound, I am influenced by clinical experience and by reports of research on absorbability of different preparations, especially those of Lomholt, and prefer a compound such as the oxychloride suspended in a watery medium to either of the other two B.P. preparations. In some cases I have been convinced that the precipitated bismuth I have injected has not been absorbed at all satisfactorily, and excretion experiments which show that a higher percentage of a small dose than of a large one are absorbed in a given time argue against the employment of such a concentration of bismuth in the suspension as that in the injectio bismuthi, B.P. Between the salicylate or any of the other insoluble salts and the oxychloride there may possibly be little to choose, but Lomholt's experiments on absorption certainly showed that, other things being equal, a more rapid absorption would follow injection of a watery suspension than that of an oily one, such as injectio bismuthi salicylatis, B.P. On the other hand, the oxychloride is pure and stable

and in watery suspension, provided it is not too finely powdered (particles of 3 to 5 μ dimensions are suitable), it is absorbed at a satisfactory rate without causing undue discomfort. This work confirms the favourable impression I have formed of the oxychloride in watery suspension in an experience of more than fifteen years.

A quicker absorption of an insoluble compound is secured by giving the weekly dose in two injections at an interval of 3 to 4 days, or by dividing the dose between two sites injected at one sitting. In some cases it may not be possible to employ an arsphenamine preparation at all, or only in less than efficient dosage, and one has to depend more on the bismuth to stop the spirochætal activity quickly. In such a case one may give one of the oil-soluble preparations twice a week or proceed on the lines recently recommended by Sollmann and colleagues in U.S.A. In this a soluble preparation is administered two or three times weekly concurrently with an insoluble one once weekly for 5 or 6 weeks, and then the insoluble preparation is continued in weekly injections for 5 more weeks to complete the course.

It will be judged from the above that usually an insoluble compound is injected about once a week, and a soluble one, two or three times. One insoluble compound, however, the iodo-bismuthate of quinine, which is not greatly used in early syphilis, but is valuable in cardio-vascular and neuro-syphilis, contains such a low percentage (20) of bismuth that the dose is contained in a large volume; consequently when employing this compound it is customary to give the weekly amount of bismuth in two injections. This compound is absorbed rather more quickly than most others in the insoluble class. In certain cases one may have reason to fear that the patient might become seriously intolerant, and it may not be desirable that the remedy should continue to be absorbed for long after suspension of the treatment. It would then be advisable to proceed cautiously with an oil-soluble preparation.

In average cases of primary and secondary syphilis I give bismuth concurrently with arsphenamine preparations, believing that when the latter are used alone at the commencement and in such doses as effectually to stop the interaction between parasite and skin, there is a much greater likelihood of the parasite getting a footing in the central nervous system. In this matter of concurrent arsphenamine with bismuth and of alternating arsphenamine courses with bismuth ones, there is a difference of opinion amongst syphilologists, probably the majority in Great Britain believing in the concurrent plan. My own views are based largely on the facts that in the early days of arsphenamine treatment, when great reliance was placed on the administration of "606" *in full or nearly full doses* without the concurrent administration of mercury, syphilitic neuro-recurrences were common, and that in more recent years in certain clinics where the first course of treatment consists entirely of arsphenamine or neoarsphenamine in such doses as we know rapidly bring about the disappearance of *S. pallida* from the secretion of superficial lesions, the incidence of such neuro-recurrences has also been high. Certain clinics in which the alternating plan is followed have not had this experience, and the explanation of the difference may lie in the dose of the arsphenamine preparation. If the dose of arsphenamine used alone in a first course given to an early case of syphilis is not so high as that mentioned above, it may be that the interaction between skin and parasite continues, and so evokes an

immunity response which prevents the spirochæte from stimulating a big enough reaction in the meninges to cause symptoms.

Iodine preparations.

These promote the resolution of syphilitic processes and are most useful in the later stages. The tissue reaction is qualitatively the same in all stages, however, and there are grounds for supposing that the syphilitic infiltrate tends to bury the parasites, making them inaccessible to anti-syphilitic remedies, so that there is a use for iodine preparations in all stages. The favourite preparation is potassium iodide, in doses of 15 to 30 grains thrice daily. It may cause gastro-intestinal disturbance, even when given very dilute in water, and is then better tolerated if made up in a cent. per cent. solution and the dose dropped into milk. The depressing effect of potassium iodide is overcome by giving it with nux vomica. Many proprietary preparations are advertised as superior to potassium iodide, but they should be reserved for cases where the older preparation cannot be tolerated. Sodium iodide is probably the best preparation for intravenous injection. In this case, after testing the patient's tolerance by giving some potassium iodide by mouth, a dose of 150 grains of sodium iodide dissolved in 100 c.c. or more of sterile distilled water is given intravenously every 24 to 48 hours up to a total of 20 to 30 injections per course.

General management of syphilis.

The main principles to be observed in the treatment of syphilis are—(1) to begin as early as possible, before the micro-organism has become buried in the sclerosed primary sore or entrenched in comparatively inaccessible regions, such as the central nervous system; (2) to continue as long as experience shows that there is a possibility of the patient relapsing if treatment ceases; (3) to exploit the patient's natural resistance, by maintaining his general health in the highest possible condition.

Since the decision as to cure has to be postponed for some years after suspension of treatment, and relapse cases are particularly difficult to cure, it is better to treat all cases as if they were of the resistant type. It is a great mistake to stop treatment as soon as the serum reactions become negative, or to continue then with only a feeble form of treatment, such as mercury by mouth.

With regard to the programme of treatment to be followed in an ordinary case of early syphilis in a man of average weight *without clinical* signs of disease of the central nervous system or of any viscus, two alternative plans have been recommended by the Committee of Experts on Syphilis convened by the League of Nations Health Organisation; the plans were based on an analysis of over 13,000 records of early cases of syphilis treated in five countries. By early syphilis the Committee meant primary and secondary syphilis such as constitute the vast majority of syphilis cases seen within the first few years of infection, but, with the reservations as to disease of the central nervous system or of any viscus mentioned above, the recommendations are applicable to most cases within the first three or four years of infection. One plan is described as "intermittent treatment," because in it the arsphenamine and the bismuth preparation are for the most part given concurrently, and intervals of three to five weeks are allowed between courses of

injections. Actually its effect is continuous because the insoluble bismuth administered during each course continues to be absorbed during the interval. The second plan is termed " alternating continuous," since for the most part series of arsphenamine injections alternate with series of bismuth, and no interval longer than a week is allowed between injections. In framing both plans the principles laid down by the Committee were :

" (*a*) To employ a comparatively heavy individual dosage of the arsenobenzene and of the bismuth or mercurial compounds, the doses being administered in comparatively rapid succession, especially at the commencement ;

" (*b*) To maintain a persistent attack on the disease, avoiding intervals of such lengths as to afford the parasite an opportunity of recovering ;

" (*c*) To administer approximately as much treatment to primary as to secondary cases."

The plan of " intermittent treatment " prescribes a series of courses as follows, with intervals of three to five weeks between any two courses. In the first seven weeks 8 injections of 0·6 to 0·75 g. neoarsphenamine (or other arsphenamine preparation in equivalent doses) concurrently with the same number of doses of an insoluble compound of bismuth, each containing 0·20 to 0·24 g. metallic bismuth (*e.g.* 0·25 to 0·30 bismuth oxychloride), or else twice the number of injections of a liposoluble compound of bismuth, each containing 0·10 g. metallic bismuth ; in the next two weeks only bismuth is given.

The blood is tested at the end of each course. The minimum number of courses for any case which remains or becomes serologically negative during or by the end of the first course is four. For cases that are not negative by the end of the first course the minimum is three beyond that course which ends with negative reactions. For non-pregnant females the treatment should be on similar lines, with the individual dose of neoarsphenamine reduced by 0·15 g.

In the recommended plan of " alternating continuous " treatment for an adult man, after three doses of " 606 " or alternative arsphenamine preparation totalling 0·1 g. per 25 lb. weight in the first week, 0·4 g. " 606 " is given in each of the 3rd to 7th, 12th to 17th, 24th to 29th, 38th to 43rd, and 54th to 59th weeks, 29 injections in all ; and a bismuth compound containing 0·2 g. Bi. is injected weekly in the 8th to 11th, 18th to 23rd, 30th to 37th, 44th to 53rd, and 60th to 69th weeks, 38 injections in all. Potassium iodide is given during the administration of the bismuth. It is recommended in this plan that the blood be tested on the 1st day and in the 7th, 12th, 13th, 17th, 38th, 43rd, 54th, and 59th weeks ; and the spinal fluid in the 18th to 23rd weeks.

J. E. Moore, who is otherwise an advocate of the alternating system, gives 4 doses of Bi. (0·2 g.) concurrently with the first four of arsphenamine, then continues at weekly intervals with 4 doses of the latter, followed in turn by 4 Bi., 6As., 6 Bi., 6 As., 8 Bi., 6 As., 10 Bi., 6 As., and 10 Bi.

For reasons already given, my strong preference is for the plan of intermittent treatment. For men of average weight a dose of 0·6 g. neoarsphenamine seems to be sufficient, and for pregnant women 0·45 g.

Before suspending treatment the cerebro-spinal fluid should be negative. After suspending treatment the patient should be put under observation, being examined clinically once a month, and by blood test every 3 months for a year. At the end of the year the cerebro-spinal fluid is examined. During the second year the blood tests are at intervals of 6 months, the examination of cerebro-spinal fluid being repeated at the end. As a rule it is not advisable to allow a patient to marry until after 5 years from infection and after remaining free from all signs, clinical and serological, for at least 2 years following suspension of all treatment.

In all cases of primary sore it is very important to apply local treatment to destroy the organisms *in situ*; otherwise they may escape the remedies circulating in the blood. If the sore is indurated and the induration does not disappear quickly under general treatment, it should be removed by circumcision, destroyed with the cautery, rubbed with mercurial ointment or injected with a solution of neoarsphenamine (say, 0·15 g. in 0·5 c.c. water).

In later syphilis, *i.e.* after the third or fourth year, the line of treatment depends very much on the involvement of viscera and/or nervous system, the treatment of which is discussed elsewhere in this work. It is very important in these later cases to examine carefully the cardio-vascular and nervous systems. If the cerebro-spinal fluid is positive, there is little hope of restoring it to normal by ordinary anti-syphilitic treatment. In such cases tryparsamide is probably the best remedy to employ at first. It is given intravenously in weekly doses, commencing with 2 g. for an adult and increasing at once to 3 g., dissolved in 10 c.c. distilled water, in courses of about 10 injections, with intervals of about 6 weeks between courses. The concurrent use of bismuth seems to be advantageous in these cases. Assuming that, as is usual, no sign of optic nerve disturbance appears, patients commonly tolerate very large total amounts of tryparsamide—as much as 10 or more courses. The cerebro-spinal fluid should be examined periodically, and the tryparsamide treatment is continued in regular courses, with intervals, so long as improvement is steady. If no improvement in the state of the fluid is apparent by about the end of the third course, one considers the institution of pyretotherapy, of which probably the most effective form (apart from the use of physical apparatus for production of fever) is malarial inoculation, and usually about ten paroxysms of fever are allowed before interference by means of quinine or some similar remedy.

Both malaria and the use of physical apparatus may be impracticable, as the patient usually feels well and also may be a busy man unable to spare the time for, or perhaps explain to his family the necessity of, entering a nursing home or hospital for a course of malarial paroxysms, or of fever produced by physical agents. For this reason it is usually more practicable to try at first a course of fever induced by simpler means, such as the intravenous injection of a vaccine. The most popular for this purpose seems to be antityphoid vaccine, of which the dose may begin at 200 millions and be increased with successive injections, given every other day, by about 80 per cent. The aim is to provoke a rise of temperature to about 104° F., which is reached a few hours after the injection. The vaccine of the Ducrey bacillus, sold as dmelcos, is perhaps more convenient and less toxic than antityphoid; the first dose is usually 1 c.c., and the dose is increased with successive injections to 5 c.c. or more. The disadvantage of vaccine injections given in this

way is that the patient quickly becomes tolerant, and even large increases of the dosage produce very disappointing results in respect of temperature rise, so that there is much to be said for the method of Nelson whenever it is practicable. In this the patient receives two doses each day, each smaller than would be necessary by the single-dose method, the second being given 2 or 3 hours after the first, when the fever produced by this is at its height; the effect is to flick up the temperature to a much higher level. The scheme shown in Nelson's paper used T.A.B. vaccine. After preliminary single doses of 70 and 140 millions on the first and second days, resulting respectively in temperatures of 103·6° F. and 103° F., on each of the next 11 days two doses were given. The first of these ranged from 25 to 75 millions, and the second was sometimes the same as the first, and sometimes as much as 80 per cent. higher. If the second dose does not produce a sufficient rise, a third given before defervescence may do so. Many workers have now reported well on this method. Another method is to inject intramuscularly a solution of sulphur in oil, such as sulfosin, beginning with 1 c.c., and increasing to 10 c.c., according to the temperature provoked. After the fever treatment it is best to continue with the tryparsamide and bismuth, or with some form of ordinary anti-syphilitic treatment.

For cases of tertiary syphilis affecting the external and supporting structures and for latent ones, when the cerebro-spinal fluid is negative, the first course can usefully be on the same lines as shown above for early cases, while in later ones it may be preferable to rely more on bismuth, giving this entirely, or interspersing a few doses of an arsphenamine preparation. It is well also to administer considerably more iodine to later cases. In these later cases it is often very difficult or even impossible to convert the serum reactions to negative, and many syphilologists will not treat them beyond the stage when they show no clinical signs, maintaining that it is hopeless to convert the reactions, that the treatment only gets on the patient's nerves, and so forth. I am sure that this view is mistaken. Patients with latent syphilis who have not complained of any particular feeling of ill-health commonly remark after the first or second course of treatment that they now feel better than they have done for years; it is as if an insidious depressor of health had been removed. Moreover, it is not true that treatment of these cases has no effect on the serum reactions. If a serum test is employed which measures the strength of reaction in units, the effect of treatment is obvious. Thus, in a case tested by the Sigma method before treatment the reaction may be, say, 36 units; at the end of the first course in such a case it is often 18 or 20 units; at the end of the second course, 8 or 10; and so it gradually becomes reduced to 2 or 3, a number which is still regarded as positive, and at this it is apt to remain, but at this stage a change to mercury by mouth for some months often reduces the strength of the reactions quite remarkably. I usually treat steadily until the figure indicating the strength of serum reaction has not been reduced for two or three courses, and then advise continuation treatment at the rate of about three courses in 2 years.

Pregnant women are treated on much the same lines as early cases, the dose of the neoarsphenamine or the sulpharsphenamine preparation not exceeding 0·6 g. The point of greatest importance in these cases is to prevent the spirochæte reaching the circulation of the fœtus, and this can generally

be done by starting treatment in the first half of pregnancy, the earlier the better, and continuing it almost to the end. On account of the susceptibility of the kidneys, it may be advisable to withhold mercury or bismuth for the first few injections until it is seen how the injections are tolerated.

Syphilitic infants.—The following rules may help in deciding whether or not the infant should be treated, and the lines of treatment in the event of this being necessary:

As already mentioned, it is unsafe to rely on a positive serum reaction for a decision to treat, or on a negative one for a decision to withhold treatment.

(1) *S. pallida* can usually be prevented from entering the fœtus by commencing the treatment of the mother in the first half of pregnancy.

(2) The older the infection of the mother, and the earlier she is treated in her pregnancy, the greater the justification for a "wait and see" policy in regard to treatment of the offspring after birth.

(3) If the mother's syphilis has been treated indifferently and is of less than five years' duration, and if her treatment in this pregnancy was started later than the 4th month, it is safest to treat the offspring.

(4) Either the infant is infected or it is not infected. Precautionary treatment, so called, is given on the assumption that it may be infected and should be as complete as if infection had been proved completely.

(5) CURATIVE TREATMENT.—(*a*) If it is decided to give arsphenamine and bismuth, the scheme of treatment may be on the lines set out in the League of Nations Schedule, giving intramuscularly, 0·02 g. sulpharsphenamine and 0·004 g. bismuth metal per kg. infant (say 0·08 g. sulpharsphenamine and 0·20 c.c. of a 10 per cent. suspension of the oxychloride, or 0·8 c.c. of a similar suspension of the iodo-bismuthate of quinine for an infant weighing 9 lb.). (*b*) In place of sulpharsphenamine it may be more convenient to give acetarsol (p. 214), by mouth. In this case the following, in conjunction with heavy metal, would probably suit most cases. The dose of the drug is given in water half an hour before the first feed. Probably the best scheme of dosage is one based on the infant's weight as follows:

1st week, 0·005 g. per kg. per diem.
2nd ,, 0·010 ,, ,,
3rd ,, 0·015 ,, ,,
4th to 10th week, 0·02 g. per kg. per diem,
4 weeks' rest.

The course of acetarsol and bismuth should be repeated three times after the blood has become negative. (*c*) Instead of bismuth treatment shown in (*a*) and (*b*), inunctions with mercury ointment (15 to 60 grains of the B.P. preparation, according to age) can be given daily throughout each course except in the fifth week, or yellow mercurous iodide $\frac{1}{8}$ grain dropped into the milk three times a day.

In older children and adults with congenital syphilis the treatment is on similar lines to those employed in corresponding stages of acquired syphilis, but there is here probably more reason to supplement the injection treatment by pyrogenetic measures.

Needless to say, the hygienic conditions of the patient must be such as are likely to raise his general resistance to infection.

L. W. HARRISON.

YAWS

Synonyms.—Framboesia; Framboesia tropica; Pian; also many vernacular names such as Parangi (Ceylon), Bubas (Brazil), Coco (Fiji), etc.

Definition.—A contagious, inoculable, tropical disease caused by *Treponema pertenue*. The primary lesion is of non-venereal origin and is followed by the secondary stage consisting of an eruption of typically granulomatous papules. The tertiary stage, occurring a few or many years later, is characterised by destructive lesions.

Ætiology.—Yaws is essentially a disease of indigenous populations of tropical countries. Europeans are rarely affected. It is prevalent in the West and East Indies, Ceylon, the Philippines, Oceania and New Guinea, and parts of tropical Africa and South America. It is only present in a few isolated communities in India. Infection usually occurs in childhood, although a few adults escaping infection then may contract it later, often from their own infected children. The disease is not transmitted congenitally, and infection is generally regarded as occurring only once in a lifetime. Both sexes are attacked. The cause is the *T. pertenue* (Castellani, 1905), which is morphologically indistinguishable from the spirochæte of syphilis; on animal inoculation, however, constantly different reactions have been observed by a number of observers. Animals infected with either of these organisms become resistant to inoculation with the same spirochæte earlier than to that with the other. This is probably true also in the case of man. The similarity of yaws and syphilis is greatest in the tertiary stage. Although some authors regard these diseases as identical, the present state of knowledge does not warrant this. Bejel, the non-venereal syphilis of the Bedouin Arabs, has certain epidemiological and clinical similarities to yaws. *T. pertenue* enters the skin through minor abrasions, cuts or previously existing ulcers, most commonly on the limbs and especially the legs. It is possible that some insects may transport the Treponemata and thus spread infection.

Pathology.—The primary and secondary lesions are characterised by interpapillary down-growths of epidermis into the corium. There is also œdema and infiltration with polymorphonuclear leucocytosis and plasma cells both in the proliferated epidermis and in the corium. Spirochætes are more numerous where the cellular infiltration of the epidermis is most pronounced, but they are also present in the adjacent corium. The tertiary lesions are characterised by necrosis and ulceration with granulation tissue and dense fibrous tissue. Giant cells are frequently present, but spirochætes are not numerous. Peri-vascular cellular infiltration and vascular endothelial proliferation are usually said not to occur in yaws lesions, but recent work indicates that there are no generally reliable histological criteria for the differentiation of yaws and syphilitic skin lesions.

Symptoms.—The incubation period in man is 4 weeks or longer (in monkeys 3 weeks), and may be accompanied by mild general symptoms.

The primary lesion, which is not always demonstrable, resembles the typical secondary lesions but is often larger. It is usually single and extragenital, and may heal before the secondary eruption appears or outlast it. The adjacent lymphatic glands may be enlarged.

The *secondary stage*, which may appear within 3 weeks of the primary

lesion, may be heralded by irregular intermittent fever, headache, bone and joint pains, often worse at night, and a characteristic more or less generalised papular eruption. This commences as small, yellowish papules, which increase in size or coalesce to form larger lesions. The stratum corneum is shed, exposing a granular surface of minute pinkish elevations, separated by a whitish groundwork. Serum containing treponemata exudes and dries, forming a yellowish crust, which later may become discoloured and polished, especially in the case of less active lesions. Pus is not usually present. Healing occurs sooner or later, often leaving but little scarring, although hyperpigmentation, which later disappears, may be seen. The lesions may itch, and, although not very painful, are sensitive to minor irritation, such as flies. The distribution is general, but the trunk is often relatively spared. The body orifices and the soft skin of flexures are particularly involved. Successive crops may appear for from 2 or 3 years. Other types of skin lesion, pathologically related to those just described, are often seen, but usually typical secondary lesions are also present. A fine desquamation is sometimes present, and general enlargement of the lymphatic glands is often found. The eruption of a yaw on the sole, clavos or crab yaws, is particularly painful, and may occur many years after the earlier lesions have healed. Yaws papules may also occur on the buccal mucous membrane. Bone lesions are frequent during this stage, and are characterised by swellings. Periosteal deposits and rarefied foci in these deposits and in the cortex are seen radiographically. Sabre-tibia may develop, but destructive bone lesions do not occur. Multiple dactylitis is frequent. Ganglia and synovitis with free fluid are seen. Goundou belongs to this stage. All secondary lesions heal spontaneously, although bony deformities remain. The general health is not usually seriously affected.

The *tertiary stage* may be reached within a year of the healing of secondary lesions, or after a quiescent period of many years. Lesions at this stage are characterised by tissue destruction and ulceration. In the skin superficial ulceration or deep gummatous-like processes may occur, which on healing leave hyperpigmented atrophic scars and occasionally contractures. In the bones, swellings with ulceration associated with bony necrosis (" gummata "), spontaneous fractures, deformities of the digits, periostitis, nodes, synovitis and arthritis are seen. Destructive processes in the mouth and nose may lead to palatal perforation and to gangosa. Epidermal thickening, erosions, fissures and coarse desquammation occur on the palms and soles, some of which may return to normal, but others result in atrophic changes, pigmentation and contractures of the fingers. Juxta-articular nodes, chronic bursitis and patchy depigmentation of the skin are also met with.

Complications and Sequelæ.—In severe tertiary cases with many lesions, cachexia may result. One or more intercurrent diseases may be present. In Fiji and Haiti aneurysm and lesions of the central nervous system have been attributed to yaws, but the evidence is not convincing.

Diagnosis.—In localities in which yaws is prevalent there is usually no difficulty in diagnosing the early lesions, but congenital and acquired syphilis, bejel and bromide rashes may occasionally call for consideration. Treponemata can usually be found in serum from early lesions. The differentiation of tertiary lesions from syphilis may be impossible on clinical or pathological evidence, and a history of yaws in the past may be the only guide. Cutaneous leishmaniasis, blastomycosis, leprosy and tuberculosis may lead to confusion.

The Wassermann and Kahn reactions are positive in yaws and syphilis after the first few weeks. The absence of mucous patches, visceral, vascular and central nervous system lesions in yaws and its ready response to modern arsenical and bismuth preparations may help to differentiate the two diseases.

Prognosis.—All secondary lesions heal spontaneously in a few months or years, and probably some cases become spontaneously cured and develop a negative Wassermann reaction. Yaws is rarely fatal, most deaths being due to intercurrent disease. Modern therapy is very effective. In tertiary lesions more intensive treatment is required to produce healing and here, too, spontaneous cure probably occurs although less readily.

Treatment.—PROPHYLACTIC.—The recognition of the infectiousness of yaws and ordinary cleanliness are adequate. Cuts, abrasions and ulcers should be covered.

CURATIVE.—Neoarsphenamine and allied drugs are as specific for yaws as they are for syphilis. A single injection may clear up secondary lesions and occasionally even change the Wassermann reaction to negative ; after four or more injections (0·6 g., adult) probably more than 40 per cent. of cases will be cured. Bismuth preparations are much cheaper, but although almost as effective are not so rapid in their action. Intramuscular injections of insoluble bismuth are probably not completely absorbed after 6 months or more (Hackett), and stomatitis and albuminuria may occur. Sodium-potassium-bismuth-tartrate, bismuth oxide (0·2 g., adult), and other bismuth preparations in water or oil may be used ; at least six injections are given once or twice weekly. When feasible, combined treatment is the method of choice. In tertiary lesions potassium iodide is of value. Intercurrent diseases, if present, need treatment.

GOUNDOU

Synonyms.—Anakhre ; Gros Nez ; Dog Nose.

Definition.—Symmetrical bony tumours of the sides of the nose commencing during the secondary stage of yaws.

Ætiology.—This condition is probably to be found wherever yaws is prevalent, but has been reported most often from tropical Africa, especially in the west. It is seen in children and adults. Some reduction in size of the lesions in early cases may occur spontaneously or after treatment.

Pathology.—There is thickening of the periosteum with production of spongy tissue in which are fibrosis and perivascular plasma cell infiltration. The bony tissue is usually bounded by a thin layer of cortical bone. This hypertrophic osteitis involves the nasal process of the superior maxilla. In marked cases the tumour may encroach upon the nasal passages, orbit, or palate.

Symptoms.—Osteocopic pain, headache, and a thin blood-stained purulent nasal discharge may occur in the early stages, but later these subside. The paranasal swelling on one or both sides increases outwards, and may become large enough to obstruct vision. Facial deformity may be the only symptom, but nasal obstruction may result from extension to these passages. The over-lying skin is not implicated. Sometimes similar tumours elsewhere on the superior maxilla, or on the inferior maxilla, and other yaws bone lesions may also be present.

Diagnosis.—In yaws communities the paranasal swellings are characteristic, but in isolated cases differentiations may be needed from syphilitic osteitis, leontiasis ossea, and possibly acromegaly.

Prognosis.—Though it may be distressing, the disease rarely causes death.

Treatment.—Energetic anti-yaws therapy is indicated in early cases, and surgical removal of the bony tumour in advanced ones.

Gangosa

Synonym.—Destructive Ulcerating Rhino-pharyngitis.

Definition.—An ulcerative process of tertiary yaws resulting in destruction of the palatal and nasal structures.

Ætiology.—This condition is probably to be found wherever yaws is endemic. Its presence in the Pacific Ocean Islands and the East Indies has been stressed. It may commence in older children and adults.

Pathology.—The process begins with ulceration of the palate or in the nose, and is followed by destruction of soft tissues and bone. The histopathology is that of tertiary yaws.

Symptoms.—Pain, purulent discharge and foul odour accompany the ulceration mentioned above. The amount of destruction produced varies from a small perforation of the soft or hard palate, or some falling in of the nose to complete destruction of the palate, nose, nasal contents, and adjacent tissue of the cheeks and orbit so that the roof of the nasal cavities, pharynx and tongue are exposed. Arrest of the process, either spontaneously or following therapy, may occur at any stage. The larynx is probably not affected.

Diagnosis.—In yaws communities this is usually easy, but differentiation from American dermal leishmaniasis, syphilis and leprosy may be necessary.

Prognosis.—The progress of the destruction and healing is usually slow and often progressive, and although the response to adequate treatment is good, tissue losses remain. Death may result from general exhaustion, sepsis, insufflation pneumonia, or other intercurrent disease.

Treatment.—Energetic anti-yaws therapy is indicated, and intercurrent disease may need treatment.

Juxta-Articular Nodes

Definitions.—Multiple, painless, fibrotic nodules occurring in the vicinity of joints and bony prominences in the later stages of yaws.

Ætiology.—This condition is probably found wherever yaws is prevalent, and has been reported from most tropical countries. It is rare in childhood and is characteristically seen in elderly people often together with chronic pre-patellar bursal enlargement. Similar lesions are occasionally met with in late syphilis and in bejel.

Pathology.—The nodules consist of hard, greyish-white, avascular fibrous tissue, in which may be opaque yellow spots and occasional areas of necrosis. Foci of chronic inflammatory cells are found microscopically; endarteritis is said not to occur but treponemata have been demonstrated in

them. The tumours have no capsules, and merge into the neighbouring connective tissue.

Symptoms.—The nodules appear as small round multiple tumours in the subcutaneous tissue about joints and bony prominences, especially the knee, elbow and over the femoral trochanter. Only a few are present at any one situation; they are painless, firm and even cartilaginous in consistency, and only rarely break down and ulcerate. They are usually freely movable under the skin, but later some attachment to the skin at the most prominent point may occur. Their development is slow, and the nodules may resolve spontaneously or remain stationary. Their usual size is 1 to 2 cm., but some may become much larger.

Diagnosis.—Differentiation from syphilitic, rheumatic and onchocerca nodules may be necessary. Biopsy may be of assistance. In onchocerciasis the tumours are often softer, and embryos may be demonstrated in aspirated fluid; on section they are loculated, and filariæ and embryos are present.

Prognosis.—The nodules may cause some discomfort at points of pressure, but do not endanger life.

Treatment.—If necessary, troublesome nodules may be excised. Intensive anti-yaws therapy may cause resolution in some and regression in others.

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LEPTOSPIROSIS

Since the causative organism, *Leptospira icterohæmorrhagiæ*, was first demonstrated in Japan by Inada and Ido in 1915, spirochætosis icterhæmorrhagica has been recognised in many different countries. The earliest observations indicating that strains of leptospira other than the classical spirochætosis icterohæmorrhagica strain might produce disease in man was made two years later in Japan when *L. hebdomadis* was shown by Ido, Ito and others to cause Japanese seven days' fever or Nanukayami disease. Subsequently several strains differing in antigenic structure were discovered in the Dutch East Indies and Malaya. In Europe swamp fever was recognised as a leptospirosis caused by *L. grippo-typhosus*, and in 1932 *L. canicola*, which commonly affects dogs, was shown to produce leptospirosis in man. More recently in Australia three new strains have been isolated. Schüffner has recently classified the leptospiras pathogenic to man on the basis of different antigenic structure as revealed by serological reactions and animal inoculations, the clinical picture, epidemiological considerations and geographical distribution. Nine different strains are recognised, and these are separated into two groups, *i.e.* those capable of producing jaundice and those which fail to do so, but it should be remembered that even in classical spirochætosis icterohæmorrhagica only 50 per cent. of patients develop jaundice. The clinical picture in leptospirosis caused by any of these strains include conjunctival congestion, fever, prostration, severe headache and generalised muscular pains; meningeal symptoms and rashes may also develop. A neutrophil leucocytosis is characteristic. The outstanding difference is in prognosis, for while many cases of classical spirochætosis icterohæmorrhagica die, patients infected with

other strains almost invariably recover. Early blood culture, inoculation of guinea-pigs with blood or urine, serum agglutination reactions and other serological tests are essential to establish the diagnosis of leptospirosis and determine the strain of leptospira implicated.

I. Leptospirosis associated with Jaundice

Four strains pathogenic to man are included in this group:

(1) The classical Weil strain, *L. icterohæmorrhagiæ*, is cosmopolitan in distribution and lethal to guinea-pigs. The natural reservoir is *Rattus decumanus*, and it is known that in many different countries rats of this species pass *L. icterohæmorrhagiæ* in large numbers in the urine; these organisms infect man through skin abrasions or via the nasal mucous membranes during submersion in contaminated water. Only rarely the disease is acquired from infected dogs and cats.

(2) Akiyami A strain is similar to *L. autumnalis* of Japan and the Rachmat strain of the Dutch East Indies. The natural host is *Apodemus speciosus* in Japan where it has an autumnal prevalence.

(3) The Salinem strain, or *L. pyrogenes*, of the Dutch East Indies is probably identical with the Zanoni strain, which is one of the two leptospiræ responsible for leptospirosis amongst the cane-cutters of Queensland, Australia, in the rainy season. It has been found in a local species of rat—*R. culmorum*. The strain is lethal to guinea-pigs.

(4) The Batavia strain is found only in Java where *R. decumanus* appears to be the reservoir host. It is less pathogenic for guinea-pigs than the other strains described above.

II. Leptospirosis without Jaundice

Five strains pathogenic to man are included in this group:

(1) *L. hebomadis* causes seven days' fever in Japan. It is primarily an infection of the field vole, *Microtus montebelli*, and appears in the urine, which contaminates soil or food. It has recently been found in Sumatra in dogs and man.

(2) *L. grippo-typhosus* gives rise to summer epidemics amongst field workers in Europe, but the reservoir host and mode of infection is unknown. The disease runs a benign course. It has also been isolated from patients with leptospirosis in the Andamans (Andaman B strain).

(3) *L. canicola* produces an epizootic in dogs, from which man acquires the disease by contact. The rat is not a reservoir host. In Canicola-fever, though jaundice is absent, the meningitic symptoms often appear more severe than in classical Weil's disease. In inoculated guinea-pigs its virulence is enhanced with passage.

(4) The Pomona strain produces fever lasting 3 to 8 days, and has been isolated from agricultural workers in Queensland. It occurs after rain.

(5) The Ballico strain causes leptospirosis in Queensland on the cane plantations after rain. It produces a mild fever lasting a week. It is lethal to guinea-pigs and has been found in local rats.

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SPIROCHÆTOSIS ICTEROHÆMORRHAGICA

Synonyms.—Spirochætal Jaundice; Weil's Disease.

Definition.—An acute febrile disease with a world-wide distribution, caused by *Leptospira icterohæmorrhagiæ*, and generally occurring in people with an occupational relationship to rats. In its typical severe form it is characterised by fever, profound prostration, headache, generalised pains and acute muscular tenderness, conjunctival hyperæmia, leucocytosis, albuminuria, jaundice, and a tendency to hæmorrhage. Subclinical infections may occur, and jaundice is absent in about 50 per cent. of cases.

Ætiology.—In 1886, Weil first directed attention to this disease, which is now associated with his name. In Japan it was well known amongst miners and labourers in the rice fields, and in 1914 Inada and Ido infected guinea-pigs with blood from human cases and demonstrated *L. icterohæmorrhagiæ* in the tissues. Later, rats (*Rattus decumanus*) were found to be the reservoir host; the leptospiras, which were localised in the kidney, escaped in the urine and often contaminated water, fungal slime and soil. In man infection generally occurs in people who work in rat-infested places, and follow occupations in which minor injuries and abrasions of the skin are common; this accounts for its incidence in sewer labourers, bargemen, canal and dock workers, fish and tripe cleaners, coal miners and farm labourers. In Great Britain the disease is recognised as an occupational one, for which compensation may be claimed under the Workmen's Compensation Act. In trench warfare troops may become infected. The disease may also be acquired via the nasal passages from infected water when bathing or during immersion accidents, which mode of infection is particularly common in Holland.

Pathology.—(1) Morbid Anatomy.—In fatal cases there is an acute hepatitis with jaundice, while parenchymatous degeneration of the tubular epithelium of the kidneys, perhaps associated with hæmorrhages into Bowman's capsules, is characteristic. Large and small hæmorrhages are often scattered throughout the tissues and particularly affect the stomach, intestinal mucosa, and the lungs.

(2) Isolation of the Leptospira.—*L. icterohæmorrhagiæ* may be isolated by blood culture on Fletcher's medium during the first week, or by injecting 5 c.c. of infected whole blood intraperitoneally into the guinea-pig up till the tenth day of the disease. In the cultures there is a time lag of 3 to 5 days before leptospiras are found, and of 5 to 8 days before they appear in the viscera or blood of inoculated guinea-pigs. Where meningeal symptoms develop leptospiras may be found in the cerebrospinal fluid, and they are often demonstrable in the urine after the second week.

(3) Serological Reactions.—The agglutination reaction, using formalised cultures as advised by Schüffner, yields satisfactory results. Agglutinin appears in low titre about the fifth or sixth day, and rapidly increases during the second and third week of the disease; maximal titres up to 1/4000 have been recorded. Agglutinins persist for many years after an attack, and multiple observations to determine an increase in titre may be necessary in cases in which the titre is low and residual agglutinin may have persisted from a previous infection. The adhesion test of Brown and Davis has also proved of definite value.

Symptoms and Course.—The incubation period varies from 6 to 12 days. In moderately severe cases presenting the classical clinical picture three stages are recognised: (1) a febrile stage, with sudden onset; (2) an icteric stage, associated with renal features, and sometimes hæmorrhage; and (3) a convalescent stage, in which febrile relapses are common.

(1) Febrile Stage.—This generally lasts 6 to 8 days. As a rule the onset is sudden, with shivery feelings and definite rigor. Headache, nausea, vomiting, profound asthenia, backache, photophobia, and generalised muscular pains are characteristic. So severe may the muscular pain and tenderness be that the patient cries out with agony on the slightest movement. Conjunctival injection is common and herpes with hæmorrhage into the vesicles not infrequent. The muscles of the limbs and the abdominal muscles are often exquisitely tender on palpation. There may be some enlargement of liver or spleen but often this is absent even in the icteric stage of the disease. A neutrophil leucocytosis is characteristic; the total count varies between 10,000 to 20,000 leucocytes per c.mm., and the neutrophils equal 80 to 85 per cent.

(2) Icteric Stage.—An icteric tinge of the conjunctivæ and lemon yellow tinting of the skin appear from the fourth to the sixth day, but is only found in about 50 per cent. of cases. The jaundice gradually deepens and may become a deep orange in colour. A direct biphasic van den Bergh reaction develops, with well-marked hyperbilirubinæmia; in a recent series one patient whose plasma contained 56 units recovered, and another with a maximum value of 29 units died of cholæmia. With the onset of jaundice the urine becomes dark brown, and contains bile salts and bile pigments. The stools contain excess of fat, which is adequately or excessively split, and are often pale brown or even white in colour, the result of a decrease of stercobilin.

Evidence of renal involvement is not infrequent and the urine, which is decreased in quantity, contains albumin, renal casts, pus cells and perhaps red blood corpuscles. As renal function fails the nitrogenous constituents of the blood increase and the blood urea attains high values. Anuria may ensue. Hiccough, Cheyne-Stokes respiration, subsultus tendinum, delirium and coma are features common to cholæmia and uræmia, which are frequent causes of death. Skin petechiæ or purpuric patches sometimes appear and bleeding gums, hæmoptysis, hæmatemesis, melæna and hæmaturia may complicate the picture.

(3) Convalescence.—This generally commences in the third or fourth week, by which time the renal and hepatic manifestations have subsided, but it is often 5 or 6 weeks before the patient is fit to leave hospital. Not infrequently in the third week a relapse of fever occurs, which may last from a few days to 3 weeks; it is unaccompanied by icterus or other severe symptoms.

Atypical Clinical Types: These are frequent, and may or may not be associated with jaundice. They include:

(*a*) *Anginal type.*—The patient complains of fever, generalised pains and sore throat, and is usually diagnosed as influenza, tonsillitis or rheumatic fever. Unless jaundice develops or the occupation of the patient suggests the possibility of spirochætosis icterohæmorrhagica, laboratory

investigations are not made and the true nature of the infection remains unrecognised.

(*b*) *Abdominal type.*—There is fever, abdominal pain, vomiting and localised or generalised rigidity associated with acute tenderness of the abdominal muscles; the picture may resemble an acute abdominal condition, such as appendicitis, cholecystitis, pancreatitis or peritonitis. A neutrophil leucocytosis is present, and when hæmatemesis occurs, perforated gastric ulcer may be diagnosed.

(*c*) *Respiratory type.*—There are physical signs of pulmonary consolidation resembling pneumonia, and hæmoptysis may supervene. Jaundice may never develop.

(*d*) *Meningeal type.*—Not uncommonly leptospiral meningitis, with neck retraction, Kernig's sign, etc. may develop at the onset. Lumbar puncture reveals a clear fluid under increased pressure, containing neutrophil leucocytes, lymphocytes and perhaps monocytes, while leptospiras may be demonstrated by animal inoculation or culture. More rarely, chronic meningitis may supervene months after the acute stage of the disease has subsided, but notwithstanding this the cerebrospinal fluid contains pus cells and leptospiras.

Subclinical infections also occur in which people like sewer workers acquire a symptomless leptospirosis; there is no history of illness yet the blood shows definite agglutination against *L. icterohæmorrhagiæ*.

Diagnosis.—Few diseases are more protean in their clinical manifestations or have remained for such long periods undetected in communities. Spirochætosis icterohæmorrhagica is not generally suspected until the patient develops jaundice and there is known to have been an occupational relationship to rats or a recent water-immersion accident. An appeal to the laboratory under such circumstances will generally enable a delayed diagnosis to be made, either by isolating the leptospira or by serological tests. Apart from jaundice, a history of possible contact with rat-infected material, the extreme prostration, the conjunctival injection and the severity of the muscular pain and tenderness, and the neutrophil leucocytosis, should arouse suspicion.

Prognosis.—Fatal cases are almost invariably jaundiced and die between the ninth or fourteenth day as a rule from cholæmia or uræmia. The mortality rate appears to vary in different outbreaks, but where the diagnosis is reasonably good it is about 15 per cent.

Treatment.—PROPHYLACTIC.—This includes the protection of bathing pools, abattoirs, fish shops, etc., from rats, and the immediate treatment and protection of any skin abrasions in people whose occupation brings them in contact with rat-infected material. Prophylactic vaccination is under trial. Nurses should be instructed to disinfect the patient's urine.

CURATIVE.—Chemotherapy has proved disappointing and intravenous injections of anti-leptospiral serum in large dosage at the earliest possible moment is the only specific treatment holding out any prospect of success. Owing to the hepatitis and renal involvement, the protein content of the diet should be minimal and fluids and dextrose given in large quantities. Intravenous dextrose (5 per cent.) and citrates are of special value.

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RELAPSING FEVER

Synonyms.—Spirochætosis; Febris Recurrens; Spirillum Fever; Famine Fever.

Definition.—A group of specific infectious fevers due to spirochætes (treponemata) and spread by lice or argasine ticks, characterised by a variable number of febrile relapses.

Ætiology.—Relapsing fever occurs in many parts of the world and is often seen in epidemic form during wars and famines. It is rare in England, but occurs in parts of Europe, including Russia, and in Turkey, India, Cochin-China, Algiers, Egypt, Africa and the United States it is not infrequent. All ages and both sexes are liable. The different varieties of the disease are caused by spirochætes demonstrable in the peripheral blood during the febrile paroxysms, and they may be divided into the lice-borne and tick-borne fevers. The varieties transmitted by lice include (1) European relapsing fever due to *Treponema recurrentis* (the old spirillum of Obermeier); (2) Northern African relapsing fever produced by *T. berberum*; (3) Indian or Asiatic relapsing fever caused by *T. carteri*; (4) North American relapsing fever attributed to *T. novyi*. The varieties transmitted by the argasine ticks include (1) Central African tick fever due to *T. duttoni* transmitted by *Ornithodorus moubata, O. erraticus* and *O. savignyi*; (2) Palestinian tick fever caused by *T. sogdianum* and transmitted by *O. papillipes*; (3) Persian and North-West Indian relapsing fever caused by *T. persicum* and transmitted by *O. papillipes* (*tholozani*) or *O. lahorensis*; (4) Spanish relapsing fever attributed to *T. hispanicum* and transmitted by *O. maroccanus*; (5) Central and South American relapsing fever due to *T. venezuelense* is transmitted by *O. venezuelensis* in Columbia and Venezuela, and by *O. talaje* in Panama; (6) Californian tick fever due to *T. turicatæ* and transmitted by *O. hermsi*. At present it appears somewhat doubtful whether the creation of the numerous species of spirochætes detailed above is justified on grounds other than those of convenience. Lice become infective about the sixteenth day, and remain so for about one month. Infection is probably conveyed by the fæces, or after the louse has been crushed and the spirochætes liberated from the codomic fluid; scratching may play an important part in transmission. With ticks the spirochætes are liberated in the coxal fluid, and the anal excrement is also said to be infected; from this source man generally acquires the disease, but it is also possible that it may be transmitted during biting, as spirochætes are demonstrable in the salivary glands of ticks. The ova become infected and new generations of ticks can pass on the disease in hereditary fashion.

Pathology.—In uncomplicated cases petechial hæmorrhages and occasionally jaundice are found. The spleen is soft and congested and often the site of multiple infarcts, while the liver is enlarged, friable and hyperæmic, and along with the kidneys and heart shows cloudy swelling and fatty degeneration. The long bones contain red marrow. Congestive changes in the cord and brain and iritis have also been described, especially with *T. duttoni*. Microscopically, spirochætes are demonstrable in endothelial cells throughout the body, especially in the liver and spleen, and also in the

brain and cerebrospinal fluid. Monkeys are susceptible and, as in the case of rats and mice, are actively immune after recovery. Krantz has applied the Reichenberg reaction or "adhesion test" to relapsing fever spirochætes, specific immune serum causing the spirochætes and blood platelets to adhere together.

Symptoms.—A. The Lice-borne Relapsing Fevers.

1. *European form.*—The incubation period varies from 2 to 12 days, and in accidental inoculations it is about 5 to 7 days. During this period slight prodromata may occur. The onset is sudden with a rigor, frontal headache and intense pains in the back and limbs. Anorexia, nausea and vomiting are common, and in children convulsions may occur; the temperature and pulse rise rapidly, the former often reaching 104° F. on the evening of the first day. The tongue is coated and moist, the spleen is enlarged, and in some epidemics jaundice and a tender enlarged liver may be present. Herpes labialis may develop, and occasionally an erythematous rash appears at onset. Later, rose-coloured spots may involve the skin of the neck, trunk and inner aspect of the thighs. Petechiæ are observed only in severe cases. After the fever has persisted for 5 to 7 days the temperature falls by crisis, accompanied by profuse sweating and possibly diarrhœa and collapse. The patient rapidly improves, but after an apyrexial period a relapse ensues, generally about the fourteenth day, followed by a second crisis about the end of the third week (twenty-first day). This usually terminates the illness, but occasionally a third relapse is noted. Spirochætes are present in the blood until 24 hours before the crisis, when they rapidly disappear, and are not demonstrable except possibly in thick smears during the apyrexial period when a leucopenia replaces the characteristic febrile neutrophile leucocytosis. The blood remains infective between relapses, and if injected into a mouse or white rat spirochætes appear in 24 hours.

2. *Asiatic relapsing fever* closely resembles the European form, but rigors are not so common, collapse is more frequent at the crisis, and relapses more numerous. Carter describes two varieties: (*a*) a short irregular remittent fever; (*b*) the so-called bilious remittent or icteric fever. This is a severe form of infection associated with spirochætal hepatitis. There is high fever, intense toxic jaundice, skin petechiæ, splenomegaly, and an enlarged tender liver. The urine contains albumin, bile pigments, bile salts and urobilin. There is hyperbilirubinæmia associated with a direct biphasic Van den Bergh reaction in the plasma. Toxæmic features are marked, and include a dry brown tongue, diarrhœa, abdominal distension, hiccough, stupor, delirium and coma. Death not infrequently results.

3. *North African relapsing fever* is found in Algiers, Tunis and Egypt, and closely resembles the European form. The number of relapses rarely exceeds three, but fatal cases may show jaundice, bilious vomiting, hepatomegaly, splenomegaly with infarctions, and albuminuria, necessitating differentiation from yellow fever.

4. *American relapsing fever* due to *T. novyi* has a low mortality rate and not generally more than one relapse.

B. The Tick-borne Relapsing Fevers.

1. *Central African relapsing fever.*—**Synonyms.**—Tick Fever; Tete Disease; Carapata Fever.

This form is found throughout British and Portuguese East Africa, Nyasaland, Uganda and the Congo Free State.

It differs from the European form in the shorter duration of the initial fever (3 days), the irregular incidence, greater number of relapses and the scantiness of spirochætes in the peripheral blood. The incubation period varies from 3 to 10 days, generally being about 1 week. The tick bites may be accompanied by local inflammatory changes and the prodromata include mental lethargy and sweating. The attack may start gradually with malaise, vomiting and slight temperature which gradually increases, or suddenly with dizziness, headache, and generalised pains, the temperature rapidly reaching 104° F. After the pyrexia is established these symptoms may persist and, in addition, chilliness, pain over the spleen, bilious vomiting, bronchial catarrh, diarrhœa, enlargement of the spleen and liver, albuminuria and herpes may occur. Generally after 3 to 4 days the fever terminates by crisis with profuse sweating. The patient feels weak and tired, but slowly regains his appetite and strength until the next febrile paroxysm, which may occur after an interval of 3 to 8 days. Third and fourth relapses are frequent and as many as ten may occur, weakness and emaciation then being marked. In severe and fulminating cases epistaxis, hæmaturia and jaundice may be met with, also occasionally involvement of the central nervous system, with coma and death due to cerebral embolism caused by tangled masses of spirochætes. Cranial nerve pareses are described, and spirochætes may be present in the cerebro-spinal fluid, which may show increased pressure and lymphocytosis.

2. *Persian and North-West Indian relapsing fever* presents a primary fever of some 4 days' duration followed by short bouts of pyrexial recurrence; five or more relapses are not uncommon. Some epidemics are very mild, others more severe. Often the spleen is not palpable, and icterus is uncommon except in the more severe epidemics.

3. Spanish relapsing fever caused by *T. hispanicum* resembles the tick fever of Central Africa. The initial fever lasts about 4 days, and is associated with splenomegaly and neutrophil leucocytosis. Iritis and facial neuritis are not infrequent complications during relapses, which do not generally exceed four in number.

Complications and Sequelæ.—Bronchial catarrh is not infrequent during the initial fever, and pneumonia and parotitis may also occur. In some epidemics hæmatemesis and hæmaturia have been noted; in others jaundice and hepatomegaly are not infrequent. Rupture of the enlarged spleen has been reported, also ophthalmia, adenitis, neuritis and diarrhœa. In *T. duttoni* infection conjunctivitis, iritis and cranial nerve palsies coming on in the late relapses may be encountered. Optic atrophy has also been described.

Diagnosis.—Relapsing fever has to be distinguished from influenza, typhus, malaria and trypanosomiasis, and, if there is jaundice, from yellow fever and Weil's disease. This is done by finding the specific parasite in the blood.

Prognosis.—The prognosis varies. With the European types the mortality rate is only 3 to 5 per cent., but with the Asiatic type it is much higher. Jaundice is an unfavourable development. African tick fever is not infrequently fatal, especially in the aged and debilitated, and Central American tick fevers resemble the Central African variety.

Treatment.—PROPHYLACTIC.—Avoidance of contact with lice and ticks is necessary if infection is to be prevented. Delousing of troops in war-time is important. With *O. moubata* the avoidance of native dung huts, especially at night-time, and of old camping sites, is essential.

CURATIVE.—Good nursing is important and strict dieting necessary especially where there is icterus and hepatomegaly. Arsphenamine (0·3 to 0·6 g.) and neoarsphenamine (0·6 to 0·9 g.) are specifics in all types of the disease, and generally not more than two injections are needed for cure: resistant strains, however, do occur in which much more intensive treatment is necessary. The injections should be given during the pyrexial period, and preferably when spirochætes are demonstrable in blood smears and not immediately before the crisis. This is especially so in resistant cases of the Central African type for which combined treatment with Solganal B and neoarsphenamine may prove necessary. Collapse at the crisis may require stimulants like digitalis, pituitary (posterior lobe) extract and strychnine. If the nervous symptoms be severe, lumbar puncture may be advisable to reduce intracranial pressure.

RAT-BITE FEVER

Synonyms.—Sodoku; Sokoshio; Rat-bite Disease.

Definition.—A chronic relapsing type of fever following the bite of rats, and due to the *Spirillum minus* (Carter, 1887); it is characterised clinically by a return of the inflammation in the healed wound, lymphangitis, adenitis, rigors, fever and a macular or papular purplish rash.

Ætiology.—The disease is common in Japan, China and Bombay, and cases have been reported from France, Italy, Spain, Britain, East Africa, West Indies and Australia. Any one bitten by an infected rat may acquire the disease. In man the spironemata were found in the bitten tissues and in the lymph glands by Futaki; they are demonstrable with difficulty in the peripheral blood, appearing as thick, short forms (3 to 6 microns), which on cultivation increase in length (20 microns). About 3 per cent. of house rats in Japan are carriers, and after experimental inoculation spirilla are present in the blood for the first fortnight of infection.

Pathology.—In human cases, degenerative changes in the liver and kidneys have been reported, while animals show congestion and swelling of the lymph glands and spleen.

Symptoms.—After being bitten the wound heals up in an ordinary manner, but in from 2 to 6 weeks pain and swelling appears at the site of the old bite and the scar breaks down. The lymphatics draining the area of the bite become inflamed, with enlargement of the corresponding glands; a definite ulcer may now mark the site of the bite, with an angry inflammation spreading away from it, and small vesicles may break out around it. When this has continued for some time, general symptoms make their appearance; the temperature rises to 103° F. or over; there may be rigors, vomiting, nausea, severe headache, joint pains, diarrhœa and general malaise. A specific rash then usually appears as dusky-coloured, purplish red spots, or a coloured, patchy erythema over the limbs, trunk and face, which lasts for some time and slowly disappears. After remaining high for 3 to 8 days, the temperature drops, often by crisis, and the symptoms generally ameliorate. After a

varying period of time the first relapse appears with a return of the former symptoms. Pyrexia then disappears, only to be followed by further relapses, which in some of the reported cases have continued for months or even years. Considerable debility follows the attacks, and finally the patient may pass into a very poor state of health. A transient or permanent nephritis may result, and exophthalmos and paresis have been seen in some cases. Ultimately the infection tends slowly to disappear.

Diagnosis.—The history of rat-bite, the local lesion associated with lymphangitis and adenitis, the specific rash, and recurrent fever are typical. In some ways the disease resembles syphilis, but the Wassermann reaction is negative. Spirilla are difficult to demonstrate in the peripheral blood, and white rats or mice should be inoculated with human blood.

Prognosis.—With modern treatment this is quite good, but previously it was not so, many cases continuing with chronic symptoms for years. A mortality of 10 per cent. has been given by some authors.

Treatment.—Arsphenamine or some of its derivatives should be given, commencing with doses of 0·3 gram. One or two injections are usually sufficient to abolish completely all the symptoms and bring about a permanent cure.

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E. PROTOZOAN INFECTIONS

MALARIA

Synonyms.—Ague; Paludism; Remittent, Intermittent, Marsh or Jungle Fever.

Definition.—A protozoal disease of man caused by various species of *Plasmodium* which infect the red corpuscles and give rise to periodic fever, splenomegaly and anæmia; transmission is by anopheline mosquitoes.

Historical.—Malarial fevers were recognised by Hippocrates in the fifth century B.C., while in the time of Cæsar, Varro suggested they might originate from swamps. In the Middle Ages, Europe suffered severely from the ague, being saved from its ravages by Cinchona bark brought back from Peru by the Jesuits in the first half of the seventeenth century, and not by the Countess del Chinchon, as is generally believed; this remedy also enabled Sydenham and other physicians to separate malaria from other fevers. Laveran (1880) discovered both the parasite and the phenomenon of flagellation in shed blood, but differentiation into the three species was not made until later. Manson (1894) formulated the hypothesis of mosquito transmission, inducing it from the phenomenon of flagellation of the male gamete, but he thought man acquired the disease from infected mosquitoes via water and not by biting. McCallum (1897) recognised the fertilising function of the "flagellating body." Ross (1898) worked out the correct transmission and developmental cycle of bird malaria (Proteosoma) in culicine mosquitoes, and having previously observed the partially developed oöcysts of human malaria in dappled winged mosquitoes (anophelines) he predicted a human life cycle

similar to that observed in bird malaria. Later in the same year, Grassi, Bignami, and Bastianelli (1898) observed the complete development of malignant tertian malaria in *Anopheles maculipennis* and transmitted the disease to man by the bite of infected mosquitoes.

Ætiology.—Malignant or subtertian malaria greatly preponderates in tropical and benign tertian in temperate zones, while in the subtropics all three forms may occur. Quartan has a patchy distribution. Some islands, such as Fiji, are free of malaria. All races are susceptible, and in endemic areas the infection is commonest in children. An infected population gradually acquires a certain degree of immunity, and in avian and simian malaria this has recently been shown by Taliaferro and others to depend on an enhanced phagocytic function and hypertrophy of the reticulo-endothelium, especially of the spleen and liver. In Europe the disease disappears at 3000 feet, and in India and Africa at 6000 feet. Seasonal prevalence, which is not marked near the equator becomes so farther from it. Malignant tertian malaria is responsible for most fatal epidemics, which are generally associated with excessive rainfall. The great Ceylon epidemic of 1934–1935 was an exception, for the benign tertian parasite played an important rôle and it was associated with failure of the South-West Monsoon. Drought conditions followed, and in water holes caused by drying up of the rivers and lakes the mosquito vector, *Anopheles culicifacies*, bred in great numbers. Famine conditions due to failure of the crops further lowered individual resistance, and within 7 months 80,000 people died from malaria.

The parasites of malaria belong to the *Sporozoa*, sub-order *Hæmosporidia*, genus *Plasmodium*. Four forms affect man—benign tertian (B.T.) due to *Plasmodium vivax* (Grassi and Feletti, 1890), a tertian malaria due to *Plasmodium ovale* (Stephens, 1922), quartan malaria due to *P. malariæ* (Laveran, 1881), and malignant or subtertian malaria (M.T.) due to *P. falciparum* (Welch, 1897) (*Laverania malariæ* or *præcox*). The parasites undergo two cycles, one in man, the other in the mosquito.

Human phase (endogenous, asexual or schizogony). The sporozoites, inoculated by the mosquito, pass into the blood stream and enter the red cells where they change into little rings which gradually develop more protoplasm and black pigment. Quartan fills the corpuscule, while benign tertian actually expands it. The pigment collects centrally, and the protoplasm and chromatin divide into spores (sporulating body, rosette or schizont). The envelope bursts and the spores (merozoites) are scattered in the plasma whence they penetrate new corpuscles restarting the cycle.

Mosquito phase (exogenous, sexual or sporogony). When the sporulation of the asexual cycle takes place in benign infections certain large non-sporulating sexual forms (gametocytes) fill the corpuscles. Malignant tertian gametes are crescentic, and when taken up by suitable mosquitoes revert to circular bodies. Subsequent development is as follows: from the male gamete flagella become detached which penetrate the female bodies and fertilise them (sexual act, zygosis). The resulting body now elongates (travelling vermicule or oökinet), penetrates into the stomach wall, where it again takes on a circular form, developing into oöcysts which, after becoming filled with numerous spindle-shaped bodies (sporozoites), protrude like little herniæ or warts. Finally these rupture and the sporozoites escape into the body cavity and thence into the salivary glands. The infected mosquito inoculates man

with the saliva during biting, and the sporozoites, passing into the corpuscles, start the infection. (See Human phase.) At suitable temperatures, development in the mosquito takes about 10 days, and following human inoculation by the mosquito there is an incubation period of from 9 to 21 days or longer, varying with the species of parasite.

Cases of *Plasmodium ovale* infection (Stephens, 1922), have been reported from South, East and West Africa and Venezuela. Though morphologically it resembles *P. malariæ*, the infected corpuscles show Schüffner's dots, and are often oval or distorted in shape, with serrated edges; the schizogonous cycle takes 48 hours and tertian fever is produced. After experimental infection of man, either by direct inoculation with infected blood (Yorke), or following bites from artificially infected mosquitoes (James), the parasite preserves its morphological characters in blood smears.

Mosquito Vectors of Malaria.—It is not every anopheline mosquito which can transmit malaria successfully. Perhaps the best-known transmitter of malaria is *A. maculipennis*, which is nocturnal in habit, and has been specially studied in Europe and the Eastern Mediterranean. The recent work of Hackett, Misseroli and others have shown that *A. maculipennis* is not a uniform species but is divided into "biological races" or varieties. These races cannot generally be distinguished either as adult or larvæ, but only by their egg characteristics. The breeding grounds, sexual behaviour and feeding habits differ. Thus, the race called *elutus* bites man for choice, and is a dangerous carrier of malaria; other races, like *typicus* and *messeæ*, bite cattle for choice, and therefore are much less dangerous to man. The larva of *elutus* needs traces of salt in water, and for this reason it tends to have a coastal distribution. In the Balkans, malaria of the plains is mainly transmitted by *A. maculipennis* var. *elutus*, whereas malaria of the hills is solely transmitted by *A. superpictus*, which especially breeds in running mountain streams with rough rocky beds. *Anopheles sergenti* occurs in Syria and Palestine, and breeds in water which is still or running slowly. *A. bifurcatus*, which occurs in Europe and has generally little relationship to malaria, used to be a common source of this disease in Palestine; it bred in underground cisterns, inside towns and villages, and produced much urban malaria. *A. culicifacies*, which causes malaria in Ceylon, breeds in the dry season in trickles of water and water holes in the empty beds of rivers. It follows that the mosquito vector must be carefully studied in every country and special local methods devised for its extermination. Other mosquito vectors in other parts of the world include: *A. funestus* and *A. costalis* in Africa; *A. albimanus* and *A. argyrotarsis* in the West Indies; *A. culicifacies*, *A. turkhudi* and *A. maculipalpis* in India; *A. umbrosus*, *A. maculatus* and *A. minimus* in Assam, Burma and the Federated Malay States. Mosquitoes are not liable to develop infection unless the carrier has more than 12 gametocytes per c.mm. (Darling), and development of the malarial oöcyst in the mosquito's stomach is temporarily inhibited by low temperatures.

Parasites in blood smears.—All forms of benign tertian and quartan parasites are met with in the peripheral blood, but in malignant tertian malaria, owing to sporulation in the internal organs, generally only the small rings and the large crescents appear. Smears are stained by Leishman's or Giemsa's stain, and the following points assist in differentiating the different

species. *Ring forms.*—The rings of *P. falciparum* occupy about one-sixth of the cell, which may show Maurer's spots; they are often fine and hair-like and show irregular or flattened marginal forms: two chromatin dots and multiple infection of the same corpuscle may occur. Occasionally this is seen with *P. vivax*. The rings of *P. vivax* and *P. malariæ* occupy about one-third of the cell, are larger and contain more cytoplasm, but often the species cannot be determined if only ring forms are present (Wenyon). *Partly grown forms.*—In *P. vivax* the infected corpuscle is enlarged, Schüffner's dots are often present, and the parasites are of irregular shape and contain light brown pigment. With *P. malariæ* there is no enlargement of the corpuscle, the pigment is dark brown or black, band forms are common, and Ziemann's stippling may be demonstrated in the red cells by special staining. *Adult forms.*—In *P. vivax* and *P. malariæ* the schizonts have 16 and 8 nuclei or merozoites respectively, in contrast with which the gametocytes have a single nucleus and a different distribution of pigment and chromatin.

Pathology.—*Clinical.*—In severe infections, especially with M.T. parasites, there is considerable blood destruction. The intracorpuscular parasite probably uses hæmoglobin as a pabulum and produces brownish black malarial pigment, which is a hæmatin compound of unknown composition found in the parasites, the parasitised corpuscles and in the R.E. cells of the liver, spleen, serous membranes and marrow. The hæmatogenous bilirubin may attain a concentration of 3·0–6·0 units, and is responsible for the hæmatogenous jaundice observed clinically. The hæmatogenous bilirubin is converted by the liver cells into bile pigment, and pleocholia ensues with dark coloured stools containing an excess of stercobilin which on re-absorption produces urobilinuria, especially if there is an associated malarial hepatitis. The malarial anæmia in uncomplicated cases is generally normocytic in type, and in severe infections the blood picture may show anisocytosis, poikilocytosis, polychromasia, punctate basophilia, and occasionally normoblasts. Though there is no demonstrable hæmoglobinæmia, Schumm's test for methæmalbumin is generally positive in febrile malaria, indicating that lysis of corpuscles is occurring during the paroxysms.

Morbid anatomy.—In a fatal case of acute malignant tertian malaria the spleen need not necessarily be much enlarged; it is blackish red in colour, with a soft, diffluent pulp. The liver is congested and plum-coloured, the lungs darkish red and œdematous, and the peritoneum and intestinal mucosa leaden in colour. The heart may be dilated, and the brain may show œdema, congestion, punctate hæmorrhages, and a distinct leaden hue. Microscopic study shows malarial pigment in the hypertrophied reticulo-endothelial cells of the liver, spleen, serous membranes and bone marrow, and sometimes pigmented mononuclears in the vessels. The liver, kidneys and heart muscle may show parenchymatous degeneration, and hæmosiderin giving a Prussian blue reaction is found in the hepatic, renal and splenic cells. The internal capillaries of the brain, and often of the viscera and serous membranes as well, may be packed with parasites, and local anoxæmia and degenerative changes ensue. In more chronic cases the spleen is very enlarged, hard, and slaty grey in colour; the capsule is thickened, and there is generally perisplenitis. Sometimes the adhesions are calcified. On section, Malpighian bodies are not in evidence. Microscopic section shows great hypertrophy of the R.E. cells, which often contain malarial pigment, atrophy of the

Malpighian bodies and lymphoid tissue generally, and an increase in fibrous tissue.

Death in benign tertian malaria, quartan malaria and chronic malignant tertian malaria is generally associated with malnutrition and anæmia, with congestive heart failure or intercurrent disease, such as pneumonia, ancylostomiasis or dysentery.

Symptoms.—The benign varieties, *i.e.* those generally unassociated with fatal symptoms, include both benign tertian and quartan fevers, whereas pernicious manifestations are restricted to malignant tertian malaria. The initial pyrexia may be continuous, remittent or quotidian in type, and only later does the characteristic intermittent periodic fever, commencing in the forenoon or early afternoon, become established.

Quartan.—The classical features of ague are present with cold, hot and sweating stages, the rise of temperature being caused by the escape of merozoites into the circulation. Headache, pains in the limbs and joints, backache, fatigue and malaise, followed by chilly sensations, often initiate the rigor; violent shivering and chattering of the teeth follow and the face is pinched and blue. As the chill passes off, blankets are discarded, the face flushes, and nausea, vomiting, severe headache and even delirium may ensue. The skin remains hot and dry until the sweating stage with its fall in temperature brings relief. The whole paroxysm generally lasts only 4 to 5 hours. Temperatures of 105° F. to 106° F. are not uncommon. Single quartan infections give rise to fever every fourth day, *i.e.* 72 hours' interval; double infections will cause 2 days' fever and 1 clear, while treble infections induce daily pyrexia. The spleen is moderately enlarged and tender, and considerable secondary anæmia may develop, often associated with albuminuria. Quartan malaria is rarely fatal, but, like benign and malignant tertian malaria, it predisposes to intercurrent infections like tuberculosis and pneumonia. It may persist as long as 8 years if untreated.

Benign tertian.—The clinical picture is very similar to that described for quartan malaria, but the paroxysm lasts 8 to 12 hours. A single infection causes fever every third day with 48 hours' interval between the paroxysms, while a double infection gives rise to quotidian fever. Herpes is common, and in addition to splenomegaly the liver is sometimes increased in size. The natural course of the untreated disease does not exceed 2 to 3 years.

Malignant tertian malaria.—**Synonyms.**—Subtertian, Æstivo-autumnal or Pernicious Malaria. The Italians have described two quotidian and one tertian variety, but quotidian fever is due to a double cycle, just as continuous or remittent fever is attributable to several generations at slightly different times; such charts show small pyrexial peaks corresponding to the successive generations of parasites. Recently James has shown that the different strains of malignant tertian vary considerably in their virulence and response to treatment. Three types of fever are seen: (1) A typical tertian temperature; (2) Quotidian fever; (3) Continuous irregular or remittent fever resembling enteric. In malignant tertian the initial rise of temperature is abrupt; chilliness may be present, but there is no rigor (dumb chill), the hot stage is considerably prolonged, and the sweating stage is not marked. The paroxysms may last some 12 to 20 hours, but frequently the fever never intermits, remaining remittent in type. Headache, backache, nausea, vomiting and anæmia tend to be more severe than in the

benign forms, and as fever becomes more chronic ague-cake spleen and malarial cachexia ensue. Severe hæmolytic anæmia may develop within the first few weeks. The gravest cases, clinically somewhat resembling pernicious anæmia, may show dyspnœa, palpitation, hæmic murmurs, retinal hæmorrhage, hyperbilirubinæmia and urobilinuria; the counts in extreme instances reach 1 to 2 million erythrocytes per c.mm., but the colour index does not exceed 1·0, megalocytosis is not evident, nor is the average diameter of the corpuscle greater than normal (7·6 microns).

Bilious remittent fever.—Two types are encountered: one is characterised by splenomegaly, hæmolytic jaundice, bilious vomiting and perhaps bilious diarrhœa, associated with hyperbilirubinæmia, pleocholia and mild urobilinuria; the immediate direct van den Bergh reaction is negative, and bile pigments and salts are absent from the urine. The other has similar clinical features, but in addition there is a tender enlargement of the liver, epigastric distress and sometimes gastro-intestinal and other hæmorrhages: the jaundice comes on early and a biphasic van den Bergh reaction may be found. Urobilinuria is marked, and there are often bile pigment and salts in the urine. In the latter type degeneration and necrosis of the polygonal cells of the liver occur, and a toxic factor is superadded to the jaundice of hæmolytic origin characteristic of the milder type.

Blackwater fever.—This complication of subtertian malaria is dealt with separately.

Forms of pernicious malaria.—Apart from the hæmolytic effects of parasites on the red cells and their destruction within reticulo-endothelial cells, internal sporulation and clumping of corpuscles causing plugging of the visceral capillaries in the brain, lung, liver, heart, intestines, spleen and bone marrow may give rise to a variety of pernicious manifestations, which may simulate almost any disease in medicine. For clinical purposes they may be classified as follows: (1) *Cerebral.*—Cases may show coma, convulsions, aphasia, paraplegia, hemiplegia, meningismus and perhaps hyperpyrexia. (2) *Spinal.*—Clinical syndromes simulating spinal meningitis may also be encountered. (3) *Abdominal.*—Choleraic and dysenteric types may develop, also intestinal hæmorrhage. In the peritoneal type appendicitis or acute pancreatitis may be diagnosed, and the patient erroneously operated on. (4) *Cardiac.*—Syncope associated with a dilated right heart and various forms of disordered cardiac action may develop. (5) *Respiratory.*—Mild bronchitis and broncho-pneumonia relieved by quinine are reported. (6) *Sudoral.*—Here excessive sweating results in collapse and syncope. (7) *Hyperpyrexial.*—The clinical picture simulates that of heat stroke, and is often classified under cerebral malaria.

Complications and Sequelæ.—Malarial cirrhosis of the liver does not occur, but the tendency to the formation of soft pigment stones in the gall bladder appears to be increased. Twisting of the pedicle or rupture of the spleen from slight trauma may be encountered. Lack of mental concentration, amnesia and certain psychoses may follow cerebral malaria. Neuralgia, neuritis, corneal ulceration, iritis, retinal hæmorrhages, optic neuritis and orchitis occasionally occur. Herpes labialis is common, especially in benign infections. Hepatitis with jaundice may occur, and nephritis with œdema is not infrequent in quartan malaria. In pregnancy, abortion often results unless the fever is stopped by giving atebrin, quinine or other specifics.

Diagnosis.—Special points of clinical importance are splenomegaly, secondary hæmolytic anæmia, periodic fever commencing in the forenoon or early afternoon, and the therapeutic response to quinine. In the apyrexial phase a leucopenia and monocytosis of over 15 per cent., especially if associated with urobilinuria, are highly suggestive of malaria, while the demonstration of parasites completes the diagnosis. Blood smears should, when possible, be made before quinine is administered, and the examination of thick films may be of considerable diagnostic value where parasites are scanty in the peripheral blood.

Prognosis.—Malaria is the chief cause of death in the tropics, being specially serious amongst young children and in those suffering from intercurrent disease like dysentery and ancylostomiasis, as well as in undernourished or famine populations, and those on deficient diets. Furthermore, the debility and leucopenia induced by malaria render the individual more susceptible to incurrent infections like broncho-pneumonia and sepsis. In benign forms the prognosis is generally good as regards life, but cases may relapse repeatedly even after intensive and prolonged quinine treatment; in the Ceylon epidemic, however, especially in cases in which pregnancy or ancylostomiasis co-existed, death not infrequently resulted. In malignant forms the death-rate will be proportionate to the skill of the clinician in diagnosing his cases: speedy recognition of the complaint means early treatment and saving of life. In the absence of treatment, pernicious forms generally die, and intravenous quinine is essential in cerebral malaria or where there is much vomiting.

Treatment.—PROPHYLACTIC.—Destruction of adult vectors, anopheline larvæ and their breeding-grounds by drainage, etc., and the application of oil or spraying with Paris green should be carried out. Tropical residents should obliterate potential breeding-places in their bungalows and gardens, sleep under mosquito nets and, where possible, live in mosquito-proof houses. After sunset mosquito boots and the application of oil of citronella to the wrists and neck may be useful. Prophylactic quinine, grains v. daily, though it does not prevent infection, prolongs the incubation period and tends to keep the infection subclinical. Pamaquin (plasmoquine), on account of its lethal action on gametocytes, may prove more valuable.

CURATIVE.—The drugs which are of specific value in malaria are quinine, pamaquin and mepacrine hydrochloride (atebrin). Arsenic compounds have a distinct therapeutic action on *P. vivax*, but exert little effect on *P. falciparum*. Bed rest is essential during the febrile period and is advisable for several days after cessation of fever. Constipation must be avoided, and sodium sulphate or similar aperients should be administered regularly. Aspirin during the paroxysm is useful, and iron in full dosage assists in blood regeneration.

Quinine.—This remains the sheet anchor of malarial therapy and generally should be given by the mouth. In the acute attack quinine is most potent in benign tertian, less active in quartan, and least so in malignant tertian malaria. Regarding cure of relapses, it has less effect on *P. vivax* and *P. malariæ* than on *P. falciparum*, in which the relapse rate is considerably less than in benign tertian malaria. Quinine acts effectively on the subtertian schizonts and allays acute symptoms, but does not affect the development of either the gametocytes or the sporozoites. Various salts are available,

ine + Pulv. Rhei Co helps to disguise the bitter taste. (Dr Haq)

including the bihydrochloride, hydrochloride, bisulphate, sulphate, euquinine and tannate. Opinions vary regarding the optimum dosage and duration of treatment, and James suggests that a delay in quinine administration may be advisable in non-urgent cases until natural antibodies have developed. Regarding dosage, some advocate 30 grains daily for 1 month; others give 10 grains thrice daily for 1 week and thereafter 5 grains night and morning for 2 to 3 weeks. The dosage should certainly not be less than 15 grains daily for 10 days. Owing to its solubility the bihydrochloride should be used for both intramuscular and intravenous injections, the dosage being 7½–10 grains in 10 c.c. of distilled water. Quinine by the mouth may be given in solution or cachets, but not in pills made with insoluble salts as they may fail to dissolve and not be absorbed. Children bear quinine well, the dosage being appropriate to the age. In malarial patients its administration is advisable in the puerperium and before operation or anæsthesia (10 grains daily). Intramuscular injections of concentrated quinine may cause necrosis of muscle and sterile chemical abscess may result; bacterial abscesses, tetanus and gas gangrene have also been reported following injection with contaminated material. Intravenous injections are much preferable provided the solution is adequately diluted and injected slowly; it can be employed (1) where vomiting is excessive; (2) where quinine is ineffective *per os*; (3) where absorption of quinine is defective as shown by its absence from the urine when tested with Mayer-Tanret's reagent; (4) in such pernicious manifestations as cerebral and algid malaria where speed is essential to save life. Occasionally in the tropics malarial fever proves refractory even to intravenous quinine, and similar findings have been recently recorded by James, with certain strains in experimentally induced malaria. The toxic effects of the drug include tinnitus, visual and gastric disturbances, deafness and amblyopia: idiosyncrasy may result in severe erythematous and urticarial rashes. Cinchona febrifuge, consisting of the combined alkaloids of cinchona, is advocated by Acton on economic grounds; the dosage is 21 grains daily for 10 days.

Mepacrine hydrochloride (*quinacrine, atebrin*), a synthetic acridine derivative which, like quinine, acts on the asexual parasites within the corpuscles, but has little action on the gametocytes and none on the sporozoites. It is given in tablet form in doses of 0·1 g. thrice daily after food for 5 to 7 days, and this course can be repeated once or twice after a week's interval. It is at least as effective as quinine in ridding the blood of parasites, relieving symptoms and preventing relapses. Headache, abdominal discomfort, intestinal colic and a transient yellow staining of the skin may result from its administration; troublesome dreams, mental disturbances and certain psychoses have been recorded as occasionally associated with its administration. When doubt exists as to whether atebrin is being absorbed from the intestine, its excretion in the urine should be tested by adding sulphuric acid; in the presence of atebrin an intense yellow colour is produced and the solution gives a marked fluorescence with ultraviolet light.

If the drug is not being absorbed, or in cases of urgency, a soluble preparation—atebrin musonate—can be injected intramuscularly. It is available in ampoules containing a dosage equivalent to 0·1 g. or 0·3 g. atebrin. Local pain and toxic cerebral features were recorded following its use in the Ceylon

epidemic. Mepacrine hydrochloride should be given in preference to quinine in pregnancy and in patients who have previously had blackwater fever; in the latter the urine should be rendered alkaline with citrates.

Pamaquin (prœquinine, plasmoquine)—a synthetic quinoline derivative—was shown by Rochl to destroy malignant tertian gametocytes, but to have practically no effect on schizonts, whereas in benign tertian and quartan infections it probably acts on both phases of the parasite; sporozoites are also affected, but too large a dose has to be employed prophylactically to prevent infection entirely. It is put up in tablets—plasmoquine simplex—containing 0·01 g. and 0·02 g., one tablet being given thrice daily after food for 5 days. Toxic symptoms include headache, abdominal pain, cardiac arrhythmia, cyanosis and methæmoglobincythæmia, the methæmoglobin being found within the corpuscle and not free in the plasma.

Combined Treatment.—Pamaquin (0·01 g.) can with benefit be given with quinine (0·125 g.) in the form of pamaquin-compound, two tablets being taken twice daily after food for 7 days. It is advised to repeat such a course of treatment four times with a four-day interval between each course. Pamaquin used to be given simultaneously with mepacrine hydrochloride, but owing to the frequency of abdominal pain and other toxic complications, it is now customary to give a course of mepacrine hydrochloride (0·1 g., t.d.s., p.c.) for 7 days and after an interval of 3 days to give a course of pamaquin (0·01 g., t.d.s., p.c.) for 5 days. The same treatment can be repeated after an interval of 7 days. This combination of mepacrine hydrochloride followed by pamaquin gives excellent results and has much to recommend it.

Another synthetic drug—certuna—with strong gametocidal action has recently been described by Kikuth, and as its toxicity is less marked than pamaquin and it can be given along with mepacrine hydrochloride, it may possibly replace pamaquin in malaria therapy.

Patients with latent malaria must be specially warned against getting wet, bathing, excessive exertion and alcoholism, as these factors precipitate relapses.

BLACKWATER FEVER

Synonyms.—Hæmoglobinuric or Melanuric Fever; Malarial Hæmoglobinuria.

Definition.—An acute complication of chronic malignant tertian malaria, characterised by one or more intravascular hæmolyses of considerable severity, hæmoglobinuria, fever, vomiting, jaundice and anæmia.

Ætiology.—Blackwater fever occurs in Nyasaland, Uganda, the Sudan, East Africa, West Coast Colonies and other parts of tropical Africa, in the Duars, the Terai and the Jeypore Hill tract (Madras) in India, in Italy, Greece, Macedonia and Palestine, in the southern states of the U.S.A., Panama, etc. It invariably originates in an endemic zone heavily infected with malignant tertian malaria. Native populations may enjoy immunity, while colonists, imported natives and even visitors are attacked. Its most

frequent incidence occurs from 1 to 5 years' residence, but it may appear within 3 months. Multiple attacks are common. Though seen more frequently in males, both sexes and children as well as adults are susceptible. Practically every case gives a history of chronic malaria, often associated with irregular quinine intake, the rare exceptions being examples of latent infection. Quinine is the great factor precipitating the attack, but chill and over-exertion sometimes do so as well. Pamaquin (plasmoquine) also may precipitate blackwater, but mepacrine hydrochloride (atebrin) infrequently does so. Some have regarded the condition as due to a biological lysin, others suggest it may have an anaphylactic origin or be caused by a direct hæmolytic action of quinine on the corpuscle. There is no evidence of dermal hypersensitivity or of idiosyncrasy to quinine, and no lysin has been demonstrated. Possibly the intracellular lysin normally contained in R.E. cells which have hypertrophied as a result of chronic malaria, is suddenly liberated into the blood. Such lysin may become immediately fixed to the corpuscles in the visceral vessels and so be no longer demonstrable in the peripheral blood.

Pathology.—*Morbid anatomy.*—The skin is jaundiced, the blood watery, the serum sometimes tinged with hæmoglobin, while malarial pigment may persist in the viscera although not in large amounts. The liver is enlarged and soft, the bile thick and tarry, the spleen big and its pulp almost diffluent; the kidneys are dark, swollen and intensely congested. Microscopically, hæmosiderin is found in the liver and spleen in which malarial pigment may also be evident. Eosinophilic, granular debris blocks the tubules of the kidney, and there is toxic degeneration and desquamation of the cells of the convoluted tubules. Cloudy swelling and necrosis of liver cells, especially of the centre of the lobule, may occur generally associated with malarial pigment in Kupffer's cells.

Clinical pathology.—Malarial parasites, often present in blood smears at the beginning of the attack, are rare after 24 hours, and generally absent at autopsy. The urine shows albumin, oxy-hæmoglobin and urobilin in excess; methæmoglobin is generally demonstrable. Bile is present only in the most severe cases, and ketones may also appear. The characteristic sediment consists of brown, granular debris and granular casts. Red blood corpuscles are scanty or absent. The plasma contains oxyhæmoglobin, and after some hours methæmalbumin as well. There is an intense hyperbilirubinæmia with an indirect van den Bergh reaction of 5 to 85 units, but immediate direct reactions only occur in the severest cases with toxic changes in the liver. The blood urea is markedly raised, the excess being derived partly from destroyed corpuscles and partly from renal retention; one case in our series which recovered showed a blood urea of 450 mg. per 100 c.c. When only a limited number of nephrons are blocked, urea retention leads to polyuria; where blockage is extensive oliguria or even anuria results. In the latter type of case renal acidosis may develop; this is associated with lowering of the CO_2 combining power of the plasma, a decrease in serum calcium, and an increase in the blood phosphorus. Anæmia is frequently profound, and in severe cases 50 per cent. of the corpuscles may be destroyed overnight. A study of the excretion curves of urinary hæmoglobin shows that several distinct intravascular hæmolyses may occur.

Results of Hæmoglobin Disintegration.—In malaria red cells are destroyed

during sporulation when malaria pigment and some undestroyed hæmoglobin gains access to the blood stream. Many of the parasitised corpuscles, however, are phagocytosed by the hypertrophied reticulo-endothelial system, where they undergo intracellular lysis, with the production of bilirubin and hæmosiderin. In blackwater fever the circulating corpuscles are destroyed *in situ*, and frank hæmoglobinæmia results; also hæmoglobinuria whenever the concentration of the extracorpuscular hæmoglobin exceeds the renal threshold. If the reaction of the urine be acid the oxyhæmoglobin tends to be converted into methæmoglobin and acid hæmatin which is precipitated along with granular debris, causing a variable degree of blockage of the tubules. Some of the circulating hæmoglobin is absorbed directly by the reticulo-endothelial cells, with the production of hæmosiderin and bilirubin. The resulting hyperbilirubinæmia accounts both for the hæmolytic jaundice and the pleocholia, with bilious vomiting and dark brown stools; while the absorption of surplus stercobilinogen causes urobilinuria, especially in the presence of liver damage. Finally, any residual circulating hæmoglobin is split into globin and reduced hæmatin (ferrous), which is immediately oxidised to oxyhæmatin (ferric) and unites with serum albumin to form methæmalbumin (Fairley, 1938). It is this pigment which in the past has been confused with methæmoglobin, but which differs from it in its extra-corpuscular distribution, and in having an α band at 623 $\mu\mu$ which is not altered by Stokes's reagent, but is dispersed by strong ammonium sulphide with the production of a hæmochromogen having an α band at 558 $\mu\mu$.

Symptoms.—No recognisable pre-blackwater fever stage exists, and the patient generally thinks an ordinary attack of malaria is impending. The onset is generally sudden, with chill and loin pain, but in mild cases red or black urine may be the first indication. A rise of temperature is almost invariable, rigor is common, and nausea, bilious vomiting and epigastric discomfort are characteristic. The urine, which may be pinkish or red at first, soon becomes port-wine or porter-coloured, presenting the characteristics described. As the condition progresses polyuria, oliguria or anuria may develop. Within a few hours yellowish discoloration of the skin and conjunctivæ is apparent; this increases in intensity as hæmoglobinuria continues, but only in the severest cases is bile found in the urine. The pulse is rapid and of low tension at first, and the blood pressure in severe cases is markedly depressed (S/D = 80/50) at onset, though later it rises. Hiccough is a serious feature and there may be great restlessness, anxiety, pallor, cold extremities, and thready pulse occasioned by the rapidly developing anæmia. As many as 2,000,000 red cells per c.mm. may be destroyed in 24 hours by recurrent hæmolyses. Headache and lumbar pain are characteristic. The spleen and liver are generally demonstrably enlarged and tender, and may cause discomfort; the spleen decreases in size during the attack. Localised tenderness over the distended gall bladder may also occur. The fever at onset resembles a malarial paroxysm, is highest at first, becomes intermittent or remittent later, and generally declines in 3 to 4 days as the vomiting subsides and the urine clears. Post-hæmoglobinuric fever may appear after hæmoglobinuria has ceased and persist well into convalescence. Hyperpyrexia may develop especially in the late phases of the disease, while some cases show a marked tendency to hæmorrhages in

the skin and the gastro-intestinal tract. In one of our series the rash simulated that of typhus fever.

Several different clinical types are encountered: (1) Mild hæmoglobinuria, especially common in children, in which blood pigment in the urine is only found for a few hours. (2) Severe hæmoglobinuria, associated with the clinical features already described. These are separated into two groups: (*a*) the polyuric type in which renal excretion is well maintained despite evidences of nitrogenous retention, and (*b*) the oliguric and anuric types. Catheterisation at first shows small quantities of highly albuminous, perhaps bile-stained, urine, followed later by complete suppression. Anuria may set in early, and is associated with a normal or subnormal temperature. Hepatogenous jaundice not infrequently develops. Life may be prolonged for many days, and death occur without signs of uræmia.

Toxæmic features are common in both these types. Their differentiation is important, since blood transfusion is a life-saving procedure in polyuric cases. (3) Intermittent hæmoglobinuria, in which blood pigment is present in the urine from time to time, though in the intervals it disappears entirely. In these cases the temperature continues and post-hæmoglobinuric fever is common; icterus and anæmia are well marked.

Course and Complications.—Complications include anuria, post-hæmoglobinuric fever, anæmia, retinal hæmorrhages, biliary colic, pigment calculi and cholecystitis. About 10 per cent. of cases relapse during the course of an attack (Ross). Convalescence may be prolonged owing to anæmia and transient renal dysfunction, but there is no evidence that chronic nephritis results.

Prognosis.—The prognosis depends to a considerable extent on the quantity of corpuscles destroyed, and if during any single rapid hæmolysis this amounts to half a litre of normal blood, and the reaction of the urine be acid, a fatal anuria appears inevitable. The mortality rate varies from 20 to 40 per cent., and though some cases are doomed from the onset, in others modern therapy favourably influences the course of the illness. Unfavourable features include rapidly increasing jaundice, grave anæmia, severe hiccough, anuria and hyperpyrexia, while bile in the urine or a persistent increase in the blood urea and bilirubin is a grave prognostic omen.

Treatment.—Prophylactic.—The prophylaxis of blackwater fever is that of malaria. Where there is a previous history of hæmoglobinuria, the urine should be alkalinised with citrates and atebrin given in preference to quinine for febrile malaria.

Curative.—The causes of death in blackwater fever are well known, and in the absence of knowledge concerning the mechanism of the hæmolysis and of specific remedies for terminating it, the therapeutic indications are: (1) to combat the anæmia, anoxæmia and heart failure; (2) to alkalinise the urine, to prevent or relieve suppression, and to decrease the toxæmia. Measures directed to these ends include absolute rest in bed in the recumbent posture, fluid by various routes, oral and intravenous citrates, intravenous glucose and blood transfusion. Transport is justifiable only if it places the patient under better conditions for treatment. Careful nursing is all important. The diet at first should consist of bland fluids like barley water, fruit juices and glucose; later, milk, fruit jellies, junket, custard

and Benger's food are allowed. Proteins are restricted well into convalescence owing to renal involvement. Fluids are pushed *per os* and should contain sufficient sodium bicarbonate and potassium citrate to alkalinise the urine, and so lessen the clogging of the renal tubules. Should vomiting prove troublesome gastric lavage may be practised and water, alkalis and glucose given per rectum. In all cases where the urine is acid in reaction 1 pint of bicarbonate of soda solution (150 grains to 1 pint) should immediately be injected intravenously and repeated if necessary; the solution must be sterilised by filtration or by adding the bicarbonate to cooled boiled water, since actual boiling is liable to convert it into the toxic carbonate. Recent work by Busby, Hart, Kekwick and Whitby on alkalinisation of the urine indicates that 150 c.c. of a 3 per cent. solution of sodium citrate (4·5 g. = gr. eq.) is sufficient to render the urine temporarily alkaline; alternatively, 8 g. of potassium citrate given *per os* has the same effect. To keep the *p*H of the urine on the alkaline side of 7·0, 35 g. potassium citrate should be given together with 3000 c.c. of fluid in the 24 hours. Lemon juice, coffee or milk disguise its disagreeable flavour. Alternatively, a total of 600 c.c. of 3 per cent. sodium citrate (18 g.) in 2400 c.c. of 5 per cent. glucose by intravenous drip may be administered every 24 hours. The onset of alkalosis is suggested by headache, giddiness, vomiting and muscular cramp. As a clinical index to *p*H, the urine may be regarded as sufficiently alkaline if it turns red litmus blue, or if the urine is a bright red indicating unchanged hæmoglobin. When the urine has a brownish tint, or is porter-coloured, methæmoglobin is present and the urine requires alkalinisation. Intravenous injections of dextrose assist the heart's action and help to combat toxæmia and urinary suppression. One to 2 pints of a 5 per cent. solution are used, but in anuria a 10 to 20 per cent. solution is a more potent diuretic; hot fomentations to the loins, dry cupping and colonic douches with hot saline (120° F.) are all useful for this purpose. Diuretics like caffeine citrate and caffeine sodium benzoate have their advocates, and the bowels should be kept opened with salines or calomel. In collapsed cases with low blood pressure, warmth, pituitary extract and elevation of the foot of the bed may be of benefit. Transfusion is the best means of dealing with anæmia, and in severe cases manifesting rapid blood destruction and cardiac weakness 1 pint of citrated blood from a suitable donor should be given without delay even during the hæmolytic period and repeated if necessary. In polyuric cases blood transfusion is a life-saving procedure, but its effect in the anuric type of case is more uncertain, for though it may improve the blood count, death from uræmia may still ensue. Once the hæmolysis has stopped marked reticulocytosis, followed by blood restoration, generally proceeds automatically in the well-fed European, but iron in adequate dosage and liver injections are beneficial in vegetarians and in people living on diets deficient in good animal protein; in addition, blood transfusion may be advisable under such circumstances. Regarding specific therapy opinions differ. The tendency of the hæmolysis is to destroy the great mass of the parasites and occasionally natural cure results. Where parasites persist in the blood a course of mepacrine hydrochloride should be given; otherwise treatment with anti-malarial drugs is better postponed until convalescence.

LEISHMANIASIS

Leishmaniasis is the term applied to a group of diseases caused by parasites of the genus Leishmania. Some of these are general infections, others are local. Of the first, we have kala-azar, due to *Leishmania donovani* (Laveran and Mesnil, 1903) and infantile or Mediterranean kala-azar caused by *L. infantum* (Nicolle, 1908). Both morphologically and serologically they are the same parasite, no marked differences occur in inoculated animals, and there seems no reason to separate them. Oriental sore, due to *L. tropica* (Wright, 1903), and American dermal leishmaniasis, due to *L. braziliensis* (Vianna, 1911), are, however, distinct species belonging to the second group, and according to Noguchi are separable serologically.

Kala-azar

Definition.—Kala-azar, or black fever, is a specific disease associated with enlargement of the spleen and liver, anæmia, great emaciation and irregular fever of long duration caused by the protozoon *L. donovani*, present in the peripheral blood and reticulo-endothelial cell system.

Ætiology.—The disease has definite geographical limitations, being commonest in India, Assam and the Mediterranean littoral, where 90 per cent. of the cases occur in children ; it is also found in China, Indo-China, the Sudan, Abyssinia, Russian Turkestan and Mesopotamia. Natives appear more susceptible than Europeans, probably owing to different habits of life. In Assam villages the introduction of an infected case generally precedes other cases, and often it appears to be a house infection (Rogers). Children and young adults are specially liable, and males appear more susceptible than females.

The rounded non-flagellate stage of the parasite is a small oval body, 2 to 5 μ long by 1 to 2 μ broad, containing two structures, one a large round laterally placed nucleus (macronucleus or trophonucleus) staining bright red with Romanowsky's stain, the other (kinetoplast, micronucleus, centrosome), which is usually rod-shaped, stains a deep reddish-purple and has one end pointing toward the nucleus. It can be cultivated on rabbit-blood agar (N.N.N. medium) if grown for 2 to 3 weeks at room temperature (22–25° C.), provided the culture material has not been contaminated (Rogers). During growth Leishmania bodies develop into leptomonads measuring up to 24 microns in length, with a flagellum and centrosome at one end and a central macronucleus. This flagellate undoubtedly represents an intermediate stage in some insect vector which is almost certainly the sand-fly. In India it was Sinton's original observation that the local distribution of *Phlebotomus argentipes* coincided with that of kala-azar, which led to the transmission experiments of Knowles, Napier and Smith. It is now known that if sand-flies be fed on kala-azar cases, heavy leptomonas infections develop in the mid-gut, œsophagus and pharynx, these parasites being capable of producing the disease if artificially injected into hamsters. Infection, however, has only once been successfully transmitted by the actual biting of infected sand-flies. In the Mediterranean area very young children and dogs suffer from kala-azar, whereas in India

and North China infections occur mainly in older people and extremely rarely in dogs. Adler suggests that the former infections result from biting, the latter from crushing these insects.

Pathology.—The parasites are very generally distributed in the endothelial cells of the capillaries throughout the body, where they multiply, eventually burst through, and are subsequently taken up by phagocyte cells of the blood and tissues. Common sites for the parasite are the reticulo-endothelial cells of the liver, spleen, lymphatic glands and bone-marrow; less commonly they occur in the lungs, pancreas, kidneys, adrenals, testicles, intestinal submucosa, intestinal ulcers and the lymphatics draining them (Manson and Low). The central nervous system is never involved. Meleney holds that the macrophage or reticulo-endothelial cells respond specifically by local multiplication in this disease, forming "clasmatocytic tissue." At autopsy emaciation is marked, the spleen and liver are generally enlarged, while dropsical effusions and intestinal ulceration may occur. The spleen is at first soft, pulpy and friable, later it becomes hard and fibrous; the capsule is thickened, and perisplenitis and infarcts may also be present. The liver is firm and friable, the capsule is thickened, and fatty degeneration and a nutmeg appearance are common; cirrhosis may eventually result. The bone-marrow is generally red and soft, showing a decrease of fat, while the mesenteric glands are often enlarged, presenting a central necrosis. The heart is dilated and flabby, while the entero-colon may show superficial or deep ulcerations. Napier holds that the latter at least are of dysenteric origin. Post-kala-azar dermal leishmaniasis has recently been described.

Symptoms.—The incubation period is probably from 1 to 4 months, but cases may occur 1½ years after exposure. The onset, especially in endemic areas, may be sudden, with fever simulating malaria or typhoid, or it may be insidious. Often in febrile cases the diagnosis is not made until relapses occur and the more classical features of the disease develop. These may be classified as follows: (1) Irregular remittent or intermittent pyrexia which, though not necessarily high, is characteristic. Periods of apyrexia spontaneously develop, especially during the day, and may lead to confusion with Malta fever. A double daily rise may occur in the afternoons and evenings (20 per cent. of cases), but this may also be noted in other diseases and is not pathognomonic. (2) Loss of hair and deepening colour or pigmentation of the skin—hence the name black fever. (3) Anæmia with the characteristic blood changes. (4) Rapid loss of weight and cachexia. (5) Splenomegaly, which may be the first sign or only be noted after 1 to 2 months of fever. In the early stages the spleen feels soft and doughy, but not tender; later it hardens and may reach very large dimensions. (6) The liver is generally palpable (88 per cent.), presenting a sharp lower edge. (7) Diarrhœa.—There is good appetite associated with poor digestion which itself may lead to intermittent diarrhœa (Napier). If blood and mucus be present, intercurrent dysentery should be suspected. (8) Other features include night sweats, persistent irritating cough, palpitation, dyspnœa, low blood pressure, *i.e.* below 100 mm. of mercury, œdema of the extremities and occasionally puffiness of the face. Amenorrhœa often develops, but conception may occur with congenital transmission from the mother (Low and Cooke). The blood changes, which include anæmia, leucopenia and reduction in the platelet count, are due to replace-

ment of both the leucoblastic and erythroblastic marrow by clasmatocytic tissue. The hæmoglobin is often proportionally reduced, so that the colour index may equal 1·0; in other cases it is 0·7 or 0·8. The blood picture may show anisocytosis, poikilocytosis, polychromasia and normoblasts. The leucopenia is extreme, often sinking to 2000 per c.mm., and in 80 per cent. of cases it is less than 4000 per c.mm. The differential count reveals a relative increase in lymphocytes and monocytes, with a decrease in neutrophiles and eosinophiles. The coagulability of the blood may be prolonged, the calcium, blood sugar and serum albumin are reduced, and the total globulin content of the blood is raised, euglobulin increasing at the expense of the pseudo-globulin fraction.

Complications and Sequelæ.—Owing to debility and bone-marrow involvement with leucopenia, the resistance to bacterial infections is markedly decreased, and influenza, broncho-pneumonia, lobar pneumonia and tuberculosis are common causes of death; otitis media and cancrum oris may occur, especially in children. Watery diarrhœa is common and intercurrent dysentery frequent. Purpura, epistaxis, bleeding from the gums and melæna may be encountered. The sequelæ include chronic splenomegaly plus severe anæmia and cirrhosis of the liver, sometimes associated with ascites and demonstrable parasites. Jaundice frequently appears within 3 months of treatment and may persist for several months. Post-kala-azar dermal leishmaniasis has recently been described. Areas of depigmentation generally appear about a year after antimony injections, and papillomatous nodules, in which leishmania can be found, occur the following year. A xanthoma-like condition is also described, but ulceration never occurs. Parasites are demonstrable in smears and culture, and apparently they are confined to the skin as splenic puncture yields negative results. Occasionally the condition appears in persons who give no history of previous kala-azar or of treatment.

Course.—Bentley showed in the Assam epidemics, prior to the introduction of antimony, that the disease lasted 1 to 2 years in chronic cases. The mortality rate, if untreated, is about 90 per cent.

Diagnosis.—Kala-azar has to be differentiated from the febrile splenomegalies of the tropics, especially chronic malaria, undulant fever and enteric fever; schistosomiasis, Banti's disease and leukæmia must also be considered, and owing to the danger of hæmorrhage in the latter disease splenic puncture should never be undertaken until blood examination has excluded it. In childhood Mediterranean kala-azar has to be differentiated from Cooley's anæmia, commonly found in Greece, von Jaksch's anæmia and acholuric jaundice. Diagnosis is generally dependent on the demonstration of *L. donovani* in smears from the liver or spleen or cultures on N.N.N. medium obtained from the peripheral blood. Parasites are less common in the peripheral blood in Mediterranean than in Indian kala-azar. Aspirated material for microscopical examination must be collected in an absolutely dry syringe.

The formol-gel or aldehyde test of Napier is of considerable value in the diagnosis of kala-azar, especially when the result is positive and associated with a leucopenia. The test is performed by adding 1 drop of commercial formalin (30 per cent. formaldehyde) to 1 c.c. of clear serum, which is immediately shaken and left at room temperature. When the reaction is positive

the serum immediately becomes viscid, and within 1 or 2 minutes assumes a whitish opalescent appearance and sets so that the tube can be inverted without spilling. In from 3 to 20 minutes it forms a solid opaque coagulum like the white of a hard-boiled egg.

For the first three months the reaction is of doubtful value, but after this it is generally positive.

Prognosis.—Intercurrent disease, severe intestinal symptoms, and cirrhosis with ascites are of grave significance. Modern therapy generally results in recovery, provided the condition is not too advanced and intercurrent disease absent.

Treatment.—PROPHYLACTIC.—Segregation and treatment of the sick, and abandonment of infected houses and rebuilding at distances not less than 300 yards have been effective in India. Destruction of the probable sand-fly vector and of its breeding-places is indicated.

CURATIVE.—The patient is put to bed on a milk or light diet and intercurrent disease treated. Napier advocates an iron tonic mixture, and tincture of digitalis if there is cardiac weakness. Certain antimony compounds are specific, the most difficult form to cure being Mediterranean kala-azar. At first the trivalent compounds of the tartar-emetic type were employed, but now pentavalent antimony derivatives, such as neostibosan, are replacing them, owing to their rapid action, reduced toxicity for the host and increased toxicity for the parasite. *Trivalent antimony compounds.*—Antimony and potassium tartrate, and antimony and sodium tartrate are given intravenously on an empty stomach in a 2 per cent. solution thrice weekly. The initial dose is ½ grain, increasing by ½ grain until a maximum of 2 to 2½ grains is attained. Only freshly prepared solutions sterilised by boiling should be employed, and the total course is 40 to 60 grains. Effects of treatment are to reduce the temperature to normal, decrease the splenomegaly and hepatomegaly, increase body weight and restore the leucocytes to normal numbers. Cough and nausea following injections are not important, and rheumatic-like pains are frequent. Sever toxic manifestations like bradycardia, severe vomiting, diarrhœa and jaundice necessitate a suspension of treatment. Numerous other trivalent compounds have been employed, including antimosan, which is less toxic than tartar emetic, but almost as slow in producing cure. *Pentavalent antimony compounds.*—These include stibamine, von Heyden 693 or neostibosan, stibenyl, urea-stibamine, aminostiburea, neostam, urea-stibol and stibosan von Heyden 471. The dose of urea-stibamine, amino-stiburea and neostam as advocated by Napier is 0·1 g. initially, 0·2 g. as a second dose and 0·25 g. for each subsequent injection. With stibosan and von Heyden 693 (neostibosan) an initial dose of 0·2 g. with subsequent doses of 0·3 g. is advisable. Debilitated patients require smaller doses, while children, although tolerating proportionally larger doses than adults, receive smaller initial doses. The length of different courses varies from 8 to 15 daily injections. Toxic features include vomiting, giddiness, nausea, and more rarely diarrhœa, hepatitis and jaundice and an alarming anaphylaxis-like syndrome, producing puffiness of the face, urticaria and cardio-vascular collapse, etc. The beneficial effects of treatment are similar to those described with the trivalent compounds, except that the drugs act quicker and more effectively. Cure is indicated by an absence of clinical symptoms for 6 months, a negative aldehyde test, an increase in serum albumin associated

with a decrease in total globulin involving the euglobulin fraction, and a permanent disappearance of parasites.

Oriental Sore

Synonyms.—Tropical Sore; Aleppo Sore; Bagdad Boil; Delhi Boil; Biskra Button; Bouton d'Orient; Date Boil, etc.

Definition.—An infective granuloma of the skin and subjacent tissues caused by *Leishmania tropica*, producing nodular lesions which generally break down and form chronic indolent ulcers.

Ætiology.—The condition is common in parts of the East, including Mesopotamia, Arabia, Persia, Asia Minor and the North-West Frontier of India. It also occurs in Northern Africa, Egypt, the Sudan, Nigeria, the French Congo, and has been reported in Spain, Italy and Greece. Essentially it is a disease of towns, notably of Bagdad, Delhi and Lahore, and its incidence on exposed parts suggests an insect vector. Wherever it occurs sand-flies are common, and the remarkable development into virulent flagellates occurring in the mid-gut and extending forward to the proboscis after feeding them on oriental sores, indicates that these insects are the transmitters—probably *Phlebotomus papatasii* and *P. sergenti*. The parasite itself is morphologically indistinguishable from that of kala-azar and can be directly transmitted by inoculation; it is auto-inoculable, but not through the unbroken skin. Dogs, cats, guinea-pigs, etc., are susceptible.

Pathology.—Infective granulomata are produced, sections showing atrophy of the epidermis, infiltration of the corium and its papillæ with lymphocytes, plasma cells and macrophage endothelial cells containing *L. tropica*. If the nodule ulcerates secondary bacterial infection ensues. The keloid type of lesion described in the Sudan may show epithelial cell nests. Unlike the American form, the mucous membranes are rarely involved.

Symptoms.—The incubation period varies from 1 week to 6 months. Commencing as a small itching red papule, it develops into a nodule or blind boil, which occasionally persists for a year or more before disappearing. More usually the lesion becomes covered with a yellow crust and ulcerates, the ulcer having well-defined rounded edges and a granulation tissue base exuding thin pus. The sores may be single or multiple, as many as 35 having been recorded, and are specially common over the hands, wrists, feet, legs and face. Various other forms of dermal leishmaniasis due to *L. tropica* may be encountered. They include (1) small, firm, discrete nodules occurring in the course of the lymphatics; (2) warty outgrowths or papules known as the verrucose form, first described by Ferguson and Richards in Egypt; and (3) lupus-like nodules, which may implicate the cheek.

Diagnosis.—This is dependent on demonstrating the parasite. If ulceration has occurred the skin at the edge of the ulcer should be sterilised with iodine, punctured with a glass pipette, and the material so obtained inoculated on to N.N.N. medium. Bacterial contamination prevents growth. Direct microscopical examination of this material often shows *L. tropica* in the endothelial cells.

Prognosis.—The condition is practically never fatal even when untreated, but under these circumstances it may last 18 months, after which the patient generally possesses an immunity to further infection.

Treatment.—PROPHYLACTIC.—Sand-flies and their breeding-grounds should be eradicated.

CURATIVE.—In cases which have been secondarily infected, hot boracic fomentations or eusol dressings should be applied until sepsis is controlled and the crusts separate. Local treatment, like carbon dioxide snow, for 5 to 30 seconds every 10 days, X-ray, radium, zinc ionisation and diathermy are advocated as well as local applications of ointments containing methylene-blue, iodoform, salicylic acid and tartar emetic (1 to 2 per cent.): the latter may cause painful sloughing. Excellent results may be obtained with orisol ointment containing berberine sulphate and dianthrone (derobin, cignolin) paint, applied with a camel hair brush and strictly confined to the ulcer surface by covering it with paraffin wax. Vaccines have their advocates. Tartar emetic intravenously as given in kala-azar is the standard treatment, a total course of 20 to 30 grains being required. Neostibosan is also being used successfully, and is undoubtedly the most hopeful treatment when multiple lesions are present.

AMERICAN DERMAL LEISHMANIASIS

Synonyms.—Espundia; Uta; Pian Bois; Pian Cayenne; Forest Yaws; Bosch Yaws; Bubas Braziliana.

Definition.—An infective granuloma due to *Leishmania braziliensis*, producing cutaneous nodules and ulcers on exposed surfaces; the buccal and nasal mucous membranes may be extensively involved, also the lymph glands and lymphatics.

Ætiology.—It is found in South America, in Brazil, Venezuela, British and Dutch Guiana, Bolivia, Peru and Paraguay. The disease is specially frequent amongst wood-cutters and people living in forests: some wood-loving insect, tick or bug is thought to be the transmitting agent. Morphologically, *L. braziliensis* is similar to *L. tropica*, but differs serologically (Noguchi).

Symptoms.—The incubation period is about 2 months. The lesion originates as an itching papule, which may develop into a blind nodule or ulcerate, producing fungoid granulations. Later, ulcers appear at the margins of the mouth and nose, often subsequently involving their mucous surfaces, the larynx and nasal septum (20 per cent.). Fever, joint pains and bronchitic symptoms now appear, but many years may elapse before the patient succumbs to intercurrent disease.

Diagnosis.—Demonstration of the parasites either in scrapings from the spreading margin of the ulcer or by culture completes the diagnosis. Syphilis, rodent ulcer, leprosy and tuberculosis closely resemble the destructive form of *L. braziliensis* which, however, never involves bone.

Prognosis.—Untreated cases are liable to die of intercurrent disease or cachexia, but with tartar emetic treatment the prognosis is satisfactory.

Treatment.—Cases with extensive involvement of mucous membranes die if untreated, but even these recover with modern therapy, which is similar to that outlined for oriental sore and kala-azar. A full course of 30 or 40 grains of tartar emetic should be administered intravenously.

Stibophen (fouadin), a trivalent antimony compound, yields very satisfactory results: twenty to thirty intramuscular injections are given in a

graded dosage of from 1–5 c.c. Local treatment for ulcers on the lips and nose should also be instituted.

TRYPANOSOMIASIS

A group of diseases caused by flagellate parasites of the genus *Trypanosoma*. In Africa, man may be infected with *T. gambiense* or *T. rhodesiense*, and in South America with *T. cruzi*. Trypanosomes also produce disease in animals, the most important being nagana affecting horses, dogs, cattle and wild game in Africa caused by *T. brucei*, which is probably identical with *T. rhodesiense*. *T. evansi* produces surra and *T. equiperdum* dourine, the latter disease, like syphilis, being transmitted during coitus.

African Trypanosomiasis of Man

Synonym.—Sleeping sickness.

Definition.—This disease, transmitted by the bite of tsetse flies, is caused by *T. gambiense* (Dutton, 1902) or *T. rhodesiense* (Stephens and Fantham, 1910). After initial invasion by trypanosomes, blood infection ensues with adenitis, irregular remittent fever, rapid pulse, œdema and circinate erythematous rashes; later a meningo-encephalitis results with lethargy, mental and physical degeneration, tremors, shuffling gait, convulsions, coma and death. Mild cases, with headache and slight fever, are common.

Ætiology.—The disease is limited geographically to areas where the tsetse fly abounds and occurs in Western and Central Equatorial Africa, including the Congo, Uganda, East Africa, Rhodesia, Nyasaland, etc. Natives and whites are both affected, and children and adults of both sexes prove equally susceptible. The two species of trypanosome are indistinguishable in human blood; they possess a nucleus, a posteriorly situated blepharoplast and a flagellum. *T. rhodesiense* is identified by inoculating blood into white rats, when posterior nuclear forms develop; this so rarely occurs with *T. gambiense* that the test is one of real value in distinguishing these two trypanosomes. Furthermore, *T. gambiense* manifests an uncertain pathogenicity to laboratory animals, and is relatively insusceptible to the action of normal human serum. Glossinæ take up trypanosomes from the blood during biting; these multiply in the gut and pass forward via the proventriculus and salivary ducts to the salivary glands, where further development ensues. Glossinæ become infective in 3 to 7 weeks and remain so for life; they bite mainly in the daytime. *T. gambiense*, the central African type, is transmitted by *G. palpalis* and *G. tachinoides*; possibly the natural reservoir of infection is game, such as the reed and bush buck, etc., encountered near lakes and rivers by which these flies live, depositing their larvæ in shady, sandy soil. *T. rhodesiense*, on the other hand, is spread by *G. morsitans* and *G. swynnertoni* which are widely distributed independently of water. The reservoir of infection is the infected game of the area: Bruce identifies this disease with nagana and regards *T. rhodesiense* as identical with *T. brucei*. As the pathology and symptomatology produced by the two African trypanosomes are similar they may be considered together.

Pathology.—The lymph glands, which are at first swollen, congested and hæmorrhagic, later undergo degenerative changes and extensive fibrosis. Enlargement of the spleen due to lymphoid hyperplasia and proliferation of endothelial cells also occurs, while thickening of the capsule is common. In the late stages trypanosomes are demonstrable in the intercellular spaces of the brain and cord, the microscopical appearances of which resemble those of meningo-encephalitis and meningo-myelitis. Mott has stressed the resemblance to general paralysis, perivascular lymphocytic infiltrations being invariable. Neuroglial cell overgrowth is also characteristic, and diffuse glial proliferation affects both the white and grey matter in the cord: the ganglion cells show chromatolysis of their nuclei, most marked in the cerebral cortex, and endothelial proliferation in the arteries may occur.

Symptoms.—Two phases are recognised: (I.) a stage of trypanosome fever when the trypanosomes are demonstrable in the blood and gland juice; (II.) the sleeping sickness stage when the cerebro-spinal fluid contains lymphocytes, globulin and perhaps trypanosomes. The incubation period probably varies from 1 to 3 weeks, and occasionally an intense local reaction follows at the original inoculation site. In many respects trypanosomiasis resembles syphilis. (I.) *Trypanosome fever.*—This is invariably seen in Europeans, but not always in natives. Its main features are: (1) an irregular remittent or intermittent temperature low in the mornings, higher at night; apyrexial periods may occur, lasting for weeks. (2) A low tension, rapid pulse of 100 to 120 per minute, which tends to persist despite a fall in the temperature. (3) An increase in the respiratory rate to 20 or 30 per minute. (4) Patches of circinate erythema, involving mainly the trunk. (5) Localised puffiness and œdema involving the feet, legs and face: the skin may be dry and irritable. (6) Polyadenitis: enlargement of the posterior cervical glands (Winterbottom's sign) is very characteristic; the epitrochlear, axillary, supraclavicular and axillary glands may also be involved; they are soft, elastic, not tender, and do not coalesce or suppurate. (7) An enlarged spleen which is generally palpable. (8) Deep hyperæsthesia, especially over bones like the tibia and manifesting a definite latent period (Kerandel's sign). Long latent periods of several months (rarely several years) may elapse before the central nervous system becomes involved, and probably some cases undergo spontaneous cure where the virulence of the trypanosome is low. Once the stage of sleeping sickness has become definitely established, the untreated patient rarely survives for longer than a year. (II.) *Sleeping sickness.*—In the *earliest phase* the patient may complain of headache, lack of concentration, disinclination for work and insomnia, associated with loss of weight, enlargement of lymphatic glands and slight tremor of the tongue. In the *intermediate phase* the countenance becomes sad, apathetic and morose, laziness and emotional instability increase, and the patient is always dropping off to sleep, even in tropical sunlight or when eating. The speech becomes mumbled and slow, the gait shuffling, and fibrillary tremors of the tongue, lips and hands develop. The reflexes are exaggerated and Romberg's sign is present. In the *final phase* all these symptoms become more pronounced; muscular weakness is extreme, saliva dribbles from the mouth, bed-sores and flexure-contractions may develop, the patient becomes entirely bedridden, and coma and convulsions generally terminate the picture.

The classical picture of sleeping sickness described above represents that encountered in areas where the virulence of the trypanosome is high. Recent investigation has shown that in both East and West Africa many mild cases occur in which slight toxic features, such as headache and a little fever, are the only manifestations of the disease. Furthermore, people are known to have survived who have had the disease continually for 15 years or more. Lester points out that it is the severely infected patient, often with involvement of the central nervous system, who attends hospitals and dispensaries, and this has resulted in the commoner mild clinical infections remaining unrecognised.

Complications.—Intercurrent infections like dysentery and pneumonia often cause death, and, as in syphilis, abortion and still-births are not infrequent. Keratitis, iridocyclitis, and choroiditis occur, and during treatment with tryparsamide optic atrophy has to be carefully watched for.

Diagnosis.—Irregular fevers, especially if associated with cervical adenitis, should arouse suspicion in patients who have been exposed to infection, and under such circumstances laboratory assistance is invaluable. Autoagglutination of the blood is frequently observed. Trypanosomes may be found in thin or in thick blood films, or in smears from centrifuged citrated blood. Even more satisfactory is the method of gland puncture, provided the gland juice be aspirated in a dry syringe, when 87 per cent. of cases with adenitis show trypanosomes (Broden). Inoculation of white rats or guinea-pigs with blood or emulsified excised gland is also a very valuable procedure. Lumbar puncture is essential in later cases; typically the cerebro-spinal fluid, which is often under increased pressure, shows an increase in globulin and lymphocytes, and later in medium-sized and vacuolated mononuclear cells as well. The advanced cases show counts of from 15 to 100 cells per c.mm. Trypanosomes are often difficult or impossible to demonstrate, even after centrifuging the fluid, and animal inoculation.

Prognosis.—The prognosis is very hopeful in *T. gambiense*, provided modern treatment be commenced before the central nervous system is involved: after this it is more doubtful, though many cases recover. *T. rhodesiense* is a far more virulent type of disease, and most patients succumb despite treatment. Europeans appear to recover better than natives, probably because they suffer less from intercurrent disease and are treated under better conditions.

Treatment.—PROPHYLACTIC.—McLean, in East Africa, discovered that a population between 10–60 per square mile proved ideal for the spread of sleeping sickness, affording maximum contact between fly and man. By concentrating the population in certain areas in Tanganyika sleeping sickness was practically eradicated. Destruction of reservoir vectors, *i.e.* big game, has not proved satisfactory. Removal of forest and bush for 15 feet around lakes and rivers is a valuable measure with *G. palpalis*, but does not affect *G. morsitans*. Personal prophylaxis is important. White clothes are advisable; shorts should not be worn, and veils and gloves used when feasible. Where possible travelling should be done at night. Duke showed that, owing to its delayed elimination, 2 grams of germanin confers protection against either *T. gambiense* or *T. rhodesiense* for at least 3 months.

CURATIVE.—Several specific drugs are of proved value in trypanosomiasis:

(1) Suramin (Bayer 205, germanin), a complex organic urea compound

—is injected intravenously in a dosage of 1 g. at intervals of 2 or 3 days until a total of 10 g. has been administered. It is especially useful in sterilising the blood in early cases of both *T. gambiense* and *T. nigeriense*, but tends to produce albuminuria and casts in the urine. The patient should be kept at rest in bed, and throughout treatment the protein content of the diet should be limited owing to toxic effects on the kidneys.

(2) Tryparsamide (sodium N-phenylglycineamide-*p*-arsonate) is given intravenously at weekly intervals in doses of 20–40 mg. per kilo bodyweight (1·5–3·0 g. for an adult) until a total dosage of 30 g. has been administered. Children receive relatively larger doses. Untoward symptoms are jaundice and the much dreaded optic atrophy which not infrequently supervenes; its onset may be indicated by failing vision or contraction of the fields of vision, flashes of light, ocular pain, lacrymation and photophobia. Many cases of total blindness have been recorded. The greater the changes in the cerebrospinal fluid the greater the tendency to optic nerve degeneration. Although tryparsamide is less trypanocidal than orsanine for trypanosomiasis in the circulating blood, it has the advantage of acting on *T. gambiense* when the cerebral nervous system has become involved. It is not justifiable to conclude that cure has resulted until the cerebrospinal fluid has remained normal for 6 months, and when lumbar puncture shows it to be abnormal after treatment another course of treatment must be instituted.

(3) Orsanine (Fourneau "270") is the monosodium salt of 4-acetyl-amino–2 hydroxyphenylarsonic acid and is injected intramuscularly or intravenously in a dosage of 20–35 mg. per kilogram of body-weight (up to 2 grams for an adult). Injections are given once a week for 10 to 12 weeks. It produces rapid sterilisation of the peripheral blood but a very limited effect in the meningo-encephalitic stage of the disease.

In *Gambiense* infections, Yorke advocates orsanine or suramin in early cases showing a normal cerebro-spinal fluid, while in later cases with a pathological cerebrospinal fluid a course of tryparsamide is advised after a few preliminary doses of orsanine or suramin have been injected to produce peripheral sterilisation.

In *Rhodesiense* infections, early cases should be treated with suramin. Owing to the relative resistance of this trypanosome to the aromatic arsenicals the results with tryparsamide are much less satisfactory once there is pathological cerebrospinal fluid. The best results under these circumstances are obtained by combined treatment of suramin and tryparsamide. Whatever treatment is adopted, the patient's general health must be built up in every way and intercurrent disease eliminated.

Yorke and his colleagues have recently reported promising results with three trypanocidal diamidines—diamidino stilbene, diamidino diphenoxy propane and diamidino diphenoxy pentane. The dosage is 0·5 mg. per kilogram intravenously or 1·0 mg. per kilogram intramuscularly daily for 8 consecutive days. Rapid peripheral sterilisation occurs, accompanied by great clinical improvement, but the permanent results in patients with a pathological cerebrospinal fluid have not yet been determined. Patients with damage to the optic nerve resulting from the aromatic arsenicals should receive a course of sodium thiosulphate, 10 c.c. of a 20 per cent. solution being given intravenously on alternate days.

SOUTH AMERICAN TRYPANOSOMIASIS (HUMAN).

Synonyms.—Chagas' Disease; Coreotrypanosis; Schizotrypanosomiasis; Brazilian Trypanosomiasis.

Definition.—A disease occurring in parts of South America caused by the trypanosome, *Trypanosoma cruzi* (Chagas, 1909), which affects the muscles, myocardium and brain of man.

Ætiology.—The disease, which has been recorded in several states in Central and South America, affects children and adults of both sexes. *T. cruzi* is a short, broad trypanosome (20 μ long) with a central nucleus and large, ovoid, posteriorly situated kinetoplast. The disease is conveyed to man by certain reduviid bugs, of the genera *Triatoma, Rhodnius* and *Eratyrus*, which have imbibed trypanosomes during their meal of blood. After a developmental cycle of 6–15 days, metacyclic trypanosomes are discharged in the excreta and infect man via lesions in the skin or mucous membranes. In Brazil the chief vector is *Triatoma megista*. The trypanosomes are found in the peripheral blood only for a short time after infection, after which they assume a Leishmanial form within the cells of different organs where they undergo division, and from time to time pass back into the peripheral circulation.

Pathology.—The Leishmanial forms are found especially in the heart and voluntary muscles, also in the thyroid, supra-renals, ovaries, testicle and bone-marrow, where they multiply, causing cell destruction, cellular infiltration, hyperplasia of connective tissue and fibrosis. The central nervous system shows lesions resembling meningo-encephalo-myelitis. The spleen, liver and lymphatic glands are enlarged, and according to Chagas the thyroid is congested and perhaps goitrous.

Symptoms.—Recent work has raised considerable doubt on the validity of many of the thyroidic features (cretinism, myxœdema, etc.) associated with the chronic phases of this disease; Kraus attributes them to endemic goitre with superadded infection with *T. cruzi*. The incubation period is 8 to 10 days. The *acute type* occurs in infants of under 1 year and is characterised by fever with trypanosomes in the blood, enlargement of the spleen and lymph glands, puffiness and œdema of the face and swelling of the thyroid. A proportion of cases develop the picture of encephalo-meningitis and frequently die. The *chronic type* presents a symptomatology which up to the present has not been accurately determined. Five clinical groups have been described: (1) Pseudo-myxœdematous; (2) myxœdematous; (3) cardiac; (4) nervous; (5) chronic with subacute manifestations. Serious disturbance of heart rhythm and neurological manifestations with paralysis probably result from intracellular invasion with *T. cruzi*, but until more accurate information is available eliminating endemic goitre as an ætiological factor little can be said on this phase of the disease. Much chronic heart disease in Brazil, Uruguay and the Argentine is attributed to this cause.

Diagnosis.—In the early acute stages this is made by finding the trypanosomes in the peripheral blood, while occasionally puncture of the voluntary muscles may reveal the Leishmanial forms. Inoculation of guinea-pigs is sometimes successful, and a reliable complement fixation reaction has been

worked out by Machado and others, using extracts of heavily infected heart muscle or cultured trypanosomes.

Prognosis.—The prognosis in acute cases, especially where the central nervous system is involved, is grave.

Treatment.—PROPHYLACTIC.—Destruction of the reduviid bug vectors by chemical means, fumigation, etc., is necessary. Better houses and the use of mosquito nets are important factors in preventing infection.

CURATIVE.—No specific treatment is available, the various drugs successful in African trypanosomiasis being ineffective.

AMŒBIC DYSENTERY

Definition.—Amœbic dysentery results from infection of the colon with *Entamœba histolytica* (Schaudinn, 1903), and is characterised by an afebrile diarrhœa, three or more voluminous stools containing brownish mucus and dark red blood usually being passed daily. Latency is a marked feature, relapses are frequent, while amœbic hepatitis and liver abscess commonly occur.

Ætiology.—This disease is mainly distributed throughout the tropics and sub-tropics, but occasionally occurs in temperate regions. Both sexes and all ages are liable, though it is less common in young children. *E. histolytica* gains access to the body in its cystic form via the mouth in drinking water or food, especially vegetables, contaminated by convalescent or contact carriers, while flies either directly or indirectly may convey the infection. The cysts pass through the stomach safely, after which the walls are dissolved by the pancreatic juice, and the encysted amœbulæ escape and ultimately invade the colonic mucosa. During this stage it is the large, actively motile, tissue-invading amœbæ (20 to 30 μ in diameter), containing ingested red blood cells, which are present in fæcal mucus, but later, as the lesions become quiescent and begin to heal, precystic amœbæ appear in the excreta, originating superficially by binary fission from the more deeply situated tissue-invading forms. Precystic amœbæ are much smaller (7 to 18 μ in diameter), less actively motile, contain no erythrocytes, and must be distinguished from *E. coli*. Different races of amœbæ give rise to cysts of different size containing 1, 2, or 4 nuclei and the characteristic chromidial bodies; they are met with in the fæces of chronic cases and carriers (*vide* p. 264).

Clinical and epidemiological observations have suggested that *E. histolytica* may remain a somewhat inoffensive organism until its pathogenicity is changed by intestinal bacteria. Recent observations on kittens experimentally infected with *E. histolytica* also suggest that in the destructive processes accompanying successful invasion of the intestinal wall, a bacterial as well as an amœbic factor is implicated.

Pathology.—After passing into the glands of the large intestine, the tissue-invading amœbæ multiply, cause toxic degeneration of the lining cells, with blockage of the tubules and the production of slightly raised yellowish nodules (Wenyon). Simultaneously, the inter-glandular connective tissues are invaded, and a toxic, gelatinous necrosis is produced, characterised by an absence of polymorphonuclear leucocytes and occasion-

ally by thrombosis of adjacent mesenteric venules. Small abscesses form which rupture, producing superficial ulcers with undermined edges. The process now extends through the *muscularis mucosæ* to the submucosa, larger bottle-neck ulcers sometimes resulting which are even an inch or more in diameter, and are filled with mucoid material, cell debris and amœbæ. The brown mucus and degenerated blood so characteristic of the amœboid stool originate in such lesions. Following rupture of the primary ulcer others are similarly produced, the maximum involvement being in the cæcum, ascending and sigmoid colon, which may be considerably thickened, and the rectum. Ulceration rarely extends above the ileo-cæcal valve, and even in extensive colonic involvement the intervening mucosa does not generally appear inflamed. Frequently ulcers heal with pigmented scarring of the mucosa and thickening on the peritoneal surface, while in other instances ulceration extends to the muscular layers; adhesions may form, and more rarely sloughing and perforation may lead to a fatal peritonitis. Invasion of the mesenteric venules may produce so-called hepatitis (miliary amœbic abscesses), or solitary or multiple amœbic abscesses of the liver, lung, brain and spleen, the chief pathological feature of which is the presence of tissue-invading amœbæ in their non-fibrous necrotic walls.

Symptoms.—The incubation period varies from 3 weeks to 3 months. The onset is generally insidious, commencing with an afebrile diarrhœa; later, 3 or 4 bulky, fetid stools containing brown mucus and degenerate blood may be passed daily. Occasionally the onset is acute, as in bacillary dysentery, with fever, pain, griping and purging associated with the frequent evacuation of bloody, brown, mucoid stools containing *E. histolytica*; tenesmus occurs if the rectum be involved. As the condition progresses considerable weight is lost, the skin becomes dry and earthy brown, and anorexia, dyspepsia, anæmia of secondary type and a mild neutrophil leucocytosis may develop. Examination often reveals thickening and tenderness of the colon, especially of the cæcum and sigmoid. Sigmoidoscopy generally shows the typical amœbic lesions; in the early stages small superficial yellowish nodules and petechial hæmorrhages may be noted, while later painless yellow ulcers surrounded by zones of hyperæmia appear; scrapings reveal large tissue-invading *E. histolytica*. As a rule the intervening mucosa appears normal, but occasionally a generalised proctitis may be observed which completely clears up under emetine treatment.

Patients from the tropics may give no history of dysentery yet cysts of *E. histolytica* are found in the stools. In this group recurrent abdominal pain is often complained of, and physical examination may reveal localised tenderness over the cæcum, the transverse colon or the sigmoid. Nausea, flatulence and constipation are common, and though a few complain of diarrhœa this is not frequent. Sigmoidoscopy reveals no abnormality. Appendicitis, cholecystitis, gastric or duodenal ulcer, gastritis, or diverticulitis may be suspected; yet treatment with emetine-bismuth-iodide which eliminates the cysts from the fæces is frequently followed by the disappearance of gastro-intestinal symptoms and under such circumstances they can with justification be regarded as of amœbic origin.

Complications.—Post-dysenteric adhesions, retro-colic abscess, intestinal hæmorrhage and perforation with peritonitis may result by an extension of the ulcerative process. The appendix has been found involved

in 7 per cent. of cases. Amœbic hepatitis associated with fever, enlarged tender liver, shoulder pain and leucocytosis, and responding satisfactorily to emetine injections, is not infrequent, while liver abscess, often accompanied by rigors, sweating and involvement of the right base of the lung, may develop. If unrelieved the abscess may burst into the pleura, pericardium, stomach, or large bowel, etc., according to its anatomical situation. More rarely, amœbiasis of the brain, spleen, seminal vesicles and testicle has been recorded. Amœbic ulceration of the skin and subcutaneous tissues may develop around the sinus associated with a liver abscess, a colostomy wound or amœbic lesions involving the anus. Extensive gangrene involving the buttock, perineum and scrotum has been described by the Meleneys.

Course.—The majority of cases run a chronic course, and even without specific treatment the tendency for amœbic dysentery is to improve temporarily, but relapses are frequent and very characteristic of the disease. Latency is marked, and contact carriers are frequently encountered who never suffered from dysentery.

Diagnosis.—The diagnosis is made by finding the large invading-tissue amœbæ in the fresh mucus in acute cases, and the precystic forms or cysts in the fæces of chronic cases and carriers. Four other forms of amœbæ, non-pathogenic to man, occur in the fæces, namely *Entamœba coli*, *Endolimax nana*, *Iodamœba bütschlii* and *Dientamœba fragilis*; these have to be differentiated from the tissue-invading and precystic forms of *E. histolytica* in fæcal examinations. Not infrequently, scrapings obtained during sigmoidoscopy reveal amœbæ despite previous negative reports on the fæces, and in any case of doubt instrumental examination should be carried out. Cytologically fewer pus cells are present in amœbic exudate than in bacillary dysentery, and Charcot-Leyden crystals also not infrequently occur. *E. histolytica* has been successfully cultivated on special media; the amœbæ feed on bacteria, starch granules and red blood cells where available, but the method as yet is hardly applicable to routine work. X-ray examination after a barium enema eliminates many other lesions entering into the differential diagnosis, while in distinguishing malignant disease, chronic bacillary dysentery, ulcerative colitis, bilharzial and balantidial ulcerations of the colon from chronic amœbiasis, sigmoidoscopy, reinforced by laboratory methods of examination, becomes indispensable. A valuable complement fixation reaction has been perfected by Craig using an alcoholic extract of cultures of *E. histolytica* as antigen. In some 90 per cent. of cases yielding a positive reaction *E. histolytica* or cysts were demonstrated.

Prognosis.—With modern methods of treatment uncomplicated cases of amœbic dysentery almost invariably recover, and a large proportion are permanently curable. The prognosis is naturally more serious where complications like liver abscess exist, and here one or more aspirations generally suffice, unless secondary bacterial infection has ensued. Colonic perforation with peritonitis is frequently, and brain abscess invariably, fatal.

Treatment.—PROPHYLACTIC.—As the disease is acquired by fæcal contamination of food and water, it becomes important to ascertain that personal servants and cooks are not carriers. Food should be protected from flies, and measures should be taken to avoid contamination of water and uncooked vegetables.

CURATIVE.—Long before amœbic and bacillary dysentery were differenti-

ated, ipecacuanha was recognised as effective in certain cases. Later, one of its alkaloids, emetine, was proved of great value by Rogers in India, and more recently other preparations, including bismuth-emetine-iodide, emetine periodide and auremetine, have been introduced. The toxic properties of emetine and its compounds should never be forgotten, and during intensive treatment it is essential that the patient be kept in bed on a simple, non-irritating, low-residue diet, milk being citrated to avoid clot formation.

Emetine is indicated where the tissue-invading amœbæ have produced visceral complications like hepatitis and amœbic abscess, and also during the initial attack. Emetine hydrochloride is injected intramuscularly or subcutaneously in 1 grain doses daily for a period not exceeding 10 days in a normal-sized adult, but the dose should be decreased in debilitated persons and those of low body weight. Children receive a dose proportional to age, for those under 3 years never exceeding $\frac{1}{6}$ grain, and for those under 6 years $\frac{1}{3}$ grain per day. Emetine is a muscle poison and, owing to the cumulative action of the drug, treatment should not be repeated within 2 to 3 weeks. Diarrhœa is commonly induced, and toxic symptoms include asthenia, cardio-vascular depression, low blood pressure, tachycardia, extra systoles, extreme muscular weakness causing paresis or even paralysis of the limbs; death may occur from cardiac failure, with paroxysmal tachycardia or auricular fibrillation.

Emetine-Bismuth-Iodide (E.B.I.).—This drug is preferable to emetine hydrochloride in chronic cases and carriers showing cysts, but it has the disadvantage of causing considerable nausea and vomiting, and is best given on an empty stomach late at night in gelatine capsules, 4 hours after the last feed. Phenobarbitone (gr. 1) or tincture of opium (min. 15) is given half an hour previously when necessary. Nightly doses, of grs. 3, are given for 10 to 12 doses, the total course varying from 30 to 36 grains. During the course patients often lose weight at the rate of $\frac{1}{2}$ lb. daily, and usually there is a definite fall in blood pressure and slowing of the pulse. Emetine periodide (E.P.I.), in capsules in a dosage up to grs. 6 daily, for 10 days, is also effective; it tends to cause less vomiting than E.B.I.

Carbarsone, which is a pentavalent arsenical, is an effective amœbicide for both vegetative forms and cysts, and is less toxic than stovarsol, which it is largely superseding. It does not, however, cure hepatitis or amœbic abscess. The drug is administered in pulvules containing 0·25 g., one pulvule being given twice daily after food for 10 days. Carbarsone can be used in ambulatory cases on a normal diet, and from these points of view possesses distinct advantages over the more toxic emetine preparations.

Chiniofon.—Chiniofon (yatren) is an iodine-oxyquinolin-sulphonic acid combination, and can be given by the mouth or as a retention enema. The adult dose is $\frac{1}{2}$ to 1 g. of the powder in gelatine capsules thrice daily for 10 days, repeated if necessary after a week's interval. If given *per rectum* the bowel should be first washed out with 1 pint of 2 per cent. sodium bicarbonate solution to remove mucus, and an hour later 200 c.c. of a 2·5 per cent. solution of chiniofon is run into the rectum and retained for as long as 8 hours if possible.

Combined treatment.—The most favoured combination in cyst cases consists of retention enemas of chiniofon in the morning and E.B.I. at night, or a course of the double iodide followed by carbarsone. During convales-

cence a non-irritating low-residue diet reinforced with vitamins is advisable, and alcohol should be avoided; meat is allowed once daily. The results of modern therapy are as a rule satisfactory, though relapses may occur, necessitating further courses of treatment, no matter what drug is used.

Surgical complications.—Emetine should always be given in hepatitis and also in amœbic abscess before needling, to relieve congestion (Rogers) Open operation and drainage should be confined to abscesses secondarily infected with bacteria. Amœbic appendicitis is only part of an amœbic typhlitis, and responds satisfactorily to emetine. Perforation is almost invariably fatal, unless immediately operated on.

For Bacillary Dysentery, see p. 118.

CILIATE DYSENTERY

Definition.—An ulcerative condition of the colon caused by *Balantidium coli* (Malmstren, 1857).

Ætiology.—Human infections generally occur amongst those having occupational contact with pigs, which also harbour this ciliate; cases have been reported from Europe, America, Asia and Africa. The ciliate is egg-shaped, 50 to 80 μ long by 30 to 55 μ broad; large and smaller forms are described. At its anterior end is the peristome; its interior contains a sausage-shaped macronucleus, a micronucleus and vacuoles, while externally the whole body is covered with longitudinal rows of cilia. Encysted forms, 50 to 60 μ long, also occur in the fæces. As healthy carriers are frequently encountered, it is not improbable that there is some secondary bacterial or other factor which determines the pathogenicity of *Balantidium coli.*

Pathology.—The colon, and more rarely the ileum, show ulcers distinguishable from amœbic lesions only by the demonstration of *Balantidium coli*, which is found both in the cavity of the ulcer and the surrounding submucosa; it may also invade adjacent lymph glands, but not the liver.

Symptoms.—In many cases the disease remains latent and symptoms are absent. In others the onset is insidious, with loose motions, later followed by sanguineous, mucoid stools typical of chronic dysentery; anæmia may develop. Intestinal perforation has been reported, but never liver abscess.

Prognosis.—The mortality rate including latent cases is about 7 per cent. (Walker), but in those showing active dysentery it may reach 29 per cent. (Strong).

Diagnosis.—Sigmoidoscopy may show colonic ulcers, but diagnosis is dependent on demonstrating *Balantidium coli* or its cysts in the excreta, or in scrapings from the ulcers themselves.

Treatment.—Most of the remedies tried have not been satisfactory. Aguilar advises restricting carbohydrates and increasing protein and fresh vegetables. Stovarsol in doses of 0·25 g. (4 grains) twice daily after meals for one week or carbarsone in a similar dosage for 10 days holds out some prospect of cure. Methylene-blue by the mouth and as an enema (1–3000) has been advocated and Walker considers silver protein of value. High colonic

irrigation with solutions of iodine, quinine and silver nitrate have been recommended, but owing to the spontaneous disappearance of the ciliates from time to time the value of different remedies is difficult to assess.

FLAGELLATE DIARRHŒA

There are three common intestinal flagellates of man, *Giardia intestinalis* (Lambl, 1859) which inhabits the upper intestine, *Trichomonas hominis* (Lavaine, 1860) and *Chilomastix mesnili* (Wenyon, 1910) found in the cæcum and colon. Considerable controversy has arisen regarding their pathogenicity and, though admittedly they are more common in cases of diarrhœa than in healthy individuals, nowhere do they actually invade the intestinal mucosa. Encysted flagellates are frequently found in normal stools, and Dobell has pointed out that the free flagellate forms which are naturally adapted to a fluid medium only appear when the stools become liquid or loose. From a clinical viewpoint, however, *Giardia intestinalis* has some claim to pathogenicity.

Giardia Intestinalis (Lambl. 1859)

Synonyms.—*Lamblia intestinalis; Giardia lamblia.*

Ætiology.—This parasite inhabits the jejunum and duodenum and occasionally reaches the bile ducts. It is a pear-shaped flagellate (10 to 18 μ long $\times$ 5 to 10 μ broad), possessing a concave sucker on its ventral surface, and in the encysted form may persist for many years in the fæces. As with certain other flagellates decreased or absent secretion of hydrochloric acid in the stomach appears to predispose to infection, and after gastro-jejunostomy we have found them in aspirated gastric juice.

Pathology.—In animals the glands of the small intestine may be found packed with giardia, and though they never cause ulceration or hæmorrhage, hyperinfection may, as Wenyon points out, lead to surface irritation. It is probable that in this fashion catarrhal enteritis results.

Symptoms.—Though encysted forms are often found in the fæces in healthy individuals, periodic attacks of diarrhœa may occur associated with the passage of large quantities of clear mucus or ochre-yellow stools in which enormous numbers of free flagellates occur. The demonstration of these flagellates in the bile by means of a duodenal tube does not constitute evidence of invasion of the biliary passages and gall bladder, and the present tendency to attribute all manner of symptoms to Giardia infection is to be deprecated.

Prognosis.—This is good; fatal cases in man being unknown.

Treatment.—Mepacrine hydrochloride (atebrin) in a dosage of 0·1 g. t.d.s., p.c. for a period of 5 days eradicates Giardia infection completely.

G. Carmichael Low.
N. Hamilton Fairley.

F. RICKETTSIA DISEASES

INTRODUCTION

Rickettsia bodies are small, non-motile, Gram-negative bodies usually less than 0·5 μ in diameter. They are more or less pleomorphic, and are found in both host tissues and arthropod vectors. They can only be cultivated in the presence of living tissue, and are mainly located within mesothelial cells, either in the cytoplasm or nucleus. Ricketts (1909) first noted these bodies in guinea-pigs and monkeys with Rocky Mountain spotted fever, and since then several varieties affecting man have been described. Thus, classical typhus and Brill's disease are caused by *Rickettsia prowazeki*; Rocky Mountain spotted fever by *R. rickettsi*; murine typhus by *R. mooseri*; tsutsugamushi disease by *R. orientalis*; trench fever by *R. quintana*; and "Q" fever by *R. burneti*.

An ever-increasing number of typhus-like fevers is being described in different parts of the world caused by rickettsias, and carried by arthropods like lice, fleas, ticks and mites in which rodents play an important rôle as reservoirs of infection. They have been classified on a geographical basis, according to their insect vectors, or in terms of their agglutination reaction with X2, X19 and XK strains of *Bacillus proteus*.

The ætiological relationship, if any, between the rickettsias and the various strains of *B. proteus* which have from time to time been isolated from typhus cases and are agglutinated in different fashions by sera derived from typhus-like patients, remains undetermined. It is probable that there is no ætiological relationship, the Weil-Felix reaction being merely an example of heterologous agglutination.

The Weil-Felix Reaction.—Suspensions of X19, X2 and XK strains of *B. proteus* are now employed in this agglutination test. Originally the reaction was carried out with living suspension, but now the alcoholic method, which destroys the flagella and preserves solutions of "O" antigen for six months, is used. In general it may be said that X19 is the main antigen for louse and flea-borne typhus, XK for mite typhus, while the sera from patients with tick typhus, as a rule, react in low titre to all three strains. The serum from patients with "Q" fever, however, does not react with any of these strains. Felix thinks the strain forming the main antigen for the tick-borne group has yet to be discovered.

For clinical purposes, a rising titre exceeding 1 in 100 may be taken as diagnostic. The test should be made as early as possible in order to estimate subsequent rises in titre. A significant rise rarely occurs during the first week, but it is generally well established by the tenth day. The maximum titre of 1/1000 to 1/10,000 may not be attained until convalescence, after which the reaction weakens and gradually becomes negative.

Though the test is of little diagnostic utility during the first week and may occasionally fail to reveal agglutinin in significant titre in severe cases until convalescence is reached, it is a reliable test of very real clinical value. Non-specific stimulation of the proteus "O" agglutinin in other bacterial infections of man rarely occurs.

Megaw has suggested the classification of typhus and the typhus-like fevers in terms of the host vector, and this will be adopted as being the most suitable classification for present purposes.

FLEA TYPHUS

Synonyms.—Murine Typhus; Hone's Disease; Ship Typhus; Typhus Murin; Endemic Typhus; Urban Tropical Typhus; Shop Typhus; X19 Tropical Typhus.

Definition.—A mild typhus-like fever, with a world-wide distribution, generally occurring in non-epidemic form, and caused by *Rickettsia mooseri*. It is conveyed to man by the rat flea, *Xenopsylla cheopis*, from infected rats or other rodents which are natural reservoirs of the disease.

Ætiology.—That some connection might exist between the handling of grain and rats was first suggested by Hone (1922) in South Australia. Maxcy (1926) suggested that the sporadic typhus-like fever of North America was conveyed by fleas from infected rats to man, and Dyer and others (1931) found that fleas collected from rats and injected into guinea-pigs produced the disease. Nicolle (1933) described the same disease under the title "*Typhus murin*" in sailors in French war-ships in the Mediterranean.

R. mooseri has a similar morphology to *R. prowazeki*, which causes epidemic typhus, and the Weil-Felix reaction with X19 strains is similarly positive in the two diseases. The two rickettsias are differentiated by the fact that *R. mooseri* gives a positive scrotal reaction when inoculated into guinea-pigs. However, it has recently been found in Mexico that a strain which at first gave a negative scrotal reaction, later gave a positive reaction after repeated passage through these animals. *R. prowazeki* and *R. mooseri* may therefore be identical and epidemic typhus have a murine origin, the strain being modified by repeated passage through man. Similarly, Brill's disease was at one time regarded as a variety of flea-borne murine typhus, but Zinsser has proved that in America it is really a mild recrudescence of louse-borne typhus occurring in carrier immigrants who had suffered from epidemic typhus contracted in Europe as long as twenty years previously.

Pathology.—Patients rarely die with flea-borne typhus, but there is no evidence that the lesions differ from those of mild epidemic typhus. In infected animals the lesions are very similar to those caused by *R. prowazeki* except in the guinea-pig, where the scrotum becomes dusky red, swollen and inflamed, the tunica is thickened and may show hæmorrhage and exudate, and the testicle is swollen. This lasts some four days, is known as the Neill-Mooser reaction, and is feeble and inconstant with *R. prowazeki*.

Symptoms.—The incubation period is generally 8 to 14 days, but exceptionally it may be 3 weeks. The onset is generally rapid, and the clinical picture similar to that of mild epidemic typhus, the temperature rising to 102° to 103° F. and persisting for about a week; shivery feelings, headache and pains in the back, and cough may occur. The face becomes flushed and the conjunctivæ are somewhat injected, but not to the degree seen in classical

typhus. A macular or papular rash may appear about the fourth or fifth day, but even in Europeans it is faint, while in dark-skinned races it may not be visible at all. Complications are generally absent, and convalescence uninterrupted and rapid.

Diagnosis.—A history of association with rats known to harbour the disease, the mild nature of the fever, and the strongly positive Weil-Felix reaction to X19 strain of *B. proteus* and negative response to XK will enable a diagnosis to be made in most cases. Though the malady cannot be differentiated from Brill's disease on these grounds, inoculation of rats which are very susceptible to flea typhus will settle the question, for rats are resistant to the virus of Brill's disease.

Prognosis.—The mortality ranges from 1 to 4 per cent., except in cases of the Mexican *Tabardillo*, which may be as fatal as classical typhus. Mooser holds that Tabardillo can be transmitted by lice as well as fleas, so its status is problematical.

Treatment.—Prophylaxis consists essentially of rat destruction and the avoidance of contact with rats. Vaccines of formolised suspension of Mexican murine virus from injected guinea-pigs have been employed by Zinsser and Castenada, with promising results. Experimentally, immunity is good against the murine strains, but only partial against classical typhus. Nicolle and Laigret's vaccine prepared from the brains of guinea-pigs or rats injected with the Tunis strain of murine typhus is also used to immunise man against both murine and epidemic typhus.

No specific curative treatment is known. The measures outlined in the treatment of louse-borne typhus are applicable.

MITE TYPHUS

A number of varieties of mite typhus has been described due to the one virus, *R. orientalis* or *R. tsutsugamushi*. For many years the scrub or rural form of tropical typhus described by Fletcher in the Federated Malay States, and transmitted by *Trombicula deliensis* from infected rats, was regarded as differing from tsutsugamushi disease inasmuch as there was supposed to be an absence of a primary lesion, lymphangitis and bubo. Lewthwaite and Savoor (1940) have now identified the two viruses, and shown that in rural typhus there may be either a persisting necrotic ulcer or a fleeting papular lesion which often escapes recognition by its disappearance before the onset of other symptoms. The local lesion is common in the white-skinned European and rare in the dark-skinned Tamil. In Sumatra the pseudo-typhus of Deli, transmitted by *Trombicula deliensis* from infected rats, is also identical with tsutsugamushi; though the mortality is only 5 per cent. in the indigenous population, it may be as high as 40 per cent. in Europeans. Similarly, Mossman or coastal fever of Queensland is a mild type of mite-typhus conveyed from rats by the mite—*Lælaps australiensis*; sugar-cane workers are especially affected. Lymphangitis and lymphadenitis are common, but the primary lesion, with its black central eschar and surrounding red areola, has been noted only occasionally.

Tsutsugamushi or Japanese river fever will be described as the type for mite typhus.

Tsutsugamushi Disease

Synonyms.—Japanese River Fever; Pseudo-Typhoid of Deli; Mossman or Queensland Coastal Fever; Rural or Scrub Tropical Typhus; Sumatra Mite Fever.

Definition.—An acute febrile disease of the typhus group often associated with a local ulcer, lymphangitis, adenitis, and an erythematous eruption. It is caused by *R. orientalis*, and in Japan is transmitted from infected field mice by the bite of a larval mite—*Trombicula akamushi*.

Ætiology.—The disease occurs commonly in July and August amongst harvesters handling the hemp crop in the Island of Nippon, Japan. It is also encountered in Formosa, Korea, China, Malaya, the Philippines and Sumatra. The disease is primarily an epizootic in mice, rats and possibly other rodents. In Japan the field vole, *Microtus montebelli*, is the reservoir host. Trombiculid mites pass through four stages in their development, but it is only the larval stage of *T. akamushi* or *T. deliensis* which can transmit infection to man.

Pathology.—Hæmorrhages into the serous membranes, splenomegaly, pulmonary congestion, adenitis, especially involving the thoracic and mesenteric lymph glands, cloudy swelling of the kidneys and liver, and myocardial degeneration may be found at autopsy. A local necrotic ulcer, with adenitis, is often present. Rickettsial bodies are generally demonstrable in the vascular lesions of the brain; they are common in the cytoplasm of the endothelial cells of the capillaries and smaller arterioles.

Symptoms.—In the Japanese form of the disease a small papule generally appears 2 or 3 days after attachment of the larval mite to the skin, especially that of the axillæ, genitals, or limbs. The papule may subside, or become pustular and form a necrotic ulcer some 6 to 8 mm. in diameter, surrounded by a red areola. Within the incubation period the lymph glands draining the bitten area become tender, painful and enlarged, and generally there is an associated lymphangitis.

Fever commences some 5 to 14 days after the bite, and the onset is generally sudden, with shivery feelings or rigor, headache, giddiness, malaise, and perhaps vomiting and pains in the chest. Sometimes there is a period of malaise and mild headache for 2 or 3 days prior to the onset of fever. Injected conjunctivæ, a furred cracked tongue and constipation are common, while hyperæsthesia, deafness, sweating, cough and signs of bronchial irritation may develop. Diarrhœa occurs in some cases. About the seventh day a dark macular rash appears on the face, later spreading to the limbs and trunk; it may be papular, but never becomes petechial. It lasts about 5 days, and, unlike the rash of Rocky Mountain spotted fever, does not tend to involve the hands and feet. The spleen is demonstrably enlarged in over half the cases, and generalised slight enlargement of the axillary, cervical and groin glands is not infrequent.

During the second week the fever is higher (103°–104° F.), prostration and mental symptoms such as insomnia are more marked, and should delirium or coma develop the outlook is grave. The blood pressure is low, there is considerable loss of weight, and the knee jerks are often absent. Leucopænia is the rule, and a mild grade of albuminuria common. The duration of the fever is from 2 to 3 weeks, the temperature reaching its maximum about

the fifth day, and falling by lysis or by crisis after disappearance of the eruption.

Abortive cases with adenitis and transient fever sometimes occur, and patients may remember removing the larval tick from the place where the ulcer subsequently developed.

Complications.—These include acute bronchitis, broncho-pneumonia, parotitis, phlebitis, and myocardial degeneration with heart failure.

Diagnosis.—Typhoid and para-typhoid fevers, and leptospirosis may simulate typhus. The presence of a necrotic ulcer, with adenitis, followed by fever, should enable a clinical diagnosis to be made in patients whose occupation is liable to bring them in contact with larval mites. Where the local lesion and adenitis are absent or inconspicuous a Weil-Felix reaction, positive to OXK and negative to OX2 and OX19 strains, would clinch the diagnosis. In Malaya, urban typhus has to be differentiated; here the Weil-Felix is positive with OX19 type, while male guinea-pigs inoculated with the blood taken early in the disease produce scrotal swelling, which does not occur in tsutsugamushi.

Prognosis.—The development during the second or third week of delirium and coma, myocardial failure, or broncho-pneumonia is an unfavourable feature. In Japan the mortality rate is about 30 per cent., varying from 20 to 50 per cent. in different reports. In Malaya it is now about 15 per cent.

Treatment.—Prevention consists essentially in measures designed to avoid contact with larval mites. Anigstein's vaccine consists of formolised saline emulsions of blood or tissue from patients or animals infected with Malayan tsutsugamushi. Some 200 and 400 million organisms are injected at weekly intervals, but no definite statement regarding its value can yet be made.

Curative treatment follows the lines outlined in classical typhus. No specific cure is available.

TICK TYPHUS

Several strains of virus are probably concerned in the causation of tick-borne typhus. The reservoir hosts are rodents and dogs, and, as Megaw points out, the epidemiological and clinical features of the different tick-borne diseases have sufficient in common to justify their being dealt with together. The agglutination reaction to all the strains OX2, OX19 and OXK tends to be of low titre, and serum from patients with "Q" fever does not react with any known strain of *B. proteus*.

Spotted fever of the Rocky Mountains was recognised long before any other types, and includes the milder Eastern type of spotted fever and possibly the more severe Sao Paulo fever. The latter is conveyed from rats to man by the horse tick, *Amblyomma cajennense*, and has a mortality rate of 70 per cent.; it closely resembles the graver cases of Rocky Mountain spotted fever, and its virus also immunises animals against the latter disease.

Fièvre Boutonneuse and the tick-bite fevers of Kenya and South Africa have much in common. Unlike Rocky Mountain spotted fever there is usually a sore at the site of the tick bite, and in experimental animals there is cross immunisation between boutonneuse and the South African virus.

Fièvre Boutonneuse occurs in most countries bordering on the Mediterranean, and is probably conveyed from dogs by the dog-tick, *Rhipicephalus sanguineus*. Clinically, it resembles the mild form of Rocky Mountain spotted fever, but the presence of a local necrotic ulcer of dark red areola, the more nodular nature of the rash, and the low mortality rate of 1 to 2 per cent. are outstanding differences. Furthermore, the virus of *boutonneuse* fever does not, as a rule, produce scrotal swelling in guinea-pigs, nor does it give cross protection against Rocky Mountain spotted fever virus.

"Q" fever, which is caused by *R. burneti*, gives rise to a mild typhus-like fever in man and inoculated guinea-pigs. In mice inoculated with human blood collected during the fever, *Rickettsiæ* are found in the spleen and suspensions obtained from mouse tissue are agglutinated in high titre by human serum from infected cases. The Weil-Felix reaction with the serum, however, is negative to all the known strains of *B. proteus*. In Australia the bandicott is a natural reservoir of infection and infected ticks of the species, *Hæmaphysalis humerosa*, have recently been collected from these animals. "Q" virus has also been found in *Dermacentor andersoni* by Dyer, in Montana, where the inhabitants of certain villages acquire the disease. Guinea-pigs, injected with a vaccine which will protect against Rocky Mountain spotted fever, are not protected against "Q" fever.

Rocky Mountain Tick Typhus

Synonyms.—Rocky Mountain Spotted Fever; Spotted Fever of Eastern Type.

Definition.—A non-epidemic severe typhus-like fever long recognised in the Rocky Mountains. It is generally unassociated with a local lesion or adenitis, and is transmitted to man from infected rodents by the bites of several different species of ticks including *Dermacentor andersoni*. The disease may have a high mortality.

Ætiology.—The disease primarily affects wild rodents, and, as shown by Wilson and Chowning (1904), is conveyed to man by ticks. Larval and nymph ticks transmit the virus from rodent to rodent, but human beings are usually infected by adult ticks of the species *Dermacentor andersoni*, *D. variabilis* and *Hæmophysalis leporispalustris*. Infected ticks transmit the infection to their offspring. It is said that a single infected tick may contain 15,000 infecting doses. The causal organism, *rickettsia rickettsi*, was described by Ricketts (1909) in the blood of guinea-pigs and monkeys infected with Rocky Mountain spotted fever. *R. rickettsi* produces a well-marked scrotal reaction in inoculated guinea-pigs, and can be demonstrated in the fluid exudate of the tunica vaginalis prior to generalised dissemination in the blood stream.

Most infections are found in people whose occupations brings them in contact with ticks. Where town dwellers are affected, dogs probably are implicated. Most cases occur in April and May in the Rocky Mountains, and in the summer in the Eastern States of the U.S.A.

Pathology.—Pathological changes include petechial hæmorrhages involving the skin and serous membrane, enlargement of the spleen and lymph glands, and degenerative changes in the kidneys, liver and heart. Proliferation of the vascular endothelium often leads to thrombosis and possible secondary gangrene. *R. rickettsi* is found within the nuclei of mesothelial

cells, not in the cytoplasm as with *R. prowazeki*. Vessels of the brain as well as the viscera are affected.

Symptoms.—The incubation period is from 3 to 14 days. A local lesion at the site of the tick bite with adenitis is rare. The onset is generally sudden, with headache, lumbar and generalised pains, and sometimes sweating, rigors, anorexia, malaise and vomiting. The tongue is coated, the conjunctivæ injected, and the temperature rises rapidly to 103° or 104° F., the maximum being reached in 3 or 4 days time. By then, in severe cases, the face is becoming dusky and a rose-red macular or papular rash appears. Later the macules turn darker, cease to fade on pressure, and may become obviously hæmorrhagic. The rash is first seen on the wrists and ankles ; later, it extends to the body generally, including the palms, soles and face. The fever lasts 2 or 3 weeks, and falls by rapid lysis. Constipation, restlessness and insomnia are usual, while severe cases may show stupor, delirium, coma and convulsions. Enlargement of the spleen is common, and may be an early feature. Later, there may be jaundice and hepatomegaly, and where the central nervous system is involved altered reflexes, and Babinski's and Kernig's signs may be elicited. A leucocytosis of 15,000 to 20,000 per c.mm. is not infrequent, but leucopenia may occur ; the lymphocytes are increased. Albuminuria is the rule in severe cases.

Apart from this average classical type there are abortive cases, with transient fever lasting 3 or 4 days ; ambulatory cases, with scanty rash and fever lasting 7 to 10 days ; and fulminating cases, which die with marked nervous symptoms either before the rash has appeared or with a hæmorrhagic type of eruption.

Complications and Sequelæ.—Convalescence tends to be prolonged, especially in severe cases. Bronchitis, pneumonia, femoral and other thromboses, parotitis, hæmaturia, epistaxis and malæna may complicate the picture. Iritis, nephritis, otitis media and gangrene of the fingers, toes, tonsils, prepuce and scrotum have been recorded.

Diagnosis.—The differential diagnosis includes epidemic and other forms of typhus, typhoid and the para-typhoid fevers, and cerebrospinal meningitis. Geographical considerations, the character of the rash, and the serological and other laboratory findings are of importance. Positive serological reaction may be obtained with OXK, OX2 or OX19 strains of *B. proteus*, but often reactions in significant titre are not evident until the fever is subsiding ; a steadily rising titre is, of course, diagnostic.

Prognosis.—The mortality rate varies from 5 to 50 per cent. in different geographical areas. Apart from fulminating cases, the onset of profound nervous symptoms, severe cardiovascular depression and a hæmorrhagic rash indicate a severe infection and imply a correspondingly grave prognosis.

Treatment.—In endemic areas tick-proof clothing should be worn and the body carefully searched for ticks ; iodine should be applied locally after their removal. A prophylactic vaccine has been prepared by Spencer and Parker in the form of a carbolised emulsion of heavily infected ticks. It gives satisfactory protection against both Rocky Mountain and Sao Paolo fevers. Medicinal treatment follows the lines outlined for louse typhus. No specific therapy is available.

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LOUSE-BORNE TYPHUS FEVER

Synonyms.—Typhus Exanthematicus; Epidemic Typhus; Jail, Camp or Famine Fever.

Definition.—A highly contagious fever characterised by sudden onset, severe prostration, a characteristic rash, and termination by crisis about the fourteenth day. The infection is conveyed by body lice, perhaps through their bites, but more probably by cutaneous inoculation of their excreta by scratching. Head lice are also believed to be possible vectors. The disease is one of a group transmitted by lice, ticks, rat fleas, and larval mites.

Ætiology.—Most of the factors which conduce to the spread of typhus operate by their influence on the parasites by which the disease is conveyed. The lice pass directly from the sick to the healthy, or indirectly by means of garments, bedclothes and mattresses. Lice which have fed on infected persons can, after 8 or 10 days, transmit the disease and remain infective for the rest of their lives. Crowding of the sick together in dark, ill-ventilated rooms greatly favours the possibility of infection, whilst in the presence of free ventilation very close contact is necessary before the disease is contracted.

Exhalations from the lungs, emanations from the skin, and the excreta are believed to be capable of conveying the infection, and the bodies of those dead of the disease have been supposed to retain their infective powers until decomposition sets in. These beliefs, in view of the part played by lice, obviously need revision. Typhus carriers are always verminous persons. Clothes which harbour infected lice have often transmitted the disease to distant parts. The excreta of lice are also infective for a day or two, and may possibly be air-borne as dust and inhaled.

Typhus is a disease of cold and temperate climates; it occurs in those months of the year when confinement within doors and overcrowding are most likely. In hot climates frequent bathing, scantiness of attire, free action of the skin, and the lethal effect of high temperatures on lice are all factors which prevent its spread.

Predisposing causes are verminous infestation, overcrowding, and destitution. Epidemics are particularly liable to occur in times of war and famine. Typhus is rare in England, but endemic foci still persist in Irish and perhaps some Scottish towns. In Russia and Eastern Europe the disease is very prevalent, and a great epidemic ravaged Serbia in the early days of the War of 1914–1918. It has also been recognised in Canada, New York (Brill's disease), Mexico (where it is known as Tabardillo), Manchuria and other places.

Typhus attacks persons of all ages and both sexes. The greatest mortality is in those above middle age (at 50 years it may be 50 per cent., and between 75 and 80 years, nearly 85 per cent.); attacks in the young are less severe and very much less fatal. In populations where the disease is endemic attacks may be very mild, but when introduced into other places the type may prove excessively severe. In Brill's disease the mortality is less than 1 per cent.

Pathology.—The post-mortem appearances are those common to many acute infections and are not in themselves characteristic. Hypostatic congestion of the lungs and catarrh of the air-passages are common. The

absence of characteristic lesions in the bowel affords a distinction from typhoid fever. Beyond occasional meningeal congestion the central nervous system appears normal. Zenker's degeneration of muscle may be found.

Microscopical examination reveals the presence of nodules of endothelial proliferation in the small arteries of the skin and of the brain, also in those of the muscles and viscera.

Prime importance is attached to the presence of Rickettsia bodies (*Rickettsia prowazeki*). These are small and pleomorphic, not more than 0·3 by 0·4 μ in size. They are Gram-negative and stain by Giemsa's stain. Rickettsia bodies are found sparingly in the blood taken from a patient on the seventh to the twelfth day of the disease, and also in infected lice and their excreta. Similar bodies have been described in the vascular lesions and in the endothelial cells of the liver.

An agglutinative phenomenon which goes by the name of the Weil-Felix reaction affords a valuable means of recognising the disease. The reaction is named after two observers who discovered in the urine of patients suffering from typhus an organism of the Proteus group which is agglutinated in high dilution by the serum of those infected. The strain of Proteus concerned is known as the O variety of X19, and agglutinations have been obtained with dilutions of serum up to 1 in 30,000. Reactions in controls, if occurring at all, do not take place in dilutions exceeding 1 in 50 or, at most, 1 in 100. In half the cases of typhus the reaction is found by the fifth day, and in practically all by the tenth day, after which the titre rises for about a week. There is, however, no proof that Proteus X19 is capable of producing typhus, nor does it confer immunity to the disease.

The Wassermann reaction is almost always positive in typhus if the blood is examined before the crisis, but becomes negative again in convalescence (Bauer). In inoculated persons the titre of the Widal reaction for typhoid rises steadily.

Symptoms.—The incubation period in most cases is about 12 days. Eight to 10 days is a common interval when the disease is produced experimentally.

The onset is generally sudden, and ingravescence much more rapid than in typhoid. Distressing headache, giddiness, shivering or rigor, and frequently vomiting mark the accession. Pains in the limbs and back may be severe, and blunting of the mental faculties with great muscular prostration is evident from the first. The tongue is large and coated, but soon becomes brown, and finally may be dark and shrivelled. Appetite is lost, thirst is great, the bowels are generally constipated, and the urine high coloured and scanty, rich in urea and uric acid, but deficient in chlorides. Albumin may appear later and the diazo-reaction is very constant. The face is flushed or dusky, the features swollen and the appearance apathetic. The conjunctivæ are injected and the pupils contracted. Epistaxis may occur. The spleen may be palpable, but the abdomen is not distended. Even early in the disease, especially in alcoholic subjects, marked delirium, mania or stupor may be evident. Insomnia is present, or bad dreams disturb the rest. Tinnitus occurs, or deafness of nervous origin. The tongue is tremulous, and the gait tottering; if the patient has not already taken to his bed he usually does so by the third day of illness. The temperature may reach 104° F. by the first night; the acme, however, is generally attained on the third or fourth day.

Associated with the fever is a rapid soft pulse. Marked rapidity of the respirations is also noticeable and may lead to an erroneous diagnosis of pneumonia.

The fever (Fig. 5), which during the invasive stage may show remissions, after attaining its maximum, which may be as high as 105° or 106° F., shows little or no daily variation. At the end of the first week or a day or two later a sudden remission, which is rarely lasting, may occur (pseudo-crisis); from this period, however, the fever generally shows some abatement and terminates by a sudden or somewhat gradual crisis on the thirteenth to the seventeenth day of the disease.

The rash appears on the fourth or fifth day, first on the axillary folds, the sides of the chest and the abdomen. It avoids the face, which is merely

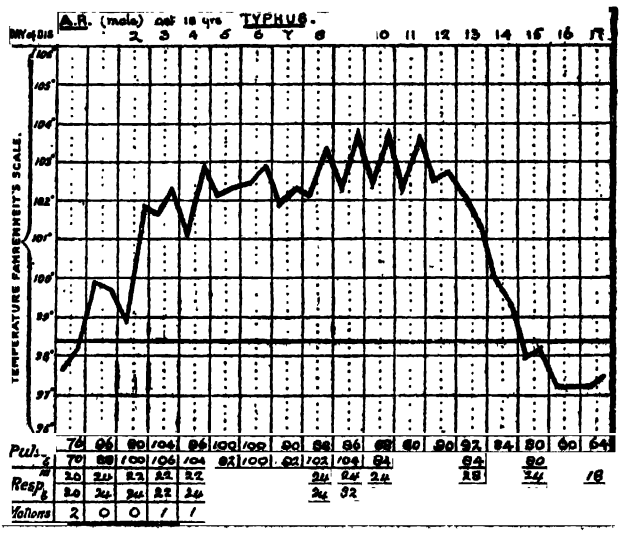


FIG. 5.—Typhus fever. Illustrating a somewhat gradual onset and abrupt termination by crisis.

flushed and congested, does not appear on the palate, and rarely on the palms and soles, but with these exceptions it may become general all over the body, although it is most profuse on the trunk, especially on the back. The three elements of which it consists are macules, papules and petechiæ. The macular elements of the rash generally appear before the papular elements and are much larger and blotchy; they appear to be in the skin rather than on it, hence the term subcuticular mottling which is applied to the appearance produced. These macules are best seen about the shoulders and axillæ, but often extend to the back and front of the chest, the thighs and arms. The papules resemble the rose spots of typhoid. At first they fade on pressure; later they may show petechiæ, becoming dull red or brown and indelible. They do not appear in successive crops. Purple petechiæ which resemble flea-bites and sometimes also purpuric patches are less constant. The latter indicate a severe infection, the hæmorrhagic character of which may be

confirmed by the occurrence of hæmatemesis, melæna or hæmaturia. Profusion of the rash in typhus is an indication of a severe attack. In mild cases the eruption is scanty, and in children it is very evanescent.

A leucopenia in the early stages is followed by anæmia and leucocytosis, in which polynuclears or monocytes may predominate.

The cerebro-spinal fluid may show a slight lymphocytosis, and also give a low positive Weil-Felix reaction. The globulin is increased.

Towards the end of the second week the patient in a grave case may enter on the second stage of his disease. There is less complaint of headache; delirium, if present, is less violent and of a muttering rather than maniacal type. Prostration may be extreme and sleeplessness pronounced. The face is dusky, sordes accumulate on the teeth, and a curious mousy odour emanates from the patient. Day by day the nervous depression increases and the patient lies helpless on his back with a tendency to sink down in the bed. The pupils are pin-hole, the eyes half open and fixed (*coma vigil*). Although deaf and unnoticing, he mutters incoherently and can be roused with some difficulty. Tremors of the tongue and tendons, and picking at the bedclothes are apt to occur. The pulse quickens and may reach 130 per minute. It is dicrotic or almost imperceptible. The heart's impulse is feeble and the first sound faint or inaudible. The blood pressure falls steadily. Acceleration of respiration is more than ever pronounced, 40 per minute not being unusual; the breathing is shallow, and hypostatic congestion of the lung bases occurs. The urine may be retained or passed into the bed, as also the fæces. Bed-sores are apt to form. The patient may pass away in coma, or hyperpyrexia may precede death, which may occur in the second week, usually it is said on the eleventh day.

On the fourteenth day, sometimes a little earlier, sometimes later, the crisis should occur. The condition suddenly improves; the temperature falls, sometimes abruptly, perhaps more frequently by a crisis which is a little more gradual. Sleep ensues and the patient awakes from his stupor with a moist tongue and skin, a clearer intellect and perhaps a slight critical diarrhœa. Inclination for food returns, but there is still extreme weakness. Some, failing to rally after the crisis, fall into a state of collapse. In less severe cases, where the typhoid state has not been pronounced, the crisis may occur rather earlier and recovery be much more rapid; this is especially the case with children.

Varieties.—Typhus may occur in forms which are characterised by extreme mildness or by fulminant severity. The milder types are particularly seen among the natives of localities where the disease is endemic, and in children. Of the severe types, that known as *typhus siderans* or *blasting typhus* is the most striking. In this form death may occur within 2 or 3 days of the onset. A meningeal variety, accompanied by head retraction, ptosis, squint and other nervous symptoms, simulates meningitis, which may indeed be present. Some cases are characterised by fierce maniacal delirium. Typhus also may assume a hæmorrhagic form, but this is uncommon. Relapse in typhus is almost unknown, and authentic second attacks are rare.

Complications and Sequelæ.—Respiratory complications in the form of bronchitis, broncho-pneumonia, or hypostatic congestion of the lungs are the commonest. Rarely laryngitis occurs and may lead to necrosis of the cartilages and œdema of the glottis. True lobar pneumonia is hardly ever

seen. Diarrhœa is sometimes troublesome; it may be accompanied by abdominal distension and the passage of blood. Femoral thrombosis, analogous to that of typhoid fever, is common. Septic or gangrenous infarcts may be formed in the lungs, and gangrene of the fingers, nose or pudenda may occur. Suppurative parotitis is a marked feature of the disease, and the inflamed gland may become gangrenous. Gangrenous bed-sores, too, are apt to form with great rapidity and pyæmic complications may ensue. When typhus is followed by hemiplegia or other forms of paralysis, thrombosis or embolism of cerebral arteries should be suspected. Mania, melancholia and dementia are occasional sequels but generally clear up, although they may take several months to do so. Amongst rarer complications may be mentioned nephritis, cystitis, orchitis, jaundice and meningitis.

Diagnosis.—For the Weil-Felix reaction a reliable smooth strain of *Proteus* X19 is requisite. A rising agglutination titre to this organism is most significant. Results with a titre of less than 1 : 200 should not be accepted as positive unless the titre has risen greatly since the onset. The agglutination may become negative in the third or fourth week of convalescence.

As compared with *typhoid*, the onset is more sudden, and prostration is earlier and more pronounced. The aspect is drunken, the face congested, the pupils contracted and the eyes suffused. Diarrhœa and abdominal symptoms are unusual. The eruption is more profuse and more widely distributed, and the spots, which are paler than those of typhoid, are accompanied by subcuticular mottling. The termination of the fever is more abrupt. Blood cultures and agglutination tests are of great value in distinguishing the two diseases, and to those acquainted with typhus the peculiar mousy odour, which is absent in typhoid, is of assistance. *Lobar pneumonia*, especially the apical form with slight meningeal symptoms, may be mistaken for typhus, but should be eliminated by careful and repeated physical examination of the lungs. The hypostatic pneumonia of typhus is bilateral and does not show frank signs of consolidation. Herpes may occur in both diseases. *Meningitis* is now easily distinguished by lumbar puncture and examination of the cerebro-spinal fluid. *Encephalitis lethargica*, with fever, headache and delirium, must be distinguished by the absence of the characteristic rash of typhus, the negative Weil-Felix reaction, and the supervention of such signs as ptosis, ophthalmoplegia, and characteristic lethargy from which the patient can be roused. The cerebro-spinal fluid may show a lymphocytosis, without globulin increase, or it may contain blood. *Uræmia* is sometimes confused with typhus, but is distinguished by the absence of fever and rash and the condition of the urine. Difficulty occasionally arises with a fading *measles* rash, but unlike the rash of typhus this invades the face. A history of catarrhal symptoms may also be obtained in measles. The *spotted fever of the Rocky Mountains* closely resembles typhus. In hot climates and on campaigns other possible sources of error in diagnosis are small-pox, relapsing fever (epidemics of which often coincide with those of typhus), sand-fly fever, and malaria. Influenza also may lead to difficulty.

Prognosis.—The mortality, which is low in childhood and adolescence, then progressively increases (see page 275). In aged patients, recovery is the exception. Clinical indications of gravity are persistent sleeplessness, marked subsultus, violent delirium or convulsions, evidence of a hæmorrhagic

tendency, a profuse petechial rash and continued high fever or hyperpyrexia. Failing circulation is shown by lividity, coldness of the extremities and hypostatic congestion of the lungs. Suppression of urine and uræmic symptoms are also of grave import. A blood urea of 90 mg. per cent. is unfavourable, and it may rise to 200 mg. in fatal cases. Gangrenous bed-sores, extensive parotid suppuration, pyæmic symptoms and peripheral gangrene are of bad augury. The disease is particularly deadly to alcoholics, and fat subjects. Doctors often fall victims.

Treatment.—PROPHYLACTIC.—Every effort should be made to get rid of lice. The patient should be stripped, the hair clipped short, and the body shaved and thoroughly washed before admission to a ward. The garments of attendants should be so arranged as to prevent as far as possible the risk of being bitten. The clothing of those infected, and of contacts, should at once be adequately sterilised and their living rooms and their contents disinfected. Cases of typhus are best treated in isolation hospitals, and when the disease is epidemic good results are obtained by forbidding movements of the populace in the infected areas. Injection of the blood serum of healthy convalescents is said to be a prophylactic.

By cultivating the virus in lice and emulsifying their mid-guts in carbolic solution Weigl produced a protective vaccine. This contains dead Rickettsia.

A quarantine of immediate contacts for at least 15 days is usually recommended.

CURATIVE.—This should be on the same lines as those adopted in typhoid fever. Free ventilation, tepid sponging night and morning, careful attention to the mouth and back, and the adoption of a fluid diet, consisting of milk, beef tea, fruit juices and plenty of water, are the essentials. The bowels are usually constipated and enemas should be used. The bladder should be watched; retention of urine may lead to great restlessness and constant overflow. When the temperature rises above 103° or 104° F., tepid or cold sponging should be repeated. In hot climates, exposure to undue heat has a very deleterious effect. For sleeplessness, paraldehyde is the most useful hypnotic, but requires to be given in large doses. Wildly delirious patients need some form of restraint, and in these cases hyoscine should be tried if other means fail. Frequent rectal salines or the administration of saline solution intravenously or subcutaneously are beneficial when toxæmia is extreme. The tendency to collapse after the crisis should be remembered, and patients carefully watched at this period. For further details of symptomatic treatment the article on typhoid may be consulted.

CHARLES R. BOX.

TRENCH FEVER

Synonym.—Volhynia Fever.

Definition.—A blood infection communicable from man to man by means of the louse (*Pediculus humanus*). Characterised by recurrent pyrexia, headache, giddiness, pain in the back, pain in the limbs, conjunctival congestion, sweating, moderate leucocytosis at the height of the fever, and slight enlargement of the spleen.

The infection is often very persistent, and acute febrile relapses may

occur after months of quiescence. The disease was first recognised as a specific entity during the War of 1914–1918, when it appeared on all the European fighting fronts—800,000 being the approximate number of cases occurring in France among the Allies during 4 years, and sporadic infections have been reported among those coming into contact with returned troops in England and elsewhere.

Ætiology.—Trench fever being transmitted by lice alone, its occurrence depends on the presence of these insects and of human carriers of the infection. As with other insect-borne diseases, considerable numbers of the vector are required before an epidemic is produced, and close contact between human beings is necessary to facilitate the transference of the lice. Both

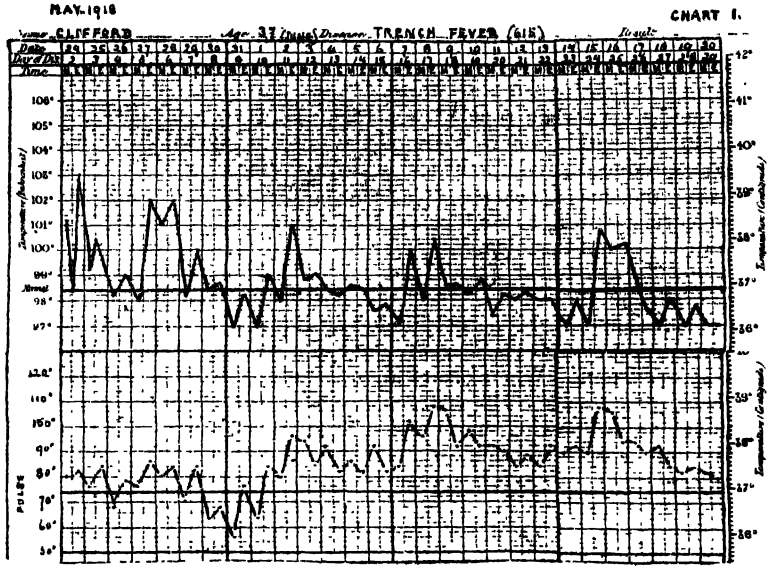


FIG. 6. Trench fever. Typical temperature and pulse curves.

the body louse and the head louse are capable of conveying infection. The disease is conveyed by the excreta or crushed bodies of infected lice; the virus may enter through the broken skin or unbroken conjunctiva; rubbing and scratching promote infection, but the bites of the lice may cause a sufficient lesion to enable infective material to enter the body.

The causal organism.—No observer, as yet, has succeeded with certainty in demonstrating the organism of trench fever in stained or fresh blood preparations, though it is known that the blood of patients is infective both during fever and in the afebrile intervals and for many months if symptoms persist. Further, the blood plasma has been shown to contain the infective agent, which in this condition is capable of passing through a Pasteur-Chamberland filter (L) with 740 mm. of mercury vacuum. Arkwright, working with excreta from lice fed on trench-fever patients, has shown that the

infectivity of the excreta for man varies very closely with the presence or absence of rickettsia bodies.

Pathology.—Very little can be said under this heading. Though German writers refer to fatal cases of trench fever, no reliable accounts of post-mortem examinations are available, and we have no knowledge of any death caused by this disease.

Symptoms and Course.—The incubation period, as evidenced by experimental infections with louse excreta, is most frequently 7 to 9 days, but the period has been prolonged to 16 days when minute doses of louse excreta have been inoculated.

The onset of the disease is sudden in the majority of cases, though about 25 per cent. of all patients complain of prodromal symptoms, such as headache, generalised pains, weakness, diarrhœa, constipation, restlessness, or insomnia, for a day or two before the temperature rises. In some instances the onset is quite dramatic in its suddenness, the patient collapsing while out walking, or even falling from his horse.

The temperature rises rapidly as a rule, and may reach 103° to 104° F. (39·4 to 40° C.) within a few hours of the onset of symptoms. A study of the chart reproduced (Fig. 6) will reveal the main features of the course of the fever; the curve may be extremely erratic. The pulse is usually accelerated, its curve corresponding to that of the temperature, its rate varying from 90 to 120 in men of military age.

In the fully developed attack, the patient's three chief complaints are headache, pain in the small of the back, and pain in the limbs. The headache is most commonly felt across the forehead and behind the eyes; usually one of the earliest symptoms, it is often one of the most severe, persistent, and commonly recurrent. When occipital, it is often accompanied by stiffness in the back of the neck. The character of the pain in the limbs is twofold: (*a*) Dull aching or gnawing, more or less continuous, always worse at night; and (*b*) acute pain—shooting or stabbing—which may last many hours, especially at night. This latter pain is nearly always felt in the bone and, most frequently, in the tibia. There is no part of the body which invariably escapes from pain. After a few days, however, the "pain all over" subsides and localised pain becomes prominent. The loins and lower limbs are most often affected. Pain is usually, but not invariably, symmetrical; its situation may vary from day to day. The pain complained of in the left hypochondrium points, in most instances, to involvement of the spleen. In early cases the splenic region is frequently so tender that examination by palpation is impossible, on account of stiffness of the muscles over the organ. When the spleen is felt, its edge is well-defined and firm. Its actual size, however, varies from day to day in the early stages, and does not remain constant until late in the disease. It is often observed to increase suddenly with the relapses and decrease during the afebrile periods (Day). Areas of tenderness are frequently associated with the pains, and may involve the spleen, tendons, bones, or joint cartilages. The nerve trunks themselves do not appear to be involved. Such tenderness may occur independently of pain, or vice versa, and either or both may persist for long periods after the fever has subsided. The extent of the areas of tenderness usually increases with exacerbations of the disease, which exacerbations may be entirely afebrile. As with the pain, the areas of tenderness are usually bilaterally symmetrical,

the skin from knee to ankle along the outer border of the tibia being most frequently involved.

The general appearance of the patient during the acute fever suggests a condition of extreme discomfort. He is restless, moving constantly to relieve the pain, and always failing to find comfort. A fairly constant feature of the initial attack is a mild degree of conjunctival congestion; it is usually transient, but frequently recurs with subsequent rises of temperature; this "pink-eye" is not accompanied by increase of secretion. At first the tongue is slightly coated with cream-coloured fur, though there is nothing characteristic about its appearance: it soon clears, and remains remarkably clean. A peculiar and very constant feature is the rapid alternations of shivering and sweating, such alternations occurring several times in the course of a single day or night. Profuse sweating, however, is rare. Rose spots upon the chest and abdomen are frequently seen during the first few days of fever. "They appear in crops, are fairly uniform in size (4 to 8 mm. in diameter), with fairly well-defined edges, varying in hue from bright pink at first to a dull red colour later. They disappear on pressure and are not raised, although vesiculation has been observed in a very few cases. They last from 6 to 48 hours and disappear suddenly, leaving no stain; at times they make their initial appearance during the relapses, which may be afebrile" (H. Fairley Marris).

The mental condition remains normal throughout the disease in the great majority of cases, though rarely there may be some delirium in the most acute attacks. The tendon reflexes are exaggerated, and a pseudo ankle-clonus is often found. During fever, lateral nystagmus on extreme deviation of the eyes is common. Frequency of micturition is complained of by about 13 per cent. of all cases, and is not associated with pain, but results in the passage of an increased amount of urine. A trace of albumin is often present. The polyuria occurs as the temperature falls.

The blood picture indicates abnormal activity of the bone marrow, and a moderate and rapidly varying leucocytosis precedes and accompanies the fever waves. The count rarely exceeds 20,000 leucocytes per c.mm. The increase of white cells is due to outpouring of immature polymorphonuclears up to 80 per cent. or more of the total. In the afebrile intervals the mononuclear elements are relatively increased. This last is probably a condition common to many soldiers in the field. In chronic cases the total of red cells is increased, the colour index as a rule being about 0·8.

Progress of the Case.—When a definite afebrile interval occurs between the initial fever and the first relapse, all symptoms usually subside as the fever abates, to return as the temperature rises. In prolonged cases, the patient's general condition obviously deteriorates and he presents an appearance of exhaustion. As relapse succeeds relapse the intervals bring less and less relief, though in some cases the later fever waves are accompanied by singularly few symptoms. The body weight steadily declines. Usually, after a period varying from a few days to about a fortnight from the onset of the disease, the acuteness of the patient's pain subsides, he sleeps well, and his appetite returns. There is even then generally some return of pain each night in some part of the limbs—most commonly the shins, calves, or ankles. If he be allowed to get up he finds walking increases the pain. During the next week or two, whether pyrexia recur or not, there are recurrences of symptoms

—especially leg pain, each exacerbation being a short replica of the original attack, or of some portion of it. In some cases such recurrences are few and slight, and the patient soon feels fit and complains of nothing but slight pain or still slighter tenderness in a limited area of the legs, from the knees downwards. In others the recurrence, even if quite late in the disease, as after months of quiescence, may be more severe than the original attack.

The Chronic Disease.—It has become evident, in a large proportion of the cases of trench fever invalided home, that there is a tendency to advance through a subacute towards a chronic condition, with symptoms of disordered action of the heart, and also in some of neurasthenia. Breathlessness on exertion, palpitation, præcordial pain, and giddiness are features of the subacute and chronic conditions. The temperature in these chronic cases varies considerably; definite fever waves lasting from a few hours to several days occur at irregular intervals, which frequently are to be measured in months.

Diagnosis.—The acute disease may be mistaken for the enteric fevers, malaria, cerebro-spinal fever, influenza, dengue, rheumatic fever, European relapsing fever, typhus, rat-bite fever, or mild infective jaundice with absence of jaundice and albuminuria. Trench fever in the chronic form is particularly liable to be mistaken for some form of cardiac disease, neurasthenia, myalgia or chronic rheumatism; and, in addition, must be differentiated from other chronic infections, such as malaria, and tuberculosis.

Prognosis.—Trench fever is practically a non-fatal disease, but may result in prolonged ill-health in from 10 to 20 per cent. of all those affected. A certain degree of immunity follows an attack of trench fever, more particularly when the attack has resulted in a complete clinical recovery; and it has been shown experimentally that such immunity may persist for six months.

Treatment. - It is a simple matter to free the individual from lice, and as regards the community this depends on successful organisation. The sick should be immediately and completely freed from vermin; but their isolation alone is not likely to control the spread of an epidemic, as mild cases are apt to escape recognition, and chronic cases remain infective for too long a period to permit of segregation till all danger is passed. The curative treatment is mainly symptomatic, the chief indication being to get the patient to bed as early as possible, and to keep him there for 8 days after the fever has subsided. In this way the incidence of chronic symptoms has been reduced. Chronic cases are best treated by healthy open-air exercise, with tonics and small doses of thyroid extract. Even when complaining of shin pain it is a mistake to allow such cases to live a sedentary indoor life.

Recent observations connected with preventive inoculation against typhus may throw light on how trench fever can be controlled.

W. Byam.

G. INFECTIOUS DISEASES OF DOUBTFUL OR UNKNOWN ÆTIOLOGY

FOURTH DISEASE

Synonym.—Filatow-Dukes Disease.

Filatow and, later, Clement Dukes described an infectious disease which they considered distinct from scarlet fever and rubella.

It is most prevalent in spring and summer. Previous attacks of scarlet fever and of rubella afford no protection. Premonitory symptoms are absent or trivial, the first sign usually being a rosy red rash, slightly raised, which covers the whole body in a few hours. The temperature may range from normal to 103° or even 104° F. The fauces are red, the tongue clean or slightly furred, and the pulse only accelerated in proportion to the temperature. The posterior cervical, axillary and inguinal lymph glands are enlarged to the size of peas, hard and somewhat tender. The conjunctivæ are pink. Desquamation may ensue.

The incubation period is between 9 and 21 days, and infectivity lasts for 2 or 3 weeks.

Most authorities either reserve judgment or refuse to recognise such a disease, alleging that some of the cases are rubella and some mild scarlet fever.

INFECTIOUS ERYTHEMA

Synonyms.—Megalerythema Epidemicum; Fifth Disease.

A mildly infectious disease of which the ætiology and mode of transmission are unknown. With slight fever, a confluent rosy eruption appears on the cheeks, avoiding the circum-oral region. The hot swelling, with its well-defined edge, may suggest erysipelas. Discrete papules spread to the forehead and neck; on the next day they invade the trunk and limbs, mainly the latter. The extensor surfaces and the buttocks are sites of predilection. The papules by confluence form patches, which may assume annular or gyrate patterns, spreading at the periphery and fading at the centres. The eruption disappears rapidly from the face and trunk, but may persist on the limbs for a week or more, and may recur as the result of irritation in a manner suggestive of urticaria. Complications are extremely rare. The incubation period is from 6 to 14 days. There is a slight polymorphonuclear leucocytosis. In contrast with rubella, eosinophilia may occur and plasma cells are scarce.

GLANDULAR FEVER

Synonyms.—Infectious Mononucleosis; Monocytic Angina.

Definition.—An acute, febrile, infectious adenitis, with a characteristic increase of mononuclear blood cells. Recovery is the rule, and complications are rare.

Ætiology.—Glandular fever is, in all probability, a virus infection. Invasion takes place through the throat, the respiratory tract or possibly the bowel. Its prevalence is world-wide. The disease is limited to small commensal outbreaks, but sporadic cases are not infrequent. It chiefly attacks children and young adults, male patients preponderating. The incubation period is about a week; it may vary from 5 to 12 days. The duration of infectivity is unknown, but appears to be short.

Symptoms.—In children and adolescents the onset is sudden, with fever and faucial injection. Stiffness of the neck, slight dysphagia or follicular conjunctivitis may occur. A rapid swelling of the lymph glands under the upper half of the sternomastoid muscle sets in. By the second or third day the glands may attain a considerable size. They are discrete and scarcely tender. The skin over them is not inflamed. In some cases, however, a definite membranous angina is already present or supervenes, and glandular tenderness is more pronounced (*anginose form*). Although the glandular swelling is at first unilateral, the glands on the other side of the neck may enlarge in turn, and minor or even primary swellings of the posterior cervical, axillary and inguinal groups may occur. The adenitis is often accompanied by sharp pyrexia, the fever being irregular, and ranging from 100° to 103° F., or even higher. Exceptionally a fleeting erythematous or rubelliform rash appears. The adenitis of glandular fever may not be limited to superficial glands or even commence in them. Paroxysmal cough, dysphagia and, rarely, even pulmonary collapse may indicate involvement of the mediastinal groups. Gastro-intestinal symptoms, such as vomiting and abdominal pain, may accompany palpable swelling of the mesenteric glands. Appendicitis may be simulated. Slight enlargement of the spleen and of the liver is not uncommon; rarely jaundice ensues. In some cases a mild lymphocytic meningitis has been observed. The blood changes are diagnostic but may be very transient. After a fleeting polymorphonuclear leucocytosis or, rarely, a neutropenia, the count shows a characteristic increase in the numbers of the mononuclear non-granular cells. These may form 40 to 90 per cent. of the total leucocytes instead of the normal 20 per cent. The cells are not of uniform type, as in acute leukæmias. Aberrant cells, which in some respects resemble large primitive lymphocytes, and in some monocytes, or plasma cells, may preponderate. The total leucocyte count is rarely more than 12,000 to 18,000, but may be 30,000 or more. The red cells are not diminished in number.

Heterophile antibodies, which agglutinate the red corpuscles of sheep, appear in the blood serum. This constitutes the Paul-Bunnell reaction. It becomes positive with the appearance of the swollen glands. A titre of 1 in 100, or possibly less, is diagnostic of glandular fever. Appearing about the fifth day, it may persist for 1 to 4 weeks. Sometimes its appearance is delayed. It may also occur in serum sickness.

The lymphadenitis is characterised by hyperplasia of the reticulo-endothelium and germ-centres which may be packed with cells like those in the blood.

The febrile stage of the disease may last for 10 days or longer, and exacerbations of fever, with involvement of fresh glandular groups, may occur. The glandular swellings subside more slowly than the fever. A subacute or relapsing type with sweats and irregular pyrexia, resembling

Hodgkin's disease, has been described. The mononucleosis may be very transitory, or may persist for some time. Convalescence is slow.

In some cases, mostly adult, glandular fever may differ considerably from the disease as described above. There is a febrile onset, with malaise, muscular pains, headache and perhaps epistaxis, but no marked soreness of the throat. Shivering, or even rigor, may occur. Towards the end of the first or second week of fever, a scanty eruption of macules or papules, like those of typhoid fever, may appear on the trunk and perhaps the limbs. The diagnosis is established when glandular enlargement, usually less pronounced than in childhood, supervenes in the third week or later, and the fever assumes a remittent type. At this stage a relative or absolute mononucleosis is most likely to be discovered, and may be evanescent or very protracted. A membranous faucial inflammation may also now be found. The spleen may enlarge. Relapses may occur, and the fever has been known to persist for many months. In some cases the Wassermann, or Kahn, reaction becomes temporarily positive. A misleading agglutination with typhoid " O " antigen in low titres may occur. Very rarely petechial eruptions have accompanied the fever, and the bleeding-time has been increased.

Complications.—There may occur a slight temporary albuminuria, with a few tube casts, but in some 6 per cent. of the cases a benign hæmorrhagic nephritis ensues. Suppurative otitis and retropharyngeal abscess have been recorded. Suppuration of the glands is rare. Serous meningitis is exceptional.

Diagnosis.—The clinical course is so characteristic and the cervical adenitis so disproportionate to the faucial inflammation that suspicion of glandular fever should be aroused, throat swabs examined, blood counts made, and the Paul-Bunnell test applied. In the adult form, fevers of the enteric group can be excluded by the usual bacteriological and serological tests. In the membranous form, diphtheria is excluded by absence of the Klebs-Loeffler bacillus and of acute toxæmic symptoms, despite persistent membrane. Resemblance to rubella is sometimes close, but there are differences in the blood films, and the Paul-Bunnell test will decide. The paroxysmal cough and leucocytosis may simulate whooping cough but the Bordet-Gengou bacillus is absent, and the Paul-Bunnell test positive. Swelling of the salivary glands and even Mikulicz's syndrome have been reported in rare instances. In such cases, if authentic, mumps may be simulated. Vincent's angina may complicate glandular fever, but the occurrence of Vincent's organisms is now regarded as fortuitous. Acute leukæmia at its onset constitutes a very real difficulty, but the leucocytosis is usually far in excess of that of glandular fever and the cell type more uniform ; anæmia is progressive, and the issue fatal. Hodgkin's disease is a much more chronic and progressive affection, and lymphocytosis rarely occurs ; biopsy of a gland is the most certain diagnostic criterion. Tuberculous adenitis has a greater chronicity ; periadenitis with suppuration and other signs of tuberculosis may be present. Septic adenitis induces a polymorphonuclear leucocytosis, and may suppurate. Agranulocytic angina is characterised by a low leucocyte count and the disappearance of all granular cells. The differentiation of glandular fever with abdominal symptoms from appendicitis is based on enlargement of the spleen and other glands, the blood picture, and the Paul-Bunnell test.

Treatment.—This is symptomatic. Ultra-violet radiation is said to hasten resolution of the adenitis. In protracted cases, injection of the blood

serum of a convalescent may bring the disease to a termination. Good results are also claimed from injection of sulphanilamide. Isolation for 7 days after the subsidence of the fever and glandular swellings is deemed sufficient in the acute cases.

CHARLES R. BOX.

RHEUMATIC[1] FEVER

Definition.—An acute, specific disease, characterised by fever, arthritis and a special tendency to carditis.

Ætiology and Pathology.—The essential cause of the disease is unknown. That the *materies morbi* is microbic there can be very little doubt, and for these reasons: the clinical features of the disease bear a strong resemblance to those seen in diseases of undoubted microbic origin, and especially in septicæmia due to streptococci and to staphylococci; the curves of incidence of the disease rise and fall with the curves of incidence of scarlet fever and of erysipelas; and the disease, if not interrupted by treatment, runs a natural course.

The essential causative factors of the disease have formed matter for discussion over a long period and are still by no means settled. At present three hypotheses are prevalent.

(i) *That the disease is a streptococcal infection.*—The close association with scarlet fever and with tonsillitis, diseases having strong affinities with streptococci, gives support to this view. But the difficulties in its acceptance are numerous: blood cultures are almost uniformly negative, even at the height of severe cases; cocci are not demonstrated in what is regarded as the essential histological lesion of the disease, the Aschoff node; the joint lesions, however severe, never suppurate; it has so far not been possible to incriminate any special variety of streptococcus as being specific.

(ii) *That the disease is due to a virus.*—As to this, though the view harmonises in many ways with the known facts, there are no data giving positive support to it.

(iii) *That the disease is a state of allergy.*—Those who hold this view conceive a focus of streptococcal infection, usually in the tonsil, which gives rise to a general hypersensitiveness of the body, and that this state, given certain conditions not yet defined, manifests itself by the syndrome which we call acute rheumatism. This hypothesis is thought by those who support it to explain the diversity of cocci associated with the disease. But, as Dible points out, that hypersensitivity should arise from infection by a multiplicity of strains of streptococci, rather than from one particular strain, constitutes the main difficulty in accepting this theory. Other difficulties are found in explaining why this particular form of sensitivity should be confined to streptococci, and why so small a section of the community should be affected. In no known state of allergy is there a specific histological lesion, nor is there a tendency to endocarditis.

Although rheumatic fever is probably not a contagious disease, an

[1] The word "rheumatic" is used throughout this article to signify conditions strictly belonging, or allied, to rheumatic fever, and not to include any of the many states loosely described as "rheumatism."

epidemic of sore throats, or of scarlet fever, is prone to produce a crop of rheumatic cases.

The disease is more common in humid and temperate *climates* than in others; it is probably more common in Great Britain than anywhere else. It is an urban, rather than a rural disease. The home environment is important as a contributory causative factor: bad general hygienic conditions predispose to it. The *sexes* are affected almost equally, but there is a slight preponderance in males, no doubt owing to their greater tendency to exposure. Rheumatic fever is pre-eminently a disease of pubescents and young adults, but it occurs at all *ages*, though it is uncommon in infants and in the elderly. If a person has had recurring attacks up to the age of 40, he is prone to them afterwards, but otherwise the susceptibility to the disease becomes greatly diminished after the age of 30. It is one of the striking facts of medicine that there are rheumatic families, in whom the tendency to the disease is highly marked. A certain *complexion* is common in them: a clear skin, with fair—often rufous—colouring.

Exposure, *fatigue* and *damp* are precipitating causes of the attack: a railway journey in wet clothes after muscular exercise, or sleeping in a damp bed, is a not unusual event in the patient's history of the onset. But it is equally true that many attacks come on in the absence of all these factors; indeed, attacks are not at all infrequent in hot weather. *Autumn* provides more attacks than any other season of the year.

Histological Morbid Anatomy.—A small cellular nodule, which is demonstrable in many cases of the disease, is thought by a number of observers to be specific. It is usually fusiform in shape, and consists of a fibrous matrix with many small round cells and some large cells, most of which are mononuclear. Later, this nodule becomes entirely replaced by fibrous tissue. Wherever this lesion is found, whether in the connective tissue of the heart muscle, in the synovial membranes or in the subcutaneous tissues—allowing for differences in the texture of the tissues themselves—these histological features are essentially the same. In the myocardium this lesion is easily recognisable ("Aschoff's node").

Symptoms.—In adults the onset is usually abrupt, with the sense of chill, accompanied almost at once by pains in the joints, the knees and ankles being the commonest. One or two joints usually precede the rest in order of invasion, to be quickly followed by others: wrists, shoulders, hips, neck, tarsus, metatarso- and metacarpo-phalangeal joints. Some degree of sore throat is very common, and may be a marked feature; when this is so, the tonsils usually show the redness and swelling more than other parts. By the end of the second or third day it is usual to find a considerable number of joints affected, so that the patient is already in much pain and great discomfort. The affected joints are swollen and red, and synovial effusions appear, especially in the knees, wrists and ankles. There is great variation in the extent and in the degree of the joint involvement in different cases. In a few instances less common joints share the inflammation: sterno-clavicular, vertebral, interphalangeal. The *fibrous tissues* suffer as well as the joints, and it is often apparent that this accounts for some, at least, of the stiffness and grave discomfort. The joint effusions never suppurate.

The *temperature* usually rises to 102° to 103° F. with the arthritis and synovial effusions, and the fever remits, or even intermits, so that the chart shows

an " irregular " curve. The pyrexia is peculiarly sensitive both to exacerbations in the disease (which are common), to relapses (which are also common) and to complications. Sweating is generally profuse, the sweat being of a peculiar " acid " smell. The *urine* is scanty and high coloured, and if the fever is marked there is usually a trace of albumin present; a deposit of urates, coloured brick-red by uro-erythrin, is a feature in most severe cases. As in most acute fevers, the *secretions* of the mouth and alimentary tract are lessened, leading to a heavily coated tongue, anorexia and constipation.

The *heart* is generally—some authorities believe always—affected, though the nature and the degree of the affection is variable. There are few, if any, cases in which careful examination from day to day does not reveal a slight degree of " softness " of the first sound of the heart, due, no doubt, to affection of the myocardium. The *pulse* is raised moderately in frequency (90 to 120), its volume is good but its tension is reduced. In more cases than not, probably, a soft systolic apex-bruit appears, not, however, necessarily indicating the occurrence of endocarditis. In about half of all cases there are reasons for concluding that *acute endocarditis* is present, as judged by the character of this bruit, its transmission towards the axilla, some evidence of enlargement of the heart and a rise in the temperature coincident with the appearance of the heart signs. This complication usually arises about the eighth to the tenth day.

The *blood* shows a considerable leucocytosis (15,000 to 30,000) and an acute " secondary " anæmia which is a constant feature of the disease and quickly reveals itself in the patient's facies. The erythrocyte sedimentation rate is increased during the active stages of the disease.

Aberrant Types.—*Subacute* attacks are common, especially in children (see p. 292) and in old rheumatic subjects. Their importance lies in the fact that all the time the heart may be suffering damage. Although this is less common in adults than in children, arthritic signs may be absent in cases of rheumatic endocarditis, as in rheumatic pericarditis.

Complications.—As already stated, about one-half of all cases develop some *heart* lesion. We have spoken of *myocarditis* and of *acute endocarditis*, and of the advent of the latter, should it arrive, about the end of the first week. The endocarditis is generally a valvulitis; most often mitral, less often aortic, but in some cases both mitral and aortic. *Pericarditis* is less common, though it may be the only manifestation of rheumatic infection; and pericardial effusion, especially of the massive sort, is nowadays quite uncommon. (For full accounts of these important cardiac complications, see special sections.)

Skin eruptions, though a specific feature of the infection, are not very common, except in children. The profuse sweating quite often leads to *sudamina*, and these, becoming inflamed, lead to *miliaria*. True *rheumatic erythemata* are much more common in the subacute cases than in the acute ones. *Purpuric* eruptions, again, are more often seen in aberrant types of the disease.

The only *pulmonary complication* of any consequence is pleurisy, and this is by no means common if we preserve the usual strict criteria of physical signs for its recognition, and omit " pleurodynia," in which condition the pain is more often intercostal than pleural. Indeed it may be said that, in the absence of pericarditis and of severe endocarditis, rheumatic pleurisy is

rare. Pneumonia also is unusual, but there is a condition of lung in severe rheumatic fever, again when complicated by grave endocardial, pericardial and pleural affections, which simulates it somewhat; the lung tissue is in a mixed state of congestion, collapse and œdema. A thin serous pleural exudate often accompanies this condition of the lung, and, no doubt, because of the associated pericarditis, it is more often found on the left than on the right side.

Hyperpyrexia was formerly a much dreaded, and not very uncommon, complication. It is now quite rare. There is, indeed, by some modern observers, doubt thrown upon the rheumatic nature of the cases described under this term. May they, for example, have been fulminating cases of septicæmia or meningitis? It is clear that no case could nowadays be termed rheumatic hyperpyrexia unless lumbar puncture and blood culture findings were proved to be negative. But the strongest points in favour of regarding some, at least, of the cases as having been rheumatic, and not meningitic or septicæmic, are (1) the very high degree to which the temperature rose (107° to 110° F.); and (2) the fact that in some of the cases, at least, the clinical picture was definitely that of rheumatic fever before the event, and when recovery occurred as the result of prompt treatment it was similar afterwards. The condition arises suddenly in most cases, though in a few there is a suspicious prodromal amelioration in the pain, sweating and general discomfort. The temperature rises rapidly to 106°, and unless checked by cold applications it may quickly reach 109° or 110° F. Before this stage is reached the patient has become tremulous and excited, then delirious and then semi-comatose, with a dusky lividity of the face and a failing pulse. Most of such cases are fatal. If prompt treatment succeeds in lowering the pyrexia it may need to be resorted to again in a few minutes or hours, since recurrence of the condition is to be expected.

Course.—Before the introduction of salicylates the course of rheumatic fever was, in the words of Sir Thomas Watson, "six weeks." Nowadays it is much shorter; 10 days to 3 weeks, if we include the joint swellings, though the fever is generally over in a shorter period than this when the treatment is prompt and thorough. If residual joint inflammations prolong the course of the disease it is important to look for contributory causes, and especially for septic foci. Recrudescences are very common, especially if full treatment be relaxed too early. Complications necessarily prolong the course of the disease.

Convalescence is often tedious, and the resultant anæmia and heart weakness warn the careful practitioner not to attempt to hurry it. Rheumatic fever patients are as liable to *relapses* as they are to recrudescences, and it is no uncommon thing to see a patient slip again into almost as bad a state as he originally was, including, it may be, painful swelling of the very same joints as were first affected. The great danger of these relapses lies in the risk of heart inflammations arising during the subsequent attacks, when perchance the patient escaped them at the first.

Prognosis.—Recovery is the rule in this disease; *death during a first attack is very uncommon.* When death occurs there is invariably serious carditis, especially myocarditis, and acute pulmonary complications (pleurisy and "rheumatic pneumonia") are usually present also. In rare cases, death occurs in a state of hyperpyrexia. When the attack supervenes upon old

rheumatic carditis, the prognosis is less good, heart failure being more easily induced. But in general it may be said that rheumatic fever is serious, not from its case mortality, but from its crippling effect upon the heart. *Residual conditions* are almost entirely cardiac injuries and chiefly scarred valves and auricular fibrillation; rarely some degree of limitation of movement in joints.

Rheumatic Fever in Children.—The disease is very common in children, in whom, however, the clinical picture as above described is apt to be departed from in several respects. (1) The arthritis is a less marked feature; it may be absent altogether, and even when it is a troublesome element in the case, the degree of pain is prone to be disproportionate to the amount of redness and swelling of the joints, and may be muscular rather than articular. (2) Skin eruptions are relatively more common—various erythemata especially, but also purpura. (3) *Rheumatic "nodules"* are almost confined to children, having the same age-incidence as *chorea* (see p. 1698). These are discrete lumps, varying in size from small peas to horse-beans; symmetrical in distribution, they are found in the scalp, along the margins of the scapulæ and bones of the forearm, about the knuckles and elbows, and, less often, in other situations. They are sometimes tender and painful. They come and go. Occasionally they are present in large numbers; the case is then most likely to be subacute in type and very tedious in its course: they are, therefore, of grave prognostic import as to the ultimate state of the heart, being indicative of a "smouldering" endocarditis. They consist of elements approximating to the "essential" lesion of the disease to which reference has been already made. (4) But the most important difference observable between the disease in children and in adults is the fact that in the former the process is not seldom subacute in its onset and course, and for this reason frequently overlooked for a time. Add to this fact that the tendency to heart involvement in these subacute attacks is no less than in the more acute and more highly febrile bouts, and it is obvious that the recognition of this state of things is of the utmost importance. Unfortunately a large number of cases of subacute rheumatic endocarditis must needs arise without the possibility of prevention, but it is probable that a large number might also be prevented, or considerably modified, by prompt treatment of the subacute rheumatism in childhood which causes the injury. These attacks of subacute rheumatism are sometimes characterised by intercostal pain, sometimes by abdominal pain, sometimes by pain in the legs without special reference to the joints. There seems no doubt that so-called "growing pains" are often rheumatic in nature. In any child so affected the heart should be examined critically, and from time to time. The presence of sore throat, of acid sweats, of one of the erythemata, in conjunction with the above-named pains, should determine a decision to treat the child as suffering from the rheumatic process. The presence of nodules is decisive in a doubtful case.

Diagnosis.—Cases of the fully developed disease do not often lead to difficulty in diagnosis, given ordinary care on the part of the practitioner. A few diseases, however, require mention. (1) *Pyæmia* due to coccal infection may lead to some confusion, and the following differential points are worthy of notice. In septicæmia, when there is arthritis, the latter is usually constant in one or two joints, not fugitive and involving many as in rheumatic fever. Moreover, the joint changes tend to suppuration and permanent

destruction of the joint structures. Blood cultures and joint-puncture fluids are not infrequently positive in pyæmia, whereas they are constantly negative in acute rheumatism. Rigors are common in pyæmia; in rheumatic fever they do not occur. If endocarditis complicates pyæmia, the heart infection is likely to lead to embolism, a condition not found in rheumatic fever. But between this type of streptococcal septicæmia and rheumatic fever all grades of cases are seen.

(2) In children *acute osteomyelitis* may be mistaken for rheumatism; rarely does the converse error arise. But the disease-process is nearly always much more severe, the temperature being much higher and showing greater oscillations. The painful part is generally the lower end of the femur or tibia, and careful examination reveals it to be epiphysial rather than arthritic. As in pyæmia, to which type of infection the disease really belongs, blood cultures are usually positive (*Staphylococcus aureus*).

(3) *Gonorrhœal arthritis* is not usually so acute a disease, nor is the patient often so ill as in rheumatic fever. The joints are fewer in number, and, as in pyæmia, the course of the individual involvement is much longer. The inflammation, too, affects peri-articular as well as articular structures; not seldom it involves adjacent tendon sheaths also. Gonococci may be isolated from the joint effusions. Although the presence of a urethral or vaginal discharge makes a diagnosis of gonorrhœal arthritis likely it does not prove it; and it must be remembered that the discharge not infrequently ceases temporarily with the onset of the arthritis.

(4) *Acute osteo-arthritis* is a rare disease, but when it occurs it produces a clinical picture that is probably closer to rheumatic fever than does any other disease-process. The patient is more often a woman than a man, and is generally older (30 to 60) than is the average case of rheumatic fever. The failure of salicylates in full doses to reduce the temperature, and to affect beneficially the course of the joint condition, should always raise doubts as to the nature of a supposed case of rheumatic fever. This differential point applies equally to diseases 1 to 3.

(5) *Gout*, when present in the acute arthritic form, may be mistaken for rheumatic fever; rarely does the converse happen. The patient is generally a man over 40 years of age; the number of joints involved is rarely more than two; the skin over these is generally dusky red in hue, and shining; there is often definite soft œdema. *The presence of severe pain when the affected joints are at rest is much in favour of gout.* The degree of fever is usually much less in proportion to the degree of joint inflammation than is the case in rheumatic fever. The presence of tophi may be taken as confirmatory of gout in a doubtful case.

(6) *Meningococcal meningitis with arthritis* rarely simulates rheumatic fever, but one of the writers (H.) has seen such a case, in which there were pungent acid sweats and purpura, and the resemblance to a case of severe rheumatic fever was for a time very close indeed.

Treatment.—(1) *General.*—With as much promptness as possible, the patient is put to bed, and is kept there until it is certain that the heart is unaffected, or, if affected, until it is certain that the inflammatory process has ceased to be active (see p. 917). The bed should be chosen carefully; narrow enough to admit of easy nursing, and having a soft but firm mattress. The patient lies in blankets with a long flannel garment opening down the front,

and having sleeves to the wrists; this garment is changed as frequently as need be, according to the degree of sweating. The position of the patient is one of recumbency, with the affected joints supported in a position of maximum comfort. Movements of the limbs are generally best carried out by the patient's own efforts, and in all except severe cases, and where the heart is affected, movements of the body as a whole may also well be left to the patient. The basis of the *diet* should be milk diluted with water or alkaline mineral waters, and so long as the fever remains a marked feature of the case nothing should be added to this unless it be whey, peptonised milk or barley water. Abundance of fluids should be allowed, for a great deal of fluid is lost to the body through the profuse sweats. Imperial drink is very useful. As the fever declines, there may be added to the milk, oatmeal, vegetable soups and chocolate. Meat should be reserved for convalescence, and even then should be given very sparingly. Tea and coffee are best omitted altogether. Fruit is disallowed. Aperients are given as necessary.

In the matter of *drugs* there is a consensus of opinion that salicylic preparations deserve the name of specific remedies. They control the arthritis, cause the fever to decline, and cut short the course of the disease-process. They also lessen the tendency to relapses, and often render these abortive when they threaten. It may be quite true that they do not prevent the occurrence of endocarditis, nor affect this inflammatory process beneficially when once established, but a remedy which cuts short the course of a disease must necessarily, in an indirect measure, act as a deterrent in respect of its complications. Thus, by prompt exhibition of salicylates an attack of rheumatic fever may be almost resolved by the eighth day, at about which period in the disease acute endocarditis is specially liable to develop. Certain it is that pericarditis, and in particular pericarditis with liquid effusion, is much less common nowadays than it was in the pre-salicylic days; so also is hyperpyrexia; and it is unlikely, in view of the more general features of rheumatic fever and its incidence, that the disease-process has itself undergone any change during the past 50 years which is likely to account for these facts. The preparation of the drug which has become most popular and deservedly so, is sodium salicylate. *It should be given in sufficient quantities, and the doses should be distributed as evenly throughout the 24 hours as is compatible with securing good sleep for the patient.* At the onset of treatment of an acute case in an adult, 20 grains should be given every 2 hours during the day, and every 4 hours during the night (200 grains in the 24 hours). Many authorities advise that twice these amounts of sodium bicarbonate be added to the salicylate to prevent acidosis; in the writers' opinion half the quantity of bicarbonate, *i.e.* 100 grains in the 24 hours, is sufficient and less likely to induce vomiting. If a child vomits a dose of salicylate, another given immediately will probably be retained. As the fever and pain diminish, these quantities may be given somewhat less frequently, a note being kept on the temperature chart of the total amount given in the 24 hours. In a child of 12 years or so, half these quantities may be given. If no amelioration follows these doses in 48 hours they should be increased by 50 per cent. (150 grains in 24 hours). If an exacerbation occurs, or a relapse threatens, after the dosage has been reduced, it should be at once adjusted to its original level. The drug is not unpleasant to take, and its taste is easily masked by liquorice water as a vehicle. Quite apart from the inestimable value of giving adequate

doses so as to gain time, there is an additional value in this procedure from the point of view of diagnosis, for a *patient suffering from acute arthritis with fever, who is not considerably better after* 48 *hours' treatment by full doses of salicylates almost certainly is not suffering from rheumatic fever.* The diagnosis in these circumstances should be at once revised. It will be found that the great majority of patients tolerate the above specified doses of salicylates without ill-effects. In the few instances in which it produces vomiting, or intense depression, or delirium, or coma, or hæmaturia—symptoms thought from time to time to be toxic effects of the drug– either aspirin in similar doses, or salicin in somewhat larger doses, may be substituted. But care must be taken in deciding that such symptoms are really due to the salicylate and are not manifestations of the rheumatic poison. Modern synthetic preparations of sodium salicylate are fairly free from the contaminations which were formerly rather common. In the early stage of the disease it may be necessary to adopt more rapid palliative measures for the *severe pain*, especially if this prevents sleep. Nothing is better than opium, either as pulv. ipecac. et opii, grs. 10, or pil. saponis co., grs. 5. It is better to avoid phenazone and phenacetin. The treatment of heart complications is discussed elsewhere (Sect. XIII.). Against the occurrence of these complications, apart from the value of early and liberal use of salicylates, we seem to be powerless. But some authors attach importance to small blisters applied to the præcordium early in the disease.

Hyperpyrexia is met by prompt application of the cold pack, with volatile stimulants; the pack may need frequent renewal, and in extreme cases the water used for it must be iced. The most constant vigilance is necessary in such cases, which, as already stated, are happily rare nowadays.

In the treatment of prolonged cases of the disease the writers believe iodine (preferably not in the form of the potassium salt) to be useful, and especially so in cases complicated by serous inflammations, whether cardiac or other. Such experimental treatment of these prolonged cases by sera and vaccines as the writers have observed has not led them to employ either in any routine fashion. "Channels of entry" should, in protracted cases, be adequately dealt with as in (4).

(2) *Local.*—The position of optimum comfort of the affected joints has been already referred to. The use of splints for fixing the joints often gives relief. In the milder cases it suffices to wrap the joints in cotton-wool and bandage them lightly. In the more severe cases a lotion of tinct. opii, 1 fl. oz.; glycerin, 2 fl. oz.; water, 12 fl. oz.; sod. carb. to saturation, used hot, gives as much relief as anything. An alternative is one of the preparations of methyl salicylate, used freely, but without rubbing. Aspiration of the effusion is scarcely ever needed; its indication, indeed, should raise doubts as to the diagnosis.

(3) *During convalescence.*—Convalescence is generally slow, and should not be hurried. If the heart has suffered by direct inflammation, the recumbent position must be prolonged until it is certain that quiescence is established in that respect; this usually means from 4 to 6 weeks after the subsidence of the fever. The disastrous effects of attempting to hasten convalescence in such cases are to be seen amongst patients who have been treated in institutions which advertise a false efficiency by reporting a "shorter average stay in hospital" than is the case in sister institutions.

The transition from strict recumbency to a sitting posture should occupy a whole week, by the gradual addition of pillows, and the further return to ordinary active life should be graduated with care.

Tonic preparations, such as quinine and hypophosphites, are useful, but the tradition that iron is not well tolerated until late in convalescence—though the state of anæmia seems to indicate it—is confirmed by experience. Diet during convalescence has already been referred to. Massage and passive movements of the affected joints may be begun so soon as the inflammation has completely subsided.

(4) *Preventive treatment.*—Failing exact knowledge of the essential causative agent in rheumatic fever, no effective mode of prevention can at present be devised. But if there be a doubtful "channel of entry" present in any case, this should be dealt with in some radical fashion, in any patient who has had an attack, or is a member of a susceptible family. "Septic" tonsils should be enucleated, and an appendix which has at any time shown signs of inflammation should be removed.

ERYTHEMA NODOSUM

Ætiology.—Although this disease is a fairly definite and easily recognisable clinical entity, it is still uncertain where it should be placed, when considered in relation to nosology or to ætiology. Formerly the favoured view was that the disease is a manifestation of acute rheumatism. Since, however, it is less often than not associated with the more definite criteria of acute rheumatism (arthritis, endo- and pericarditis), since it rarely recurs in the same patient, and since treatment by salicylates in full doses does not cut short its course, it is very doubtful if it should be regarded as a true rheumatic affection. A more recent view is that the disease is intimately related to tubercle: the lesions being toxic rather than actual areas of infection: the isolation of tubercle bacilli from them, originally reported, has not been confirmed. Alternative views are not lacking. By some erythema nodosum is thought to be an acute specific disease due to an unknown virus. Collis suggests that it is a type of hyper-reactive tissue response to different bacterial allergens and that the allergens responsible for erythema nodosum in London are commonly tuberculin and the toxin of hæmolytic streptococci.

It occurs more often in females than in males (according to Mackenzie, in the proportion of five to one), and the majority of cases are found between the ages of 10 and 30 years. There is no seasonal incidence. In the experience of the writer it is much more common in hospital than in private practice; this and some other observations suggest that bad feeding or insanitary conditions may contribute to the incidence of the affection.

Pathology.—There has been demonstrated a widespread arteriolitis in the subcutaneous fat, resolving without suppuration or residual fibrosis.

Symptoms.—The symptoms consist of: (i) the local lesions, and (ii) certain constitutional changes.

(i) The local lesions are bilateral and occur chiefly upon the lower limbs; indeed, in the great majority of the cases they are confined to these. When they appear on the arms they are most often found only in this situation, the patient is more often than not an adult, and the general symptoms are

less like rheumatic manifestations than is the case in the more common variety of the disease. The lesions are round or oval swellings, usually confined to the extensor aspect of the limbs, affecting the shin regions chiefly, and varying in size from a large pea to half an orange. There may be two or three only on each leg, or, in severe cases, the greater part of the extensor surface may be covered by them. They involve the subcutaneous tissue as well as the skin. They are very tender to touch. On their first appearance they are deep red in colour, later they become purple in hue, and still later they often show a definite ecchymotic appearance—giving rise to the name dermatitis contusiformis. In bad cases there is a good deal of associated œdema of the surrounding tissues.

(ii) The general symptoms include a mild grade of fever (not constantly present), joint pains, malaise and sore throat. But many cases occur in which the local skin condition, with pain and tenderness, covers the whole of the symptomatology. Constipation is common, and is sometimes severe: in a case of the writer's, in a young man, there had been no action of the bowels for 10 days, and the patient had suffered from constipation all his life.

The course of the disease is from 2 to 3 weeks, but some mild cases get well, if treated, within a week.

Diagnosis.—The diagnosis is not difficult. Radcliffe-Crocker says that the lesions may be mistaken for syphilitic nodes: the distinction is made by the presence of other signs of syphilis, by the fact that the pains in the latter disease precede the appearance of the node through the skin, and by the lack of response to treatment by iodide of potassium. The lesions of Bazin's disease, though they occur on the legs much more than on the arms (as in erythema nodosum), though the sex and age are the same and though the association with tuberculosis is definite, are chronic and relapsing in character, and ulceration usually occurs.

Treatment.—Rest in bed, with the legs elevated, and general hygienic conditions, suffice to bring about spontaneous recovery in all cases. No drug has credit for cutting short the course of the disease. Recovery has been found to be quite as rapid when the patient is treated by small doses of hydrarg. c. cretâ with saline aperients, as when she is given full doses of sodium salicylate. As a local application lead lotion is perhaps the most soothing.

EPIDEMIC MYALGIA

Synonyms.—Epidemic or Infectious Pleurodynia; Bornholm disease; Epidemic diaphragmatic spasm; Devil's grip.

Definition.—An acute infectious epidemic disease of short duration characterised by sudden onset of pain in the upper abdomen and lower thorax, pyrexia, sweating, and a tendency to relapse.

Ætiology.—The disease occurs usually in the late summer and autumn; it mainly affects children under 15 years of age. The exciting cause is unknown; infection appears to be spread by direct contact only, the incubation period being 2 to 5 days; the patient remains infective so long as the pain persists. One attack may not confer lasting immunity.

Pathology.—Nothing is known of the pathology. No abnormality has

been detected in those cases in which an exploratory laparotomy has been performed owing to mistaken diagnosis.

Clinical Features.—The onset is sudden, with acute spasmodic pain in the region of the xiphisternum and the attachment of the diaphragm, perhaps more on one side than the other. The pain leads to shallow rapid respiration, and is intensified by deep breathing, by yawning, sneezing or cough; a spasm during a period of quiescence may be induced by laughing. In adults, pain may also be complained of in the neck and extremities, and there may be some frontal headache. The temperature rises rapidly, perhaps to 104° F., and subsides within 24 hours. There is a marked tendency to a return of pain and pyrexia during 3 or 4 days, and the second attack may be the more severe. Profuse sweats are common, anorexia the rule, while vomiting and diarrhœa are seldom met with.

There are no physical signs, other than in the character of the respiration, of involvement of the pleura, lung or peritoneum. There may be some cutaneous hyperæsthesia and tenderness on pressure in the painful area, especially in the epigastrium. In some cases a leucocytosis occurs, and eosinophilia has been reported during convalescence. No abnormality has been detected on X-ray examination.

Complications are infrequent. Conjunctivitis, catarrh of the upper respiratory tract or orchitis have been reported in certain epidemics. There are no sequelæ. Prognosis is good.

Treatment.—The patient should be isolated, and remain in bed until 48 hours after the pyrexia and pain have subsided. Ordinary methods for the relief of pain are indicated.

HORDER.
A. E. GOW.

PINK DISEASE

Synonyms.—Infantile Acrodynia; Erythœdema; Vegetative Neurosis.

History.—The disease was first accurately described by Swift (Australia) in 1914, but Selter (Germany) had reported similar cases in 1903, and Swift records that he certainly saw examples of the disease when he was a resident at the Hospital for Sick Children, Great Ormond Street, in 1885. Feer (Zurich) is generally accepted in Europe as having described cases about the same time as Swift.

Ætiology.—The clinical syndrome is generally ascribed to the effects of a widely diffused toxin which shows a predilection for the vegetative nervous system. It frequently follows an acute infection of the upper respiratory tract and less often gastro-enteritis, either affording a possible portal of entry of a virus. Although not obviously infectious from case to case, small epidemics in localised areas have occurred in various parts of the world. This and a tendency to a seasonal incidence in spring and autumn offer obvious analogies with acute anterior poliomyelitis; and Mayerhofer has described cases following this disease. Another theory favours a vitamin or other deficiency, but usually affected children have been well fed. Hypersensitivity to sunlight has also been put forward, but claims to a cure by the exclusion of sunlight in England are balanced by equally well supported claims to great benefit by exposure to sunshine in Australia. The balance of

present evidence favours a virus. The disease occurs more especially in the temperate zones, affects the sexes equally and is almost limited to the period covered by the time of the primary dentition.

Pathology.—Apart from various findings due to secondary infections, the specific morbid pathology of the disease is said to include minor microscopical changes in medulla, cord and peripheral nerves. These consist of round-celled infiltration, demyelinisation and œdema. Some authorities maintain that even these changes are due to a non-specific terminal infection, or to secondary nutritional depletion.

Symptoms.—After a vague febrile onset, as intimated above, the infant fails to recover its previous vigour, and remains essentially miserable, with insomnia, muscular hypotonia, increasing loss of appetite and usually loss of weight. After a week or so some degree of stomatitis is commonly found, the child dribbles a lot, and just when the whole picture has been confidently ascribed to the effects of dentition the characteristic rash makes its appearance. This consists of three main features: a sweat rash, which may be present all over the trunk and proximal portions of the limbs; a curious "raw beef," puffy, non-pitting œdema of the hands, feet and frequently of the nose; and eventually various degrees of furunculosis and pyodermia. The condition of the mouth deteriorates, teeth may be shed (and swallowed), photophobia is often marked, and the child "burrows" in misery in the bedclothes, constantly scratching and rubbing the hands and feet together. In severe cases the fingers and toes may be seriously bitten and the hair plucked out. Perspiration of a cold, clammy type is present and produces a "mousy" odour. Wasting and hypotonia become extreme, the child makes no effort to stand or walk, and prolapse of the rectum may occur. Signs of affection of the nervous system are shown by a persistent tachycardia—which is constant and varies in degree according to the severity and state of the disease—the tendon reflexes are frequently diminished or lost, and it may be possible to demonstrate a diminished sensitivity to pin-prick. The disease is usually afebrile save for the effects of complications, the blood pressure is said to be raised, although the determination of this is a matter of some difficulty, and there is frequently a leucocytosis.

Complications.—The upper respiratory tract infection may spread to affect the ears and, more seriously, to produce broncho-pneumonia, which is always a menace because of the risk of aspiration with an infected mouth. Pyelitis is not uncommon. Various local infections of the skin are almost invariable in a case of ordinary severity. Sequelæ, however, are unknown and relapses seldom occur.

Course.—The whole clinical picture may be spread over three to nine months, with some variation in the severity of the symptoms.

Diagnosis.—There is no mistaking the disease once it is fully developed, and it obviously should be suspected whenever a young child appears to be seriously miserable for weeks at a time. Cases have been described with most of the classical symptoms, but without the rash or other skin changes. Tachycardia occurs in all cases, and unless the pulse rate is 140 or more a diagnosis of pink disease should not be made with confidence.

Prognosis.—In the absence of serious complications this is invariably good, and one attack confers immunity. Death is usually the result of some serious complication but occasionally is sudden after a period of increasing

rate and irregularity of the pulse. It is suggested that in such cases the end is due to ventricular fibrillation.

Treatment.—Since the exact causation is unknown, preventive measures are impossible, and most of the treatment has perforce to be symptomatic. Good nursing is essential but hospitalisation is undesirable; a well-trained nurse in the home is indicated as the patient's mother is almost invariably worn out. If weather permits the child's cot should be in the open air as much as possible, day and night. Silk or cotton clothing, frequently changed, is best, the eyes should be protected from glare, and some restraint may be necessary to prevent quite serious self-infliction of damage to the skin. The diet should be adequate, well-balanced, mostly liquid and offered cold, frequently and in small quantities. The troublesome anorexia can only be dealt with by skilful nursing. Deference to the deficiency theory of origin would indicate the administration of vitamin concentrates A, B, C and D, raw liver, and some yeast preparation, such as yestamin. Good results have been claimed for the injection of vitamin B_1 in massive doses, such as 1000 international units once a week. This has the merit of being a convenient way of treating an out-patient at a hospital. Bellergal (one to three tablets daily for several days) is believed to counteract the effects of the disease upon the sympathetic nervous system. Some sedative is essential and a mixture of chloral and bromide, according to the age, is probably the most suitable and should be used freely. For the skin a tepid bath (to which disinfectant, such as liq. hydrarg. perchlor., may well be added) once or twice daily, followed by a methylated spirit rub and copious powdering with a fine and talc (not starch) powder, will help to promote comfort. The irritation may be slightly allayed by calamine lotion or the use of menthol in paraffin (1 per cent.) dabbed on at night. The mouth requires great care. Giving the child swabs soaked in hydrogen peroxide may be recommended, and actual inflammatory lesions should be dabbed with methyl violet solution (1 per cent. in water). During convalescence an iron tonic and a change to the seaside help to promote complete cure.

ALAN MONCRIEFF.

SECTION III

TROPICAL DISEASES OF DOUBTFUL OR UNKNOWN NATURE

LATAH

Definition.—A form of cerebral neurosis, in which the patient makes involuntary movements and incoherently utters sounds or words (Scheube).

Ætiology.—The condition has been found in Java, the Philippines, Burma and Siam, and natives are affected, principally young women. Heredity may play a part, but no exciting cause is known.

Pathology.—There are no records of any post-mortem examinations.

Symptoms.—The movements and incoherent sounds are involuntary, the patient being unable to restrain them. The reflexes may be increased, and people affected take fright easily.

Diagnosis.—The disease must be distinguished from ordinary mental and nervous disorders.

Prognosis.—The disease may persist for years, and appears to be incurable.

Treatment.—None is known. Treatment by suggestion might be tried.

KUBISAGARI

Definition.—A disease associated with dimness of sight, diplopia and paresis of the cervical muscles (Miura).

Ætiology.—The condition is found endemically in parts of Japan. It attacks the agricultural natives of any age or sex, and house epidemics have been recorded. The cause is unknown.

Pathology.—This has not been established.

Symptoms.—Depression is usually present, followed by dimness of vision, often accompanied by ptosis of the eyelids; paresis of the cervical muscles, muscles of the trunk, etc., are also common. Owing to the implication of the cervical muscles the head hangs down, whence the name of the disease. The symptoms intermit, intervals of freedom alternating with new attacks.

Diagnosis.—It must be distinguished from other forms of paralysis.

Prognosis.—The disease is said never to end fatally.

Treatment.—Miura recommends potassium iodide and arsenic.

AINHUM

Definition.—A disease of the toes, characterised by a ring-shaped constriction, which finally causes amputation of the toe affected.

Ætiology.—The disease is principally found on the West Coast of Africa, but it has also been seen in Brazil, British Guiana, the West Indies, the southern states of the U.S.A. and in India. Negroes and Hindoos are attacked, adult males being especially affected. The cause is obscure. A trophic origin has been suggested; also injuries, such as cuts from grass, jiggers, etc.

Pathology.—The constricting ring is formed of fibrous tissue. An increase in the adipose tissue of the part has been noted by some, a thickening of the epidermis by others. The underlying bone may undergo absorption. Natives are very prone to fibrous tissue formation, *e.g.* keloid.

Symptoms.—The little toe is most usually affected. The disease commences by a groove or furrow, which first appears in the digito-plantar fold; this gradually deepens and spreads round the portion of the toe distal to the swelling. The change advances until the band is so narrow that the toe hangs by a thin pedicle. Finally the part may drop off spontaneously, be torn off, or be purposely cut off by the patient. The course of the malady is slow—usually several years.

Prognosis.—There is no danger to life: the disease may last 10 years.

Treatment.—Da Silva proposes vertical incisions through the constricting band in the early stages. Later, surgical amputation is advisable.

BIG HEEL

Synonym.—Endemic hypertrophy of the os calcis.

Definition.—A peculiar hypertrophic condition of the os calcis.

Ætiology.—This has not yet been established. The condition occurs in natives of the West Coast of Africa, chiefly on the Gold Coast. It is possibly connected with yaws.

Symptoms.—The disease is ushered in with fever, followed by pain and tenderness in the heel, with swelling of the os calcis of one or both feet. Cold and damp are apt to produce an increase in the symptoms, and walking is hindered. The condition may become chronic, permanent thickening of the bone resulting.

Treatment.—If the enlargement be excessive, removal of some of the hypertrophic bone may be attempted.

CHAPPA

Definition.—A peculiar affection of the joints associated with nodules in the subcutaneous tissues, which finally ulcerate.

Ætiology.—The disease was described by Read in Southern Nigerai.

Natives only are attacked as far as is known. The causative agent has eluded detection.

Pathology.—This is not yet entirely known. Nodules, as large as a pigeon's egg, form in the subcutaneous tissues, with ultimately complete destruction of the joints—the bones are also attacked.

Symptoms.—The disease, according to Read, begins with severe pains in the limbs, muscles and joints. After a time, nodules appear in the tissues, and the skin over them breaks down with resulting ulcer formation. The ulcers have no tendency to heal, but may remain for years.

Diagnosis.—The disease has to be distinguished from onchocerca nodules, tropical ulcer and yaws. Possibly it may be a late stage of the latter disease.

Prognosis.—This is bad.

Treatment.—Scraping is indicated. Arsphenamine or its derivatives may be administered, but no definite specific remedy is known.

ONYALAI

Synonyms.—Chilopa ; Kafindo.

Definition.—An acute disease affecting natives of Central Africa, characterised by blood-filled vesicles inside the mouth and involving other mucous surfaces, hæmaturia and the passage of blood per rectum.

Ætiology.—The disease may affect natives of any age or either sex, and is met with in Portuguese West Africa, along the Lualaba River, in the Belgian Congo, in Bukoba, East Africa, and in Northern Rhodesia. Gilkes believes it to be a vitamin deficiency. Blackie has recently suggested that onyalai is an acute form of essential thrombocytopenia due to defective maturation of the megakaryocytes of the marrow with an associated modification of the endothelium of the capillaries as a contributory cause in the production of the bullæ.

Pathology.—The vesicles are umbilicated, oval or circular, and about the size of a pea. They contain fluid and coagulated blood, and are trabeculated. Hæmorrhages are scattered throughout the organs, serous membranes and skin.

Symptoms.—The disease is usually ushered in by headache, vague pains in the chest and fever. After some time an eruption of small blebs and vesicles appears on the buccal mucosa and hard palate, and blood is discharged from the nose and mouth. The tongue and parotid glands become swollen. In severe cases bleeding begins from the bladder, rectum and intestines and anæmia develops. Hæmaturia appears rarer in Rhodesian than in West African cases. The temperature may rise to 103° or 104° F., though in fatal cases it may remain subnormal. Relapses are not infrequent.

Diagnosis.—This has to be made from purpura, pemphigus, smallpox and viper bites. The gums are not swollen, nor are the joints involved.

Prognosis.—Natives dread the disease. Gilkes (1934) gives 13 deaths out of 53 cases, and in a series of 17 cases seen by himself, 8 were fatal in a few days and 3 died later from relapses.

Treatment.—A high vitamin diet, including green vegetables, fruit, orange juice, fresh milk and marmite, should be given. Intramuscular injections of whole blood cure the majority of cases. Blood transfusion and iron medication may sometimes be advisable.

CHIUFA

Synonyms.—Chinkumbi; Kanyemba.

Definition.—An acute inflammation of the rectum, commencing at the anus and extending upwards, later involving the colon.

Ætiology.—The disease, which occurs especially in the hot weather and rains, has been described by Gilkes (1934) in natives of the Lunsenfwa and Luangwa Valleys in Northern Rhodesia. The cause is unknown.

Pathology.—No post-mortem examinations have so far been possible.

Symptoms.—The onset is sudden, and the disease runs an acute course which may end fatally in a few days. A white powdery condition appears round the anus, and in females the vulva and vagina may also be implicated. Later the skin becomes reddened and hard, the sphincters relax, and the anus opens out revealing a dilated and acutely inflamed rectum. When the disease involves the colon, diarrhœa and vomiting may occur. Anorexia, rapid loss of weight, and involuntary passage of fæces and urine follow.

Diagnosis.—The disease resembles epidemic gangrenous rectitis, which occurs in tropical South America and may be related to it, though gangrene is not met with.

Prognosis.—This is bad, but recovery may occur.

Treatment.—Only native remedies, so far, have been employed, a powder made from bark and leaves being blown into the rectum. These probably owe any efficacy they possess to their tannic acid content.

MOSSY FOOT

Definition.—An infective disease resulting in a papillomatous condition of the feet and legs, seen especially in natives inhabiting the Amazon valley.

Ætiology.—The disease originally met with in Brazil by Thomas has also been described in Honduras, Costa Rica and Guatemala. Some attribute it to the fungus, *Phialophora verrucosa*, others regard it as a form of tuberculosis cutis. The causative agent is not known with certainty.

Pathology.—Vascular granulomatous warty masses are found in the feet and legs, perhaps covered by yellow crusts. Sinuses do not occur.

Symptoms.—The condition starts as a vesicle on the dorsum of the foot, extending upward until the whole of its surface and possibly also the leg are covered with very vascular and painful warty masses: the sole is not affected. Elephantoid legs are sometimes attacked.

Diagnosis.—The condition has to be distinguished from verruga peruviana, Madura foot and yaws

Treatment.—The cautery is probably the best treatment. X-rays may be tried.

HILL DIARRHŒA (see p. 632)

SPRUE (see p. 638)

G. Carmichael Low.
N. Hamilton Fairley.

SECTION IV

DISEASES DUE TO METAZOA

A. DISEASES DUE TO TREMATODES OR FLUKES (DISTOMIASIS)

PARAMPHISTOMIASIS

Definition– An invasion of man with amphistome flukes of the family *Paramphistomidæ*. Two of these parasites are known. *Watsonius watsoni* (*Cladorchis watsoni*).—L. 8 to 10 mm. × 4 to 5 mm.; Ova, 120 to 130 × 75 to 80 μ. The parasite has a reddish-yellow colour when fresh and inhabits the duodenum and upper part of the small intestine. *Gastrodiscus hominis*.—L. 5 to 8 mm. × 3 to 4 mm.; Ova, 150 × 72 μ. The parasite has a large posterior disc by which it attaches itself to the mucous membrane of the bowel; it occurs in the cæcum and colon.

Symptoms.—Diarrhœa, with loose bilious stools in the case of the former parasite, and intestinal disturbances with diarrhœa in the latter. The eggs of both parasites are found in the fæces.

Treatment.—Carbon tetrachloride (3 c.c.) is probably specific.

FASCIOLIASIS

Definition.– An invasion of man and other animals with flukes of the family *Fasciolidæ*. Several of these are known.

(1) *Fasciola hepatica* (*Distoma hepaticum*), the common liver fluke inhabiting the bile ducts of sheep and other mammals.—L. 20 to 30 mm. × 8 to 13 mm. The ova are operculated and oval, measuring 130 to 145 × 70 to 90 μ. From them miracidia emerge which develop into sporo-cysts, rediæ and cercariæ in snails of the species *Limnæa truncatula*; later the cercariæ encyst on grass stems and are subsequently eaten.

Symptoms.—Man is occasionally infected; light infections may be discovered accidentally during stool examinations, while severe cases may succumb to secondary cholangitis and liver abscess. In sheep the disease produces liver rot, which may be fatal.

Treatment.—Filix-mas administered in milk or capsules in a dose of 0·1 c.c. per kilo. and repeated in 24 hours will destroy adult, but not young, flukes. Good results are reported following a course of emetine injections. Carbon tetrachloride is effective in sheep and has been favourably reported

on in human cases; it is, however, a dangerous drug where there is calcium deficiency. Success has folowed the oral administration of large doses of magnesium sulphate combined with intravenous injections of stibosan.

(2) *Fasciolopsis buski* (*Distoma crassum*)—L. 30 to 70 mm. × 12 to 14 mm; Ova, 120 to 130 × 77 to 80 μ.—This giant fluke is found in China, Borneo, Malaya, Assam, Bengal and other regions in the East: it inhabits the small intestine, particularly the duodenum, producing focal lesions. The immature eggs are voided in the fæces, the miracidium matures in 3 to 7 weeks and escapes through the operculum. It enters certain snails (*Planorbis cœnosus*, *Segmentina nitidella*, etc.) and develops into sporocysts and rediæ which generate cercariæ: the latter encyst on water plants—water caltrop and water chestnut—man becoming infected by eating the corms. The cercariæ excyst in the duodenum and mature.

Synonym.—The incubation period is 3 months. Initial symptoms include hypogastric pain, acid dyspepsia relieved by food, and diarrhœa. Later, asthenia, œdema of the face and extremities, ascites and dry, harsh skin develop.

Diagnosis.—The condition may simulate gastric ulcer or typhoid, and is diagnosed by finding the ova in the stools.

Treatment.—PROPHYLACTIC.—Consists of cooking water caltrops and water chestnuts and sterilisation of night soil.

CURATIVE.—Carbon tetrachloride (3 c.c.), hexyl-resorcinol (1 g.) and beta-naphthol (5–10 grains) are specifics. Thymol or eucalyptus mixture has also been extensively used.

PARAGONIMIASIS

Paragonimus westermani (*Distoma westermani*; *D. ringeri*)

Definition. An invasion of the pulmonary tissues by the lung fluke, a member of the family *Troglotrematidæ*.

Ætiology.—Paragonimiasis occurs endemically in the Far East, especially Formosa, Japan, Korea and China. The adult flukes (7·5 to 12 mm. × 4 to 6 mm.) form cysts in the lung, where the broad, oval, immature, operculated ova (80 to 118 × 50 to 70 μ) escape via the bronchi and appear in the rusty brown sputum: they are also found in the fæces (40 per cent.). After attaining maturity the miracidium emerges, and invades a melaniid snail, especially *Melania libertina*, where it forms sporocysts, rediæ and, later cercariæ which encyst in the gills, liver and muscles of certain fresh-water crabs or cray fish—*Potamon obtusipes*, etc. If eaten by man the adolescaria emerges in the duodenum and migrates via the peritoneal cavity and diaphragm into the lung.

Pathology.—Host reaction results in cyst formation around the fluke, which generally communicates with adjacent bronchi, into which the eggs and anchovy-sauce cyst content are discharged. Pulmonary lesions consist of fibrosis, cystic dilatation of the bronchi, pseudo-pneumonia and tubercle-like abscesses. Similar cysts may involve the intestinal mucosa, bile ducts, peritoneum, pleura, brain, spleen and liver.

Symptoms.—These are divided as follows: (1) *General*, which include adenitis and skin ulcerations; (2) *Thoracic*, characterised by cough and

hæmoptysis with physical signs of broncho-pneumonia, pleural effusions or bronchiectasis ; (3) *Abdominal*, with involvement of the liver, spleen, pancreas or intestine : if the latter, there is diarrhœa with eggs in the fæces ; (4) *Cerebral*, with Jacksonian epilepsy, hemiplegia, monoplegia, aphasia and eye symptoms. Headaches, loss of memory and insomnia may be present.

Diagnosis.—This is made by finding ova in the sputum or fæces. The complement-fixation reaction may be of assistance : eosinophilia is also present.

Prognosis.—Brain cases are fatal, and the outlook is bad in all severe infections.

Treatment.—Abstinence from eating raw fresh-water crab or cray fish prevents the disease. Emetine and tartar emetic temporarily relieve pulmonary symptoms, but cures are doubtful (Faust).

CLONORCHIASIS

Definition.—An invasion of the bile ducts of man and other mammals with trematode parasites of the family *Opisthorchidæ*, occurring in Japan, Korea, China, etc.

Ætiology.—*Clonorchis sinensis* (*Distoma sinense ; Opisthorchis sinensis*, etc.) is a spatulate fluke, measuring 10 to 20 mm. × 2 to 5 mm. Its yellowish-brown ova are oval, possess a well-marked operculum, and measure from 27·3 to 35·1 × 11·7 to 19·5 μ. Viable eggs are ingested by certain bithyniid snails (*Parafossarulus striatulus*, *Bithynia fuchsiana*), and the miracidia, penetrating the soft parts, form sporocysts, rediæ and finally cercariæ, which escape, and encyst in the flesh of certain freshwater fish of the family *Percidæ*, *Gobiidæ* and *Anabantidæ*. When the mammalian host eats infected fish the adolescaria escapes in the duodenum and directly invades the bile ducts, especially the left, owing to its straighter course.

Pathology.—Initially infection leads to primary proliferation of the biliary epithelium and thickening of the duct wall ; later this becomes greatly thickened, and finally cirrhosis of the liver with destruction of the parenchyma results (Faust). The pancreatic duct is sometimes involved.

Symptoms.—Mild cases may be symptomless, but the heavier infections show anorexia, epigastric pain, hepatomegaly, diarrhœa, wasting, jaundice, œdema and ascites.

Diagnosis.—This is made by finding the eggs in the fæces.

Prognosis.—This is dependent on the intensity of the infection ; heavily infected cases occasionally die, but mild and moderate ones invariably survive unless some intercurrent disease develops.

Treatment.—Prevention lies in the cooking of freshwater fish before consumption. Tartar emetic intravenously possibly reduces the number of worms, while gentian, crystal and methyl violet reduce the intensity of infection as measured by the egg-cell count. Gentian violet is given as a keratin-coated pill (2½ grains) thrice daily after meals for 10 days ; for intravenous use 40 c.c. of an 0·5 to 1·0 per cent. solution is injected every other day ; not more than 6 g. is advised (Faust).

When the liver is enlarged and tender, bile drainage may be accelerated by concentrated magnesium sulphate fed through a duodenal tube left *in situ*

for several days. It decreases intra-biliary pressure and absorption of toxic material, but does not cure.

HETEROPHYIDIASIS

Definition.—Infection with flukes of the family *Heterophyidæ*. Three genera occur in man.

(1) *Heterophyes heterophyes* (*Distoma heterophyes*, etc.). A minute intestinal fluke infesting man, the dog, cat, etc., in Egypt, measuring 1·0 to 1·7×0·3 to 0·4 mm. The oval, light-brown, operculated ova measure 28 to 30×15 to 17 μ. Though the life cycle is not completely known, the cercariæ encyst in mullet (*Mugil cephalus*), the ingestion of which causes infection.

(2) *Heterophyes katsuradai* differs morphologically in the great size of its acetabulum, etc.

(3) *Metagonimus yokagawai*.—This pear-shaped fluke measures 1 to 2·5× 0·4 to 0·75 mm., while its eggs closely resemble *H. heterophyes*, measuring 26·5 to 28×15·5 to 17 μ. The life cycle passes through *Melania libertina* and allied molluscs, the cercariæ encysting in the edible fish, *Plectoglossus altivelis*.

(4) A number of other heterophyid flukes, including *Monorchotrema taichi*, *M. taihokui*, *Diorchitrema pseudocirrata* and *Heterophyes brevicæca*, have been recorded by Africa and Garcia from Manila.

Pathology.—The flukes become attached to the intestinal mucosa by their suckers, inducing mild inflammatory reactions and eosinophilia.

Symptoms.—Mild digestive disturbances and diarrhœa with blood in the stools may result in severe infections. Often the condition is symptomless, the diagnosis being made by finding ova in the fæces. In their cases in Manila, Africa and Garcia have described a condition of cardiac heterophyidiasis, resembling cardiac beriberi, associated with sclerosis of the mitral valves and fibrosis of the myocardium; heterophyid ova were demonstrated in the local lesions.

Treatment.—Carbon tetrachloride, betanaphthol, thymol, the oleoresin of aspidium, or eucalyptus, castor oil and chloroform mixture are efficacious in eradicating the infection. To find the parasites, the stools must be strained through muslin.

SCHISTOSOMIASIS (BILHARZIASIS)

Definition.—Invasion of man with blood flukes of the family *Schistosomidæ*. Three species are well known—*Schistosoma hæmatobium*, *S. mansoni* and *S. japonicum*. More rarely man may be affected by *S. bovis* and *S. matthei*. *Life cycle.*—The parasites inhabit the portal veins and their tributaries, depositing ova in the hollow viscera, whence they escape via the urine or fæces; on contact with water miracidia emerge, invade the appropriate molluscan intermediary, in which sporocysts and cercariæ develop (Miyairi and Leiper). The latter invade the skin and find their way to the portal system, where the schistosomulæ mature. The tuberculated male, originally a flattish fluke, has become rounded by inrolling of its edges to

form the gynæcophoric canal, in which the thread-like female lies. Both sexes have an anterior, prehensile sucker and a posterior, suctorial sucker by which the worm maintains its position against the portal blood stream.

S. hæmatobium (*Bilharzia hæmatobia*) occurs in Africa and parts of Western Asia, etc. (♂ 10 to 15 mm.×0·8 to 1·0 mm.; ♀ 20 mm.×0·25 mm.). The ova have a sharp terminal spine and measure 120 to 160×40 to 60 μ. The intermediary hosts vary considerably, being *Bulinus contortus*, etc., in Egypt, *Physopsis africana* in Natal, and *Planorbis metidjensis* in Portugal. *S. mansoni* is found in Africa, South America, etc. (♂ 10 to 12 mm.×1·0 to 1·2 mm., ♀ 12 to 16×0·16 mm.). The ova have a lateral spine and measure 140 to 165×60 to 70 μ. The intermediary host is *Planorbis boissyi* in Egypt, and *Physopsis africana* in Natal, etc. *S. japonicum* is confined to the Far East—Japan, China, Formosa and the Philippines (♂ 12 to 20 mm.×0·5 to 0·55 mm., ♀ 15 to 26 mm.×0·3 mm.). The ova possess a lateral knob and measure 100 to 110×55 to 65 μ. The intermediate hosts are *Katayama nosophora*, *K. formosana* and *Oncomelania hupensis*.

Pathology.—In *S. japonicum* and *S. mansoni* the worms are found in the portal system, especially its mesenteric branches, ova being deposited in large numbers in the colon and liver, and to a lesser degree in the small intestine, mesenteric glands, stomach, pancreas and rarely the spleen. In *S. hæmatobium* they wander still farther afield via the inferior hæmorrhoidal plexus into the pelvic plexuses of veins, especially the vesical, prostatic and uterine; eggs are deposited in the bladder, prostate, seminal vesicles, urethra, the lower third of the ureter, cervix and vagina. These plexuses communicate with the inferior vena cava; in consequence stray ova filter out into the lungs rather than the liver. Apart from toxic effects and suctional trauma produced by the schistosomes themselves, the egg deposits cause considerable local inflammatory reaction, at first giving rise to small pseudo-tubercles initially composed of giant cells, eosinophiles and round cells; later these disappear or are replaced by whorls of fibrous tissue in which degenerated and calcified eggs are found. The characteristic papillomata form as a combined result of irritative downgrowth of epithelium produced by toxic substances liberated from worms and ova, and submucous cellular accumulations pressing the mucosa upwards from below.

Special pathology.—*S. japonicum* and *S. mansoni* produce various colonic lesions, including round, whitish, submucous pseudo-tubercles, bilharzial colitis, and papillomata, which may slough off, leaving round ulcers. All these lesions may be visible with the sigmoidoscope. In addition, marked fibroid thickening and contractures of the bowel wall, mesentery and omentum sometimes occur. Periportal cirrhosis of the liver, which may or may not be associated with bilharzial splenomegaly, is met with. Other lesions include rectal papillomata, prolapse of the rectum, perineal granulomata and ischio-rectal fistulæ. In *S. mansoni* egg deposits in the spinal cord may produce myelitis, and granuloma of the brain simulating cerebral tumour is recorded in *S. japonicum*. In *S. hæmatobium* vesical lesions are dominant, but in addition there may be involvement of the ureters (lower third), chronic fibrosis of the prostate and seminal vesicles, bilharzial infiltration of the cervix, vagina and periurethral tissues with sinus formation, and granulomata of the penis and vulva. In the bladder the earliest lesions are minute petechiæ and round, yellowish, pseudo-tubercles studding its surface; later,

papillomata and ulcers may develop, while chronic fibroid thickening and the so-called "sandy patches" are very characteristic of the chronic stages with calcified eggs. These lesions are demonstrable cystoscopically. Pulmonary fibrosis associated with egg deposits is not uncommon, but involvement of the colon and liver is minimal.

Symptoms.—Three stages can be recognised: (1) invasive; (2) toxic or anaphylactoid; (3) localised disease (*a*) early, (*b*) late.

(1) *Invasive.*—The entry of cercariæ may give rise to transient rash and local irritation lasting 24 to 48 hours (Kabure disease).

(2) *Toxic or anaphylactoid.*—Within 2 to 8 weeks a clinical syndrome may appear, characterised by urticaria and an intense eosinophile leucocytosis; in addition there may be rigors, abdominal pain, enlarged, tender liver and spleen, dyspnœa, bronchitis, anorexia, diarrhœa and fever, lasting a few days to several weeks; the severe cases often simulate typhoid. This stage is most marked in *S. japonicum* (Katayama disease), but it is also described by Lawson in *S. mansoni* and by Fairley in *S. hæmatobium*.

(3) *Localised disease.*—Local features dependent on egg deposition in the bladder or colon are not generally apparent for 3 to 9 months after infection. In *S. hæmatobium* early symptoms include scalding or frequent micturition, penile, perineal, suprapubic or loin discomfort or pain, and terminal hæmaturia, the blood being bright red and increased by exercise. At this stage the prostate may be congested and tender, cystoscopic examination shows the characteristic yellow, round pseudo-tubercles, and the urine contains leucocytes, erythrocytes and terminal-spined ova which may also appear in the fæces (40 per cent.). For years intermittent hæmaturia may be the only clinical manifestation, the subsequent course depending on such complications as carcinoma, cystitis with an alkaline urine containing much muco-pus, and renal involvement. In *S. mansoni* localised features may be absent or a chronic bilharzial dysentery may develop, characterised by colicky abdominal pain, the passage of blood and mucus, and tenesmus. Between attacks there is rectal discomfort, but the stools are solid, and coated with mucus, which may contain the characteristic lateral-spined ova. Later periportal cirrhosis and splenomegaly with ascites, etc., may supervene. In *S. japonicum* similar dysenteric symptoms are present. The chronic stage with cirrhosis and splenomegaly is characterised by weakness, emaciation, pallor, secondary anæmia, dilatation of the abdominal veins, and finally ascites and liver insufficiency.

Complications.—In *S. hæmatobium* there may be chronic nephritis or hydronephrosis due to backward pressure, or septic cystitis with pyonephrosis or ascending pyelonephritis. Carcinoma of the bladder, penis or vulva may also ensue, while bilharzia papillomata and vesical calculi are not uncommon. In *S. japonicum* and *S. mansoni* hepatic cirrhosis, liver insufficiency or carcinoma of the liver may supervene.

Diagnosis.—In the early toxic or anaphylactoid stage the diagnosis may be suggested by the intense eosinophilia and confirmed by the cercarial complement-fixation reaction (Fairley). In the localised stage the diagnosis is generally made by finding ova in the excreta, but the complement-fixation reaction, the intradermal skin test (cercarial antigen), and the cystoscopic or sigmoidoscopic findings often prove of great value. In examining for *S. mansoni* or *S. japonicum* the mucus covering of the stool should be selected,

and in *S. hæmatobium* the last few cubic centimetres of urine passed ; several examinations may be necessary and eggs may be found in scrapings from the bowel wall obtained with a blunt curette during sigmoidoscopy, when ordinary fæcal examinations are negative.

Prognosis.—The prognosis is bad in patients continuously exposed to infection, or in late cases when hepatic or renal insufficiency, septic infection or carcinoma has supervened.

Treatment.—PROPHYLACTIC.—This consists in curing the disease in man, in preventing excretal contamination of water, in destruction of snail vectors and in avoiding contact with infected water.

CURATIVE.—Two trivalent antimony compounds, tartar emetic and stibophen (fouadin), as well as emetine hydrochloride, exert a specific lethal action on the adult schistosome. During treatment rest in bed is advisable, especially if complications exist, but in Egypt and elsewhere often ambulatory treatment is alone practicable.

(1) *Tartar emetic*, first successfully introduced by Christopherson, is given intravenously in 10 c.c. of saline every second day, commencing with $\frac{1}{2}$ grain doses and increasing by $\frac{1}{2}$ grain until a maximum of 2 grains is attained. The solution must be freshly sterilised, and the total course for the adult should equal 30 grains. The drug kills the schistosomes, and viable ova rapidly disappear from the excreta. Cough, vomiting and toxic muscular pains may follow its administration, but the drug is generally well tolerated except in cases complicated by hepatic cirrhosis, renal involvement, sepsis, etc. Great care must be taken not to inject the solution into the tissues, as severe inflammation and necrosis result.

(2) *Stibophen* (*fouadin*) (antimony-pyrocatechin-disulphonate of sodium) should be given in an all-glass syringe in 6·3 per cent. solution ; the total course consists of 40 c.c. administered in nine intramuscular injections extending over a period of 15 days. According to Khalil, the therapeutic results compare favourably with those obtained by tartar emetic

(3) *Emetine hydrochloride* is advised by Tsykalas in doses of $1\frac{1}{2}$ grains for 8 to 10 days. Though lethal to schistosomes, toxic complications are liable to develop and now that stibophen is available for intramuscular injections in children there is little justification for its use. The usual medical and surgical measures should be employed for complications as they arise, and rectal and other polyps which do not resolve with specific therapy may need excision with the electric cautery.

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B. DISEASES DUE TO CESTODES

TÆNIASIS—TAPE-WORMS

Definition.—Tæniasis is produced by different forms of tape-worms occurring either as adults in the intestine (intestinal tæniasis), or as the developmental stage in the muscles and other host tissues (somatic tæniasis).

Intestinal Tæniasis

(1) *Tænia solium* (Linnæus, 1758).—The pork tape-worm measures 2 to 3 metres in length. The head is globular and possesses 4 suckers, a rostellum and a double row of hooks. The uterus never has more than 12 lateral processes (diagnostic). The ova are spherical, 31 to 40 μ in diameter, having a thick-walled shell and an oncosphere with 3 pairs of hooklets. The cysticerus stage is passed in the pig (*Cysticercus cellulosæ*), and man becomes infected by eating undercooked "measly" pork. Pickling and smoking do not kill cysticerci.

(2) *Tænia saginata* (Goeze, 1782).—The beef tape-worm measures 3 to 4 metres in length. Its head is cubical with 4 suckers, but no armature; the uterus contains 15 or more lateral processes, thus differentiating it from *T. solium*, though its oval eggs, measuring 33·40×20·30 μ, may be indistinguishable. The cysticercus stage is found in the ox (*Cysticercus bovis*) and man becomes infected by eating undercooked beef.

(3) *Dipylidium caninum* (Linnæus, 1758).—A common tape-worm of the dog is occasionally found in man. Human infestation with *Tænia confusa*, *Tænia africana* and *Bertiella satyri* has been described on two or three occasions.

(4) *Hymenolepis nana*.—This dwarf tape-worm, which is common in Southern Europe, the Southern United States and India, inhabits the small intestine of man. It measures 2·5 to 4·0 cm. in length, has 4 hemispherical suckers and a short rostellum with a single row of hooks. The eggs measure 30 to 40 microns in diameter and contain an onchosphere. No intermediary host is required, as the eggs hatch out in the intestine. After penetrating the mucosa the embryos develop into cercocysts, return into the lumen of the bowel, become attached by their heads to the villi and develop into mature worms.

(5) *Diphyllobothrium latum* (Linnæus, 1758) (*Tænia lata*, etc.).—The broad, fish tape-worm, some 2 to 10 metres long, possesses an almond-shaped head, but no armature. The immature eggs are oval, operculated and measure 70×45 μ. After 3 to 5 weeks' development in water the hexacanth embryo escapes and is ingested by some species of cyclops or allied crustacean in the body cavity of which it develops into a procercoid larva. Infected crustaceans must be swallowed by certain fish, *i.e.* before the plerocercoid larva develops. Man becomes infected by eating the undercooked, infected fish. Other species, such as *D. cordatum*, *D. parvum* and *D. houghtoni*, have been described on one or two occasions as has also *Diplogonoporus grandis* and *Braunia jassyensis*.

Symptoms.—Symptoms may be absent, or gastro-intestinal disturbances, such as anorexia, voracious appetite, dyspepsia, abdominal pain, colic and diarrhœa may result. Neurasthenia in adults, and headache, convulsions and strabismus are described in children. Occasionally *D. latum* is associated with severe megalocytic anæmia.

Diagnosis. The diagnosis is made by identifying the appropriate segments or ova in the excreta. Skin hypersensitiveness to tape-worm protein and eosinophilia may be present.

Treatment.—Filix mas and carbon tetrachloride are effective remedies for all the tape-worms, provided preliminary starvation and terminal purgation with salines be instituted. After a liquid diet, consisting of broths,

orange juice, dextrose, etc., for 2 days, during which time the bowels are well opened, extractum filicis liquidum in 30 mimim doses is given in gelatine capsules or emulsion at 8.0, 8.20 and 8.40 a.m. In obstinate cases an extra 30 minims may be given at 9 a.m. and 30 minims of oil of turpentine as well. Sodium or magnesium sulphate (gr. 240) is administered at 10 a.m., and all the motions subsequently passed must be carefully sieved and examined against a black background to identify the head; castor-oil must never be used as it dissolves out filicic acid and leads to poisoning. If the head is not recovered, treatment may be repeated in 10 days' time, or 3 months' interval may be allowed, by which time segments will have generally reappeared if the worm has survived. Carbon tetrachloride is given in capsules, the maximum adult dose being 3 c.c.; this is followed by a saline purge 3 hours later. Some report that it is advantageous to combine oil of chenopodium (1 c.c.) with carbon tetrachloride therapy, as in the treatment of ancylostomiasis.

Somatic Tæniasis

(1) *Sparganum mansoni.*—This is the plerocercoid stage of *Diphyllobothrium mansoni* (Cobbold, 1882) which has a somewhat similar life-history to *D. latum*. The adult worm infests the intestine of the dog and cat, the ciliated embryo is ingested by *Cyclops leuckarti* where it develops into a procercoid larva. When swallowed by the second intermediate host, which may be a snake, bird or mammal, including man, the cyclops is digested, the liberated larva penetrates the stomach and, travelling under the peritoneum, reaches the deep somatic muscles, also the iliac fossa, lumbar region, pleura, urethra and eye where it multiplies asexually by transverse fission, many spargana resulting from a single plerocercoid (Faust). Ingestion of sparganа-infested tissues by the dog and cat results in intestinal tæniasis, but the adult stage does not develop in man.

Symptoms.—Pain, swelling and œdema of the subcutaneous tissues and muscles sometimes occur, and in ocular sparganosis, which is common in the Tonkin delta, inflammation with pain, redness, œdema, lachrymation and ptosis may result. Human infection in China often follows the direct transference of spargana from infected frogs which are applied locally in the treatment of ulcers, etc. (Joyeux and Houdemer).

Diagnosis.—This is made by finding the unbranched sparganum larvæ embedded by their scolices in a slimy matrix in the tissues.

Treatment.—Where possible the parasite is removed surgically.

(2) *Sparganum proliferum* (Ijuma, 1905).—This species affects man in Japan, innumerable spargana producing nodules and honeycombing of the tissues, and elephantiasis if the lymph channels be involved. The adult stage and life cycle are unknown.

(3) *Tænia solium.*—The cysticercus stage of *T. solium, i.e.* cysticercosis, is occasionally found in man who may or may not have harboured the adult parasite. The cyst, which is generally surrounded by a fibrous-tissue capsule, consists of an opalescent bladder containing a single evaginated head with hooklets. Various tissues, including the brain and its ventricles, the liver, lungs, orbit and the somatic muscles and heart, may be involved. It occurs in Europe, Africa and Madagascar, and in soldiers returning from India and Egypt. Macarthur has recently found it to be a common source of epilepsy.

Man probably acquires the disease by auto-infection, or eating uncooked food, such as lettuce, to which dried segments of *T. solium* are adherent.

Symptoms.—Subcutaneous nodules ($\frac{1}{2} \times 2$ cm.), muscular weakness, cramp and pains may be encountered, also Jacksonian epilepsy, petil mal, various psychoses and occasionally focal lesions of different types, if the brain be involved (*Cysticercus cellulosæ*). The diagnosis is established by biopsy of a subcutaneous cyst, or X-ray examination revealing calcified nodules in the muscles. Ophthalmoscopic examination may show retinal lesions, while eosinophilia and skin hypersensitiveness and positive complement-fixation reactions with tænia antigens may be found. Accessible cysts can be excised, but the prognosis is bad if the brain be involved. The most dangerous period is the sixth to the eighth year, when cerebral disturbances most frequently occur. Mental deterioration and death generally result, but occasionally even those developing cysts recover. Fits should be controlled by luminal and bromide.

(4) *Tænia multiceps* (Leske, 1780).—*Cœnurus cerebralis*, the cystic stage of the canine tape-worm, *T. multiceps*, commonly affects the brain of goats and sheep; it has been recorded in man, producing epilepsy and aphasia.

(5) *Echinococcus granulosus* (Batch, 1786).—This small tape-worm (2·5 to 6 mm. in length) inhabits the intestines of dogs, jackals and wolves; it consists of a head with 4 suckers, a rostellum and hooklets and 3 or 4 segments, of which only the terminal one is gravid. In the intermediate hosts, which include sheep, cattle, pigs and man, hydated disease is produced. Man becomes infested from swallowing water and uncooked vegetables, etc., contaminated with infected canine fæces, or by handling and fondling infected dogs. Hydatid disease is frequently contracted in childhood and is most common in sheep-breeding countries like Australia, New Zealand, the Argentine and South Africa; it also occurs in Iceland but is less frequently encountered in Europe.

After the egg is swallowed, the six-hooked embryo escapes from its shell, traverses the intestinal wall, invades the blood vessels, and metastasises generally in the liver, but less frequently in the lungs, brain, bones, and muscles, etc., where it loses its hooks and forms a cyst, the wall of which consists of two layers, a laminated outer layer, the ectocyst, and a granular inner layer, the endocyst. As the cyst grows, it exerts mechanical pressure and toxic effects on adjacent host tissue, resulting in inflammatory reaction and the formation of a fibrous tissue capsule known as the adventitia. Endogenous budding from the granular layer of the cyst results in the formation of brood capsules, scolices, and daughter and granddaughter cysts. Exogenous budding sometimes occurs, especially in bone, while atypical development in viscera like the liver may result in alveolar or multilocular types of hydatid. It is improbable that a second parasite, *E. multilocularis*, exists.

Symptoms.—The clinical picture is very varied. Cysts may be symptomless for many years until pressure effects are produced, or they may rupture or suppurate with the production of acute illness. Rupture into a vein may lead to sudden death from an embolus of daughter cysts, or to an anaphylactic syndrome characterised by injected conjunctivæ, lachrymation, vasomotor collapse, urticaria, œdema, respiratory distress and eosinophilia. Rupture into the peritoneal cavity may produce an acute abdominal crisis followed by peritoneal echinococcosis, secondary cysts developing from scattered scolices, or if the cyst rupture into a bronchus natural cure may ensue. Suppuration,

especially of liver cysts, is not uncommon, while in some 30 per cent. of cases their degeneration and death with subsequent calcification lead to natural cure. The inferior aspect of the right half of the liver is the commonest site affected, while the right lung is three times as often involved as the left. Brain cysts closely simulate cerebral tumour, while echinococcosis of bone, owing to its rapid exogenous growth, often leads to a fatal issue, especially when the pelvis and vertebral column are involved ; a pressure myelitis may result.

Diagnosis.—A history of contact with dogs in childhood is important ; hydatid thrill, if present, is pathognomonic. Collapsed cysts, membrane, scolices and hooklets may be coughed up or passed per rectum, while the aspiration of a clear watery fluid containing considerable amounts of sodium chloride and hydatid elements clinches the diagnosis. Aspiration, however, should never be carried out in lung cysts except on the operating-table owing to the danger of drowning from rupture into the bronchial tract. X-ray examination is of considerable importance in localising liver and lung cysts, while the complement-fixation and precipitin reactions and the intradermal test have greatly increased the percentage of cases correctly diagnosed before operation. Eosinophilia may occur, especially if a cyst has recently ruptured.

Treatment.—No medical treatment is available except for the anaphylactic syndrome, when adrenaline (10 min. of 1 in 1000 solution) should be administered. As a rule, calcified cysts should not be operated on. After the injection of formalin to kill scolices in hepatic cysts the contents should be evacuated and the adventitia sewn up in smaller sized cysts ; suppurating and large cysts must be drained. Special care must be taken to prevent soiling of the peritoneum with the cyst contents in hepatic hydatid, as secondary peritoneal echinococcosis is liable to develop.

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C. DISEASES DUE TO NEMATODES (ROUND-WORMS)

STRONGYLOIDIASIS

Strongyloides stercoralis (Bavay, 1876).—A common tropical parasite of man, the female worms living in the jejunum and duodenum, and in massive infections invading the bile and pancreatic ducts, the stomach and colon.

Ætiology.—The eggs hatch out rhabditiform larvæ which appear in the fæces : rarely, where intense diarrhœa is present, the eggs (50–80 × 30–34 μ), which resemble ancylostome ova, may be found. The rhabditiform larvæ give rise either directly, or indirectly through a sexual circle, to filariform larvæ which invade the skin or mucosa and follow a similar route to ancylostomes proceeding via the lung to the intestine.

Pathology.—Intestinal catarrh or an enteritis, with extensive erosions of the mucosa, giving rise to a " beefsteak " appearance, may occur in heavy infections.

Symptoms.—Initial dermatitis and lung symptoms may be seen during the first few days. Mild infections show no symptoms ; severer infections

may present epigastric discomfort after meals, flatulence and diarrhœa which occasionally is very intractable. Occult blood may occur, urticaria and œdema sometimes develop at the site of entry of infective larvæ, and dermal sensitivity can be demonstrated to strongyloid extracts (Fülleborn).

Diagnosis.—This is made by finding the rhabditiform larvæ in the stools, which should be mixed with water and strained through muslin. Hook-worm embryos have a longer pre-œsophageal mouth cavity and occur within the egg.

Treatment.—Gentian violet, recently introduced by De Langar, appears to be a specific when given as a keratin-coated pill (1 grain) thrice daily before meals. It is best administered in two courses, each lasting 8 days, separated by a week's interval, during which no gentian violet pills are taken.

Allied helminths, including *Rhabditis pellio* (Schneider, 1886) and *Turbatrix aceti* (Müller, 1783), the common vinegar worm, have been reported in the vaginal exudate and urine of women.

FILARIASIS

An invasion of man by members of the family *Filariidæ*. Several species are known to infest man, *Filaria bancrofti* or *Wuchereria bancrofti*, *Filaria loa* and *Loa loa*, *Filaria perstans* or *Acanthocheilonema perstans* transmitted by *Culicoides austeni*, and *Filaria ozzardi* or *Mansonella ozzardi*, the insect vector being *Culicoides furens*. Only the first two are of clinical importance. Two larval *Filariidæ* are known in which the adults have not been found—*Microfilaria malaya* (Brug, 1927) occurring in the peripheral blood at night, and *Agamofilaria streptocerca* (Macfie and Corson, 1922) found commonly in the skin of natives on the Gold Coast.

(1) *Filaria bancrofti* (Cobbold, 1877).—This parasite has a widespread tropical distribution, being especially common in India, the West Indies, Porto Rico, Southern China and the Pacific Islands. The adults are like fine catgut (♂30 40 mm. long; ♀ 76–100 mm.×0·2 mm.); they inhabit the lymphatics and periglandular lymphatic tissue, and produce embryos which subsequently invade the blood stream, living in the lungs and thoracic blood vessels by day and appearing in the peripheral blood only at night—noctural periodicity. The embryos are enclosed in a loose sheath and measure 230–320×7·5–10 μ. As Manson first showed, the intermediate host is a mosquito (chiefly *Culex fatigans*), which sucks the embryos out of the blood at night; metamorphosis subsequently takes place in the thoracic muscles. The mature embryos are inoculated into man via the proboscis (Low). Development in the insect vector takes from 10 to 40 days, depending on the temperature, etc. In the Pacific where *F. bancrofti* is transmitted by *Aëdes variegatus*, which bites in the daytime, the filaria is non-periodic in type. It is possible, however, that this filaria is of a different race or sub-species.

Pathology.—The parent worms may produce little damage: at other times they injure the lymphatics, causing filarial lymphangitis, abscess, varicose groin glands, chylocele, lymph scrotum, filarial orchitis, hydrocoele, chyluria, chylous ascites and elephantiasis which often involves the lower extremities, scrotum or vulva. These changes are partly mechanical and partly attributable to helminthic toxins and secondary streptococcal infec-

tion, which induce lymphangitis and inflammatory changes in the tissues, resulting in fibrosis, obstruction and lymph stasis.

Symptoms.—The disease is symptomless unless obstruction to the lymph-flow and lymphangitis ensue; the latter is associated with rigors, high fever, tender enlargement of lymphatic glands and inflammatory swelling of the affected parts. O'Connor has recently described palpable focal spots, consisting of dead worms from which the lymphangitis may radiate upward or downward in the limb. Filarial abscess associated with death of parent filariæ may form in the limbs and scrotum, and is generally complicated by secondary bacterial infection. Filarial orchitis (endemic funiculitis) is really a lymphangitis involving the spermatic cord. Recurrent attacks may lead to hydrocoele. In lymphuria and chyluria the patient often passes white, milky urine which may be mixed with blood. Other clinical manifestations depend on the site and nature of the lesions.

Diagnosis.—The presence of an unexplained eosinophilia may suggest searching the blood for embryos, while the intradermal test, using *Dirofilaria immitis* extract as antigen, is of value in distinguishing the non-filarial from filarial types of elephantiasis where embryos have generally disappeared.

Treatment.—Prophylaxis depends on mosquito destruction and the use of mosquito nets, etc. No specific drug treatment is known, but the application of an ethyl chloride spray to focal points has been recently advocated to abort lymphangitis. Where secondary streptococcal infection has supervened, sulphonamide therapy is indicated. Surgical intervention may be necessary for various elephantoid conditions. In elephantiasis of the legs elastic bandaging, massage and rest, with elevation of the limbs, are desirable. Elastic stockings should be washable, porous, and made to fit, extending from the dorsum of the foot to above the knee.

(2) *Loa loa* (Cobbold, 1864).—Human infestations with this parasite occur in West Africa. The adults inhabit the subcutaneous and retroperitoneal tissues, while the sheathed embryos have a diurnal periodicity (9 a.m. to 9 p.m.); several years may elapse before embryos appear in the peripheral blood. Transmission is by certain species of mango-fly (*Chrysops dimidiata* and *C. silacea*) which feed in the daytime. Clinically the worms give rise to urticarial eruptions and puffy, painless, white swellings the size of a hen's egg, lasting 2 to 3 days, known as Calabar swellings. These are due to an œdema of the subcutaneous tissue and probably represent an anaphylactoid reaction to helminthic products or toxins. Leucocytosis associated with a marked eosinophilia (20 to 60 per cent.) is characteristic, and dermal hypersensitiveness to diro-filarial extract is shown in almost every case. Positive complement-fixation reactions are also given with diro-filarial alcoholic extracts. Neuritic pains may also be complained of. Not infrequently the worms appear about the eye, and in their migration across the conjunctivæ give rise to transient conjunctivitis and lachrymation. Where visible, the worm should be surgically removed under local anæsthesia.

ONCHOCERCIASIS

Onchocerca volvulus (Leuckart, 1893).—This nematode, found on the west coast of Africa, inhabits the subcutaneous or connective tissues of man,

often giving rise to nodular, subcutaneous, cystic tumours, 1 to 10 cm. in diameter, over which the skin is generally movable, and in which lie entangled masses of worms and embryos encased in dense fibrous tissue. The swellings are particularly common around the elbows, knees, ribs, iliac crests and great trochanter. Unsheathed microfilariæ may occasionally be demonstrated in the skin, especially of the loin and thigh, as well as in the circulatory blood and subcutaneous lymph channels, even though no evidence of disease exists. Dermal lesions, including achromia, xeroderma and pseudo-ichthyosis, are attributed to embryos located in the skin (Laigret). Pruritus may be intense, especially at night. Onchocerca tumours of the head are not infrequently associated with ocular complications. Blindness may result from retino-choroiditis or punctate iritis when embryos are found in the anterior chamber. Blacklock has shown that transmission is by the buffalo gnat, *Simulium damnosum*. Localised tumours may be removed under local anæsthesia.

The parasite called *Onchocerca cæcutiens* (Brumpt, 1919) is found in Guatemala and Mexico. Its status as a distinct species has for some time been doubtful, and the recent work of Strong indicates it is the South American form of *O. volvulus*. It produces flat nodes (Guatemala nodules) up to 2 cm. in diameter, especially affecting the scalp and face, and an eruption known as "coastal erysipelas," associated with pain, tumefaction and fever may result from secondary streptococcal infection of the skin due to scratching, the irritability being caused by microfilariæ in the corium. More important are the ocular lesions caused by microfilariæ, piercing the capsule of the nodules and invading the tissues of the eye, producing conjunctivitis, punctate iritis, keratitis and choroiditis. Blindness commonly follows (Strong). An eosinophile leucocytosis is the rule. Diagnosis is made by demonstrating the microfilariæ in the milky fluid aspirated from the nodules, or in adjacent pieces of skin shaved off and teased up in saline at 37° C. for microscopical examination. Transmission is by three different species of *Simulium*, the coffee flies living at a height of 2500–5000 feet. The nodules should be excised whenever possible, especially those in the vicinity of the eyes. Some improvement in the ocular condition may follow this procedure.

DRACONTIASIS

Dracunculus medinensis (Linnæus, 1758). — Guinea-worm disease is common in India, Persia and Africa. The adult female, measuring 40–120 cm. ×0·5–1·7 mm., inhabits the subcutaneous and interstitial tissues, and takes some 12 months to reach the skin where it secretes some toxin producing a blister which later ulcerates, and permits, on contact with water, the reflex discharge of embryos from the prolapsed uterus which perforates the base of the ulcer. The worm itself is often surrounded by a fibrous-tissue canal. Fedtschenko, in 1879, produced evidence that a cyclops was the intermediate host. Man becomes infected by swallowing these crustaceans in drinking water.

Pathology.—Three factors are responsible for pathological lesions, namely, the worm, the embryos and secondary bacterial invaders. The toxic substance responsible for blister formation may, if absorbed, lead to anaphylactoid symptoms. Premature ejaculation of embryos may produce

subacute sterile abscess. Bacterial invaders, especially *Staphylococcus aureus*, *Bacillus coli* and streptococci are responsible for acute abscess, cellulitis, bubo, synovitis, arthritis and septicæmia; these complications almost invariably result from the retraction into the tissues of a taut, elastic worm, broken during efforts to extract it.

Symptoms.—Prodromal symptoms consist of an itchy, urticarial eruption (40 per cent.) which may be associated with vasomotor collapse, vomiting, diarrhœa, dyspnœa and high eosinophilia followed a few hours later by blister formation and ulceration (Fairley). The lower extremities are commonly involved (86·5 per cent.), and in decreasing frequency the arms, trunk, buttock and scrotum. Septic complications are frequent, and contracture of tendons and fibrous ankylosis of joints sometimes result. Neuritis and muscular rheumatism may be produced by calcified worms, which on X-ray examination show a pathognomonic, convoluted, moniliform shadow.

Treatment.—This depends on the stage at which the patient is seen. Anaphylactoid symptoms are best treated by injections of adrenaline (min. x. of a $\frac{1}{1000}$ solution). A blister, if present, should be aspirated. Once an ulcer has formed it must be treated with antiseptic dressings and the worm subsequently extracted either by intermittent traction and massage, or by multiple incisions under local anæsthesia. The outline of the worm becomes more obvious if the tissues are sprayed with ethyl chloride. When the worm is closely convoluted the whole area may be excised *en masse*. The old method of gradual extraction by winding round a match and daily douching with water until the uterus is emptied still has its advocates. Localised abscess must be treated by passing a probe through the sinus and slitting up the canal in which the worm lies. Other complications are treated along general surgical lines.

TRICHINIASIS

Definition.—A disease produced by the embryos of *Trichinella spiralis* (Owen, 1835) during their migration from the human intestine to the muscles.

Ætiology.—Infection is acquired by eating raw or underdone pork in which the larvæ have encysted. After the cyst walls have been dissolved by the gastric juice the embryos mature and breed in the small intestine. The gravid female bores into the mucosa, depositing hundreds of viviparous larvæ (100×6 μ) which reach the muscles from about the ninth to the fortieth day via the liver, lung and left heart. The adults are small (♂ 1·4–1·6 mm.$\times$0·04 mm.; ♀ 3–4 mm.$\times$0·6 mm.) and live only a few weeks, whereas encysted larvæ may survive for 25 years, though they often calcify within 6 months. Rats act as reservoir hosts.

Symptoms.—For the first week during the invasion period gastro-intestinal symptoms develop with nausea, vomiting, colic and diarrhœa with perhaps blood and mucus; then when migration of larvæ commences myositis of the tongue, laryngeal and intercostal muscles and the diaphragm occurs, giving rise to difficulty of swallowing, speech and respiration. The muscles of the jaws, arms, legs and abdomen may also be involved with stiffness and pain; the affected areas are exquisitely tender and hard to the touch. Œdema, especially of the face, urticaria, leucocytosis with high

eosinophilia, prolonged remittent fever (102°-104° F.) and sweating are characteristic. Pulmonary features are common, and occasionally hæmoptysis occurs. Cachexia develops and, finally, during the period of larval encystment, the patient may succumb from toxæmia with respiratory disturbance and coma.

Diagnosis.- Early, the disease may be mistaken for ptomaine poisoning, enteritis or dysentery, and later for rheumatic fever or typhoid. The intense eosinophilia should arouse suspicion, while later biopsy of a piece of the affected muscle such as the deltoid at its tendinous insertion will often reveal precystic or encysted larvæ. Embryos may be found in the blood, especially from the twelfth to the twentieth day, by laking it with ten volumes of 3 per cent. acetic acid and centrifuging the deposit. Intradermal and precipitin tests are often positive to an antigen manufactured from the embryos (Bachman). At a late stage, calcified cysts may sometimes be visualised by X-ray.

Prognosis.—This largely depends on the intensity of the infection, the mortality rate varying in different outbreaks from 1 to 30 per cent. Convalescence is often slow and muscular atrophy may follow.

Treatment. —PROPHYLACTIC.- This depends on careful meat inspection, and adequate boiling of pork; curing by smoking and salting is ineffective. Special care should be taken at autopsy to prevent infection.

CURATIVE.--No specific treatment is known, but every effort should be made to expel the adult worms. Purgatives and glycerin, santonin, thymol and turpentine are employed for this purpose.

ŒSOPHAGOSTOMIASIS

(1) *Œsophagostomum apiostomum* (Willach, 1891).—This nematode frequently affects certain anthropoid apes and monkeys in West Africa, and not uncommonly man in Northern Nigeria. The rhabditiform larvæ exsheathe in the cæcum, invade the bowel wall and give rise to inflammatory nodules in which they develop; later they erupt into the intestine and mature. Dysentery-like symptoms, with hæmorrhage and occasionally peritonitis and septicæmia, may result. The ova are indistinguishable from ancylostome eggs, but fortunately thymol, oil of chenopodium and carbon tetrachloride are specific for the adults (Faust).

(2) *Œsophagostomum stephanostomum* (Raillet and Henry, 1909).—The adult worms present minor differences, and in the only human case recorded, by Thomas in Manaos, Brazil, nodules were found in the ileum as well as in the colon.

ANCYLOSTOMIASIS

Synonyms.—Uncinariasis; Hookworm Disease.

Definition.—Ancylostomiasis is caused by members of the family *Ancylostomidæ*. Five species may affect man—*Ancylostoma duodenale* (Dubini, 1843), *Necator americanus* (Stiles, 1902), *Ancylostoma malayanum* (Alessandrini, 1905), *Ancylostoma braziliense* (Gomez de Faria, 1910), and the *Ancylostoma caninum* (Ercolani, 1859). The first two species commonly

affect man, the third and fourth rarely, while the larvæ of the fifth may cause creeping eruption.

Ætiology.—*A. duodenale.*—Adults ♂ 8–10 mm.×0·4–0·5 mm.; ♀ 12–18 mm.×1 mm. Ova are elliptical, thin-shelled containing vitellus, segmented into 2 to 8 spherules, and measure 55–65×32–45 μ. *N. americanus.*—Adults ♂ 7–9 mm.×0·3 mm.; ♀ 9–12 mm.×0·4 mm. The ova measure 64–75×36–40 μ. The buccal armature of the two species differs. The capsule is smaller in *N. americanus*, and has an irregular border instead of the four ventral hook-like teeth of *A. duodenale*; there is also a pair of semilunar plates. All subsequent description applies to both these parasites.

When fæces containing ova are deposited on moist earth the rhabeditiform larvæ hatch out in 24 to 48 hours: later they moult twice, developing into filariform larvæ which may remain viable for 3 to 4 months. On, contact with human skin the latter bore their way into the blood vessels, pass to the right heart and lungs whence they progress via the trachea, œsophagus and stomach to their natural habitat in the duodenum and small intestine; here they mature and breed, egg-laying commencing in about 5 weeks. The worms attach themselves firmly to the mucosa, feeding on blood and may cause local bleeding (especially *A. duodenale*), though the stools generally give a negative test for occult blood. At autopsy œdema of the legs and sacrum are common, and effusions and petechiæ may involve the serous sacs. The heart is dilated and shows marked fatty degeneration, as do also the liver and kidneys. The duodenum and jejunum may present petechial hæmorrhages, especially at points where the worms are attached.

Symptoms.—At onset the larvæ may produce ancylostome dermatitis or ground itch, which clears up within 2 weeks unless secondary infection has occurred. In heavy infection symptoms may appear within 1 to 2 months. These are largely related to the anæmia which is microcytic and hypochromic in type; there is a low colour index, and an increased blood volume. The counts in a severe case would show R.B.C.'s—1,000,000–2,500,000 per c.mm.; hæmoglobin = 10–25 per cent.; colour index = 0·5. Leucocytes are normal or slightly increased in number, and eosinophilia is characteristic. Mild cases may be symptomless, and it is uncommon for the well-fed European to develop anæmia even when severely infected. Anæmia rarely occurs except in patients living on a borderline diet, poor in animal protein and iron-containing foods. Those moderately infected may complain of mental and physical lethargy, hyperacidity, epigastric tenderness, palpitations, and shortness of breath. The really severe case may show a tallow-yellow discoloration of the alæ nasi and forehead, a dry, earthy-coloured skin, pallor of the mucous membranes, mental sluggishness, dilated stomach and epigastric tenderness; earth-eating sometimes occurs and constipation is frequent. Dyspnœa, cough, palpitations, pulsating cervical veins and hæmic murmurs are common; retinal hæmorrhage, œdema of the feet and serous effusions may occur. Hook-worm disease causes great economic loss to the community by lowering the individual's physical and mental capacity for work and predisposing to secondary infections like pneumonia and dysentery. In Europe outbreaks have sometimes occurred in miners.

Diagnosis.—A microcytic, hypochromic anæmia, especially if associated with eosinophilia, should arouse suspicion in a tropical patient, and the

stools should be immediately examined for ova, preferably by the Clayton-Lane flotation method.

Prognosis.—The mortality rate varies from 1 to 3 per cent., the chief danger being anæmia, which predisposes to intercurrent disease unless specific treatment be instituted. Hook-worm infection is especially serious in children owing to its effects on their mental and physical development.

Treatment.—PROPHYLACTIC.—This includes the treatment of carriers, the substitution of latrines for promiscuous defæcation, the proper disposal of night soil, the treatment of contaminated ground and the wearing of good shoes and boots. Sanitation in mines must be satisfactory.

CURATIVE.—Many drugs have been used. The best are betanaphthol, thymol, oleum chenopodii, carbon tetrachloride, carbon ethyltetrachloride, tetrachlorethylene, and hexylresorcinol. After relative starvation or light dietary for 1 to 2 days combined with saline purgation, 30–60 grains of well-triturated thymol, mixed with an adequate quantity of milk sugar to prevent agglomeration of the crystals, are given in cachets, or 0·5 c.c. of oil of chenopodium at 6, 8 and 10 a.m., followed by magnesium sulphate (gr. 480) at noon. Some follow up a thymol treatment by oil of chenopodium one week later; the latter drug is especially valuable for associated ascaris and strongyloides infections, or if eggs have reappeared. Carbon tetrachloride, or the purified carbon ethyltetrachloride, is given to adults in doses of 3 c.c. either in liquid form or in hard gelatin capsules, but preliminary starvation is not advisable. The combination of carbon tetrachloride (3·0 c.c.) with oil of chenopodium (1·0 c.c.) is very effective; a light supper but no breakfast is allowed, and a saline purge is taken 2 to 3 hours afterwards. Tetrachlorethylene is given in doses of 3 c.c., and hexylresorcinol up to 1 g. may be administered in gelatin capsules; both are followed by sodium or magnesium sulphate purgation. Occasionally any of these drugs may cause poisoning. Thymol solvents including alcohol, fats, *i.e.* butter and milk, castor-oil, ether, glycerin and chloroform must be avoided as they lead to excessive absorption of thymol. With carbon tetrachloride, which occasionally induces acute liver atrophy, dextrose and calcium salts can, with benefit, be administered beforehand; it should not be used where there is fever or hepatic, renal, pulmonary or heart disease, or calcium deficiency. After purgation, the object of which is to get rid of both drug and parasites, the stools are examined and the number of worms counted; 7 to 10 days later the stools are re-examined; if ova have reappeared, then another course, preferably with a different drug, is advisable.

Anæmic patients should receive a diet rich in animal protein and iron-containing foods; and, in addition, iron in full doses should be administered.

ASCARIASIS

Definition.—An intestinal infection of man with the round worm *Ascaris lumbricoides* (Linnæus, 1758).

Ætiology.—Adults ♂ 17–25 cm. × 3 mm.; ♀ 20–40 cm. × 5 mm. The eggs are yellow, elliptical, possess a thick outer shell and measure 50–70 × 40–50 μ. Ova passed in human fæces develop in night soil, and the fertilised eggs, swallowed by man in contaminated water or food, pass into the intestines where the larvæ penetrate the bowel wall and migrate to

the lungs, sometimes producing ascaris pneumonia; thence, via the trachea and œsophagus, they reach the intestine (Stewart). Ova appear in the fæces in 2 to 2½ months.

Symptoms.—During larval migration urticaria, ascaris pneumonia, and, more rarely, ascaris nephritis may occur. Pulmonary complications appear early in the first week and are generally transient in nature. Adult worms may produce symptoms by toxic, reflex or mechanical means. Sensitised individuals occasionally develop rashes such as urticaria and œdema of the face, and in children, gnashing of the teeth, enuresis and convulsions are described. Reflex dyspnœa, abdominal pain and diarrhœa, with or without blood, may occur (ascaris dysentery), while masses of coiled-up worms sometimes produce acute intestinal obstruction. Perforation of the intestine leads to peritonitis or localised abscess from which worms may be discharged. Wandering worms may produce appendicitis or obstruct the pancreatic or bile ducts causing jaundice, or reach the liver producing liver abscess or cholecystitis. They have been known to enter the larynx and cause œdema of the glottis or even to appear in the antrum of Highmore.

Treatment.—Oil of chenopodium (1½ c.c.) carbon tetrachloride and tetrachlorethylene (3 c.c.) are specific remedies; in combination given as in ancylostomiasis they are particularly efficacious (see Ancylostomiasis). Santonin (3–5 grains) is the stock remedy; it may be given on consecutive or alternate days on three occasions combined with preliminary starvation and followed by castor-oil; in children, where the dosage is proportionately lowered, it may be combined with scammony or castor-oil. Hexylresorcinol in 1 g. doses is also recommended and should be followed by a saline purgative. Worms sometimes take 48 hours to be ejected, and the only index to cure is the permanent disappearance of ova.

TRICHURIASIS

Definition.—An infection of the human intestine with the whip worm *Trichuris trichiura* (Linnæus, 1771), formerly known as *Trichocephalus dispar*.

Ætiology.—Adults, 40–45 mm.; 45–50 mm. Ova are brown, barrel-shaped with terminal knobs and measure 50–54 × 23 microns. Man is infected by swallowing the fertilised eggs in food and water; on reaching the cæcum the larvæ are liberated and attach themselves to the mucosa. Occasionally they invade the appendix, colon and terminal ileum.

Symptoms.—Clinical features are generally entirely absent, but reflex symptoms are described in children and occasionally urticaria and eosinophilia are induced. Rarely verminous appendicitis and peritonitis may result, and possibly cæcal lesions may open up the way for other infections.

Treatment.—Thymol and oil of chenopodium may be effective, but worms are often difficult to eradicate.

ENTEROBIASIS

Definition.—Infection by the thread or pin worm *Enterobius vermicularis* (Linnæus, 1758), formerly known as *Oxyuris vermicularis*. Adults

♂ 3–5 mm.; ♀ 10 mm.×0·6 mm. The ova measure 50×20 μ, and are thin-shelled, colourless, plano-convex and contain coiled embryos; they are rarely found in the fæces, being mainly liberated in the perianal region from migrating gravid female worms at night, after the patient has gone to bed. The maximum length of the life cycle is 30 days, long-standing enterobiasis resulting from autoinfection via the infected fingers of the patient.

Symptoms.—The worms inhabit the colon, and when the patient is warm in bed at night may produce great discomfort and itching by migrating out through the anus. Eczema and pruritus ani may result causing sleeplessness and neurasthenia. Sexual disorders, vesical irritability, frequent micturition, prolapsus ani and mucoid secretion may be observed, also in young girls vaginal discharge. Catarrhal appendicitis sometimes occurs, and worms may wander into the stomach.

Diagnosis.—Eggs are best demonstrated by swabs made from the perianal skin. Inspection of the anal region at night immediately when itching commences may reveal the gravid female worms outside the anal canal before they have had time to retreat to the rectum.

Treatment.—The secret of successful treatment is the prevention of auto-infection. This is best done by the most scrupulous care of the hands and nails which may become contaminated (1) by scratching in the anal region, especially during sleep, (2) when completing the anal toilet with sanitary paper, or (3) from infected clothes. The nails should be kept short, and the hands well washed and scrubbed with carbolic soap immediately on waking, after defæcation, and every time there has been possible contact with infected material or clothing. Bathing drawers or pyjamas should be worn at night and sterilised each day, and infected children should occupy separate beds. Enemas of 4–8 fl. ozs. of hypertonic saline solution should be injected immediately the anal irritation commences, for at this time the worms are accessible and can be washed out from the rectum (Macarthur). The process should be repeated each night whenever anal irritability recurs. If re-infection be prevented this measure alone will generally result in cure.

Gentian violet appears to exert a specific lethal effect on the adult worms. Wright has recently advocated special keratin-coated tablets of this drug, the adult dose being 1 grain thrice daily before meals for 8 days; this course is repeated after a clear interval of 7 days. Toxic features include anorexia, nausea, abdominal cramp and vomiting. Over 90 per cent. cure is claimed.

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D. DISEASES DUE TO INJURIOUS ARTHROPODS

TICK BITES

Apart from relapsing fever, tularæmia and certain typhus-like fevers the bites of several species of ticks, including *Dermacentor andersoni, D. venustus, Hæmophysalis punctata, Ixodes ricinus* and *I. holocyclus*, may give rise to paralysis in man. Cases have been recorded from Australia, South

Africa and the United States. The incubation period varies from several hours to 6 days; the bites, which are generally situated on the nape of the neck, are painful and œdematous, and the disease, which is afebrile, may be fatal, especially in children. The paralysis is of lower motor neuron type resembling that seen in infantile paralysis, and develops first in the legs and later in the arms and neck. In removing ticks the parasite should not be forcibly extracted until paraffin or carbolised oil has been applied, as this causes withdrawal of the head and so prevents it being broken.

MITES

Apart from scabies, camel itch and copra itch, all of which are caused by different species of mites, several typhus-like fevers, including tsutsugamushi fever, are transmitted by these minute acarines. The harvest mites of temperate climates cause considerable itching and skin erythema, which comes on 12 hours after exposure and increases for 36 hours, sometimes persisting for several days. It may be prevented by sprinkling talc powder and sulphur or powdered naphthalene on the stockings, and is best treated by washing the legs with benzine, green soap or salt solution, while the itchiness can be combated, as in flea-bite, by the use of 1 in 10 carbolic lotion or an ointment composed of acid. carbol. (gr. 10), menthol (gr. 5), zinc oxide (gr. 60 and adip. præp. (1 oz.) (Roxburgh) may be used. Larval mites of the family *Trombididæ* are known to cause skin eruptions in various parts of the tropics. One, in the West Indies, produces red mite dermatitis (bête rouge), the little crimson spot in the middle of the itchy papule being diagnostic: another, in Mexico, has a predilection for the skin of the eyelids, prepuce and axilla. Owing to the fact that many adult mites have never been identified, species names are not generally available for the larvæ.

TONGUE WORMS

The adults, which are degenerated, segmented arachnids superficially resembling tape-worms, live in the lungs or nostrils of certain carnivora or ophidia, and deposit their eggs on vegetation; when these are eaten the larvæ encyst in the viscera of the intermediate host. Only two species have been reported in man, *Linguatula serrata*, which occurs in parts of Europe and Brazil, the larvæ encysting harmlessly in the human liver, and *Porocephalus armillatus*, which encysts in the mesentery, liver and lungs. The infection is not uncommon in the Belgian Congo. Pulmonary symptoms have been reported, and sometimes the larval forms wander free in the peritoneal cavity. If the cysts have become calcified they may be detected by X-ray examination (Low and Cordiner); otherwise the disease is only recognised at autopsy. No treatment is known.

INSECT BITES

Apart from specific disease transmission, bites from mosquitoes, biting flies, midges, lice, fleas, bugs, bees, ants, wasps and hornets may cause con-

siderable inconvenience to man and occasionally result in local sepsis or septicæmia, both of which may end fatally. Mosquito bites occasionally give rise to streptococcal septicæmia, and those of horse flies to anthrax.

Locally, insect venom may have hæmolytic, neurotoxic or irritant effects producing limited inflammation, or the dermal whealing which results may have an anaphylactoid origin dependent on previous sensitisation, as Boycott has proved for midge bites. The stings of bees, wasps and hornets are invariably painful, and in certain situations like the tongue and fauces may lead to respiratory obstruction, or in the larynx to death from œdema of the glottis. Anaphylaxis may follow bee or wasp stings in a sensitised individual. Such patients may suffer from profound vasomotor collapse, become comatose and die in 20 minutes. In a case of wasp sting seen by us the patient, who gave a history of having been stung on the scalp 6 years previously, was again stung on the third right finger; a wheal about 2 cm. in diameter rapidly appeared with surrounding erythema, and within 5 minutes the patient developed headache, lachrymation and injection of the conjunctivæ. Giddiness, nausea, severe vomiting, rapid low tension pulse with vasomotor collapse, generalised urticaria, especially involving the arms and neck, and respiratory distress followed; 3 hours later the general condition was greatly improved, but next day there was a large, puffy, painless swelling involving the subcutaneous tissues of the whole hand. The early and late local effects closely resembled those observed in the immediate and delayed intradermal reactions for hypersensitiveness to helminthic protein.

Treatment.—Mosquito, midge and fly bites may to some extent be prevented by the use of essential oils such as citronella applied to the clothing. They should be treated by the immediate application of iodine, the subsequent itching being relieved by a 1 in 20 watery solution of carbolic or a 1 per cent. alcoholic solution of menthol. In bee and wasp stings, the sting should be carefully lifted or scraped out, as pressure expels the contents of the poison sac. Ammonia, alkaline soap or methylene-blue may be applied locally for the acid bee stings, and vinegar for the alkaline wasp stings. Adrenaline (min. 10 of 1 in 1000 solution) should be immediately injected subcutaneously whenever anaphylactic symptoms develop. Sepsis is treated along the usual lines.

MYIASIS

Definition.—An invasion of the tissues by larvæ of dipterous insects.

Ætiology.—Many flies deposit their eggs or larvæ in decomposing discharges, and in the tropics wounds should always be protected as well as natural orifices discharging pus or fetid material. Larvæ of special flies may develop in the nasal cavities, the ear, vagina, urethra, skin or in the intestine, and the fly *Wohlfartia magnifica* may deposit its eggs in the conjunctival sac with serious consequences. Two chief varieties are distinguishable—the dermal and the intestinal.

The Screw Worm (*Cochliomyia macellaria*).—This fly, common in most of tropical and subtropical America, measures 9 to 10 mm. in length and is distinguished from the ordinary blue-bottle by the three black, linear, dorsal marks on its thorax. It lays its eggs upon foul wounds, the larvæ hatching in a few hours, and when mature measuring 2 to 3 inches in length. Super-

ficially the larva resembles a screw, being formed of twelve segments, each with a series of spines; it burrows into and feeds on the tissues, causing great destruction locally. When the nose is affected the larvæ often pass into the accessory sinuses, bore their way through the bones and even penetrate the skull, causing death by purulent meningitis. The vagina and ear may also be attacked and the middle ear destroyed.

Treatment.—PROPHYLACTIC.—This consists essentially in covering all wounds and discharging orifices, and avoiding sleeping in the open. Larvæ can be removed from wounds by ordinary antiseptic methods, and for nasal cases injection of chloroform, carbolic acid or turpentine may be used. Accessory sinuses may need to be opened.

THE MOSQUITO WORM (Ver macaque, beef worm) (*Dermatobia cyaniventris.* —This fly, common in Central America and adjacent parts of South America, measures 14 to 16 mm. in length, has a yellow head with brown eyes, a greyish thorax and dark metallic-blue abdomen. The eggs somehow become glued to the under surface of mosquitoes (particularly of the genus *Janthinosoma*), biting flies and even ticks, and in this fashion the larvæ are conveyed to the human skin where they invade the tissues via the puncture wound. A boil or warble results, containing a central opening through which the maggot breathes, discharges black excreta, and later escapes to the ground where it develops into a chrysalis and finally a fly. Cattle are also affected. Hadwen and Bruce have described a remarkable anaphylactic condition in oxen and sheep infected with larvæ of warble flies (*Hypoderma bovis*, *H. lineatum* and *Œstrus ovis*) characterised by dyspnœa, salivation, lachrymation, incontinent sphincters, vasomotor collapse, cyanosis and even death. This may be experimentally induced by injections of larval protein extracts or may result from natural trauma during life. Similar clinical features have not yet been recognised in man, though they probably occur.

Treatment.—Natives kill the larvæ with tobacco juice. The opening should be enlarged with a bistoury and the maggot removed with forceps; the cavity soon heals if treated antiseptically.

VER DU CAYOR OR TUMBU DISEASE.—This disease, common in Central and West Africa, is due to the larvæ of the Tumbu fly, *Cordylobia anthropophaga*, which is 8·5 to 11·5 mm. long, yellowish in colour, with black abdominal spots. The eggs are laid on the ground or clothing, and the emerging larvæ bore their way into the tissues by means of mouth-hooks. The first symptom is a pricking sensation, followed by the appearance of a boil or warble which commonly affects the buttocks, thighs and scalp of children, and often becomes inflamed. The larva takes about a fortnight to mature and then escapes via the central hole through which its fæces were previously excreted. Sometimes the cavity suppurates. Blacklock and Gordon demonstrated an acquired local skin immunity against cordylobia larvæ in guinea-pigs subjected to previous infection.

Treatment.—The aperture is enlarged if necessary, the maggot squeezed out, and the cavity treated antiseptically.

THE CONGO FLOOR MAGGOT.—The adult fly, *Auchmeromyia luteola*, is found throughout tropical Africa; it deposits its eggs on the floors of huts and outhouses, and when the larvæ have hatched out they suck the blood of people sleeping on the ground without causing pain. The larvæ crawl actively, are 15 mm. long and consist of 11 segments. The adult is orange-yellow in

colour, with longitudinal dorsal stripes on the thorax, and measures 10 to 12 mm. in length. Prophylaxis consists in sleeping on raised beds.

INTESTINAL MYIASIS.—Fly larvæ are common in human fæces; generally they are deposited after defæcation, but sometimes they originate from the intestine, the eggs being swallowed by man in food. Many species have been described, the genera *Sarcophaga*, *Fannia*, *Apiochæta* and *Anthomyia* furnishing the majority of examples. *Fannia canicularis* accounts for most cases in Europe. Gastro-intestinal symptoms may be mild or severe and include malaise, vomiting, diarrhœa and severe griping. General toxic features may include fever, rigors, headache, thirst and vertigo; even convulsions have been described. The bile ducts may also be implicated.

Treatment.—Castor-oil is generally sufficient, but thymol, filix mas, santonin and turpentine have also been recommended.

SPIDERS

Though spiders (Aranеæ) generally possess poison glands and inject venom into their prey, only a few species, mostly of the genus *Latrodectus*, are dangerous to man. Experimentally such venoms may slow the pulse and respiration, and produce tetanoid-like spasms and bronchial contraction in guinea-pigs. The red-backed spiders *L. mactans* in America, and *L. hasseltii* in New Zealand and Australia, and *L. geometricus*, *L. concinnus* and *L. indistinctus* in South Africa, where their colloquial name is "knoppie spider," produce local inflammation, œdema and numbness at the site of the bite as well as neurotoxic manifestations. In Peru the "pruning spider," *Glyptocranium gasteracanthoides*, causes local gangrene, hæmaturia and neurotoxic symptoms. Kobert noted oxyhæmoglobin and methæmoglobin in the urine of persons bitten by the "cross spider," *Epeira diadema*, and Sachs found in its venom a powerful hæmolysin. Probably many other spider venoms, like zootoxins generally, exert agglutinative, hæmolytic and neurotoxic effects. The tarantulas, on the other hand, give rise only to minor symptoms, though any spider with an effective biting mechanism may produce secondary bacterial infection. If seen early, treatment consists in immediate ligature, incision and suction, or washing out the wound with permanganate solution. Antiserum, if available, is effective. Morphine may be necessary to relieve pain, and injections of calcium gluconate (10 c.c. of a 10 per cent. solution) for laryngeal and muscular spasm. Intravenous saline and dextrose solution, and injections of nikethamide (coramine) and pituitary (posterior lobe) extract assist circulatory failure.

CENTIPEDES

The Scolopendridæ possess poison glands which discharge at the apices of a pair of specialised claws taking the place of the first pair of legs. The small centipede gives rise only to local manifestations associated perhaps with an erysipelas-like eruption, but the tropical species, *Scolopendra gigantea*, may cause around the punctures local necrosis and lymphangitis; headache, vomiting, fever, coma, and in children even death may follow. Treatment is similar to that of spider bites. Strong ammonia applied locally is useful.

SCORPIONS

Scorpions possess paired poison glands in the post-anal segment of the spined tail; this is thrust forward into its prey which is held in position by the formidable pedipalps. Scorpions in the tropics not infrequently kill children, and occasionally adults, and several species of the genus *Buthus* and *Centruroides*, as well as *Euscorpius italicus*, *Tityus bahiensis* and *Centrurus exlicauda*, etc., are much feared. The bite is most painful, and toxic symptoms may include fever, sweating, vomiting, diarrhœa, muscular cramps, trismus, stiffness of the neck, muscular paresis, respiratory failure and coma. Secondary bacterial infection is not uncommon. Acute abdominal symptoms due to hæmorrhagic pancreatitis have been recorded in Trinidad, and pancreatic cyst is regarded as one of the complications of scorpion poisoning there. Local treatment may be instituted as for spider bite, and the immediate application of strong ammonia or a local injection of cocaine and adrenaline relieves the pain. The intravenous injection of specific antivenene (5 c.c. for children and 10 c.c. for an adult), prepared by inoculating scorpion venom into horses, has greatly lowered the mortality rate amongst children in Egypt and South America.

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E. DISEASES DUE TO SNAKES AND POISONOUS FISHES

SNAKES

Ophidiasis or snake poisoning results from the inoculation of venom by snakes of the families colubridæ or viperidæ; non-poisonous species occasionally cause death through septic infection following their bites.

Ætiology.—Snakes are carnivorous, and Alcock and Rogers showed that even non-poisonous species may have poisonous saliva. The venom is simply a specialised secretion of the parotid (poison gland) utilised in killing and digesting prey, while the fangs are modified maxillary teeth anteriorly grooved in the colubridæ, and completely canalised in the viperidæ. The biting mechanism is vastly superior in the vipers since the fangs are longer, and capable of considerable forward rotation, whereas in the colubrines they are generally shorter and more fixed. In biting, the snake strikes with great speed, opens the jaws, rotates forward the fangs, snaps the jaws together and ejects its venom from the poison gland via the duct and fang into the tissues in one almost instantaneous movement. The vipers withdraw immediately after biting. The colubrines often hang on to the bitten part and may need to be forcibly evulsed: to inject venom effectively they must have the lower jaw fixed, and though their venoms are more poisonous the yield is, as a rule, considerably less than that of the vipers. The toxic action of

venoms is mainly dependent on (*a*) proteolytic enzymes, (*b*) phosphatidases and (*c*) neurotoxins. The proteolytic enzymes, so well represented in viperine venoms, digest the tissues and damage the vascular endothelium (hæmorrhagin), leading to the escape of blood and the liberation of histamine which causes extensive local œdema and gives rise to symptoms of cardio-vascular failure (Kellaway). The coagulant properties of venoms are due either to a direct coagulation of the fibrin by the venom or to the conversion of prothrombin into thrombin (Eagles). The phosphatidases cause hæmolysis and also directly affect the heart and circulation; the acceleration of venom hæmolysis by lecithin is attributed to the transformation of lecithin into lysolecithin, which is itself actively hæmolytic. The neurotoxin formed in colubrine venoms has a strong peripheral effect, paralysing the sensory, proprioceptive and motor nerve endings. Paresis of the musculature is due to the curare-like action on the motor endings and a further direct action on the muscle itself (Kellaway).

Pathology.—In colubrine bites there is a congestive mode of death from peripheral respiratory failure, associated with fluid blood, a dilated right heart, and congestion and œdema around the fang puncture. In fatal viperine bites there is hæmorrhage, thrombosis and digestion of tissue locally, associated with a spreading gelatinous œdema resembling "red currant jelly," which sometimes involves the subcutaneous tissue of the whole limb; multiple hæmorrhages are found in the viscera, serous membranes, etc. Ante-mortem clotting is present in small animals, but not in man where the blood is fluid unless, as rarely happens, the fangs enter a vein: death results from cardiac failure, peripheral circulatory failure, secondary hæmorrhage, or septic infection and local gangrene.

Symptoms.—The clinical picture depends on the quantity and quality of the venom injected. Symptoms appear generally within 10 minutes to 2 hours after the bite, nausea, faintness and vomiting being characteristic early manifestations. Cardio-vascular shock follows both colubrine and viperine bites; paretic features predominate in the former, and general hæmorrhagic manifestations in the latter. In colubrine bites the fang marks are not always visible, and pain and local swelling are minimal; these features, however, are marked in the case of viper bites, which show in addition much hæmorrhagic oozing. Histamine shock accounts for the cold extremities, blanched, white skin, low blood pressure, vomiting, rapid thready pulse and extreme prostration. Psychical shock is sometimes an added factor, and may produce a somewhat similar picture in terrified natives bitten by non-poisonous snakes. In the earlier stages in colubrine bites the muscular weakness, ataxic gait and blurred speech may produce a picture simulating alcoholism, and diplopia, ptosis and blunting of sensation are not infrequently added; later there is inability to swallow, the tongue appears swollen, saliva dribbles from the mouth, the breathing, which was at first stimulated, becomes shallow and slow, and in fatal cases cyanosis, coma and convulsions of asphyxial origin ensue; the respirations may become costal in type and death occurs from peripheral respiratory failure. Hæmorrhagic extravasations (viperidæ) may lead to cutaneous petechiæ, epistaxis, hæmoptysis, hæmatemesis, hæmaturia and melæna. In the early stages the gums may ooze blood and the urine contain red corpuscles.

Complications.—Blunting of the cough reflex and paresis of the muscles

of deglutition may be followed by insufflation pneumonia. After krait bites the anterior-horn cells of the cord may fail to recover or an acute ascending paralysis has been recorded some 10 days later. With viperine poisoning, local suppuration and gangrene sometimes necessitate amputation.

Course.—Death may occur within 20 minutes or many days later from complications. As a rule colubrine cases surviving for 3 days recover.

Diagnosis.—Generally this is not difficult, but cases may need to be differentiated from alcoholism and the bites of non-venomous snakes and scorpions. The grooved or canalised anterior fangs in the upper jaw make identification of a poisonous snake easy.

Prognosis.—This depends on the amount of venom injected, the efficacy of local treatment and the availability of specific antivenene. Even with really deadly snakes, factors such as clothing, inefficient biting or a poor venom yield may prevent a lethal dose being injected, and this fact accounts for many extravagant claims regarding the value of weird cures. Most first-aid measures are useless since the ligature is applied ineffectively or too late, and once a lethal dose of venom has been absorbed into the circulation, antivenene given intravenously is the only measure that will save life.

Treatment.—PROPHYLACTIC.—Snakes bite man more often by accident than design, and in snake country a little knowledge and common sense regarding the natural habits of the ophidia, the use of lanterns in walking along roads at night and the wearing of strong boots and leggings would greatly lessen the incidence of snake bite. Every second case is bitten below the knee.

CURATIVE.—Only two methods of treatment are of recognised value after a lethal dose of venom has been injected into the tissues: (1) Immediate ligature which delays absorption of venom, followed by such local measures as incision, excision, suction, or the injection of chemicals, the object of which is to remove or destroy inoculated venom before a lethal dose can be absorbed; (2) the intravenous injection of specific antivenene. By temporarily prolonging life, effective ligature may enable antivenene to be given in otherwise fatal cases.

Local Measures.—In sheep bitten by the tiger snake (*Notechis scutatus*) the absorption time of a lethal dose proved to be only 2 minutes (Fairley), so to be effective a ligature must be in position at the earliest possible moment. Pressure must be applied over a single bone proximal to the heart, *i.e.* over the femur in foot and leg bites, and over the humerus in bites on the hand and forearm; in finger and toe bites a boot lace may also be tied at the base of the implicated digit. Complete stasis of the circulation has to be attained as judged by blanching of the nails and failure of incisions to bleed. Thick rubber tubing ($\frac{3}{8}$-inch) is an ideal tourniquet, but in the field, strips of clothing, loosely knotted and twisted with a stick, are effective, and every 20 minutes the tourniquet may be loosened for 30 seconds to flush the limb with blood. After ligature the skin should always be wiped clean or washed, otherwise incision and scarification may lead to absorption of venom deposited and dried there (Ferguson). Scarification with or without the application of permanganate crystals is not effective, and mere incision is of doubtful value; it should be combined with suction either by the mouth or preferably with a breast pump or a Bier's suction glass. Excision of the bitten area and washing with permanganate solution, followed by mechanical suction is the best local treatment, and is the only one available where ligature is inapplicable as in

body bites. Polyvalent antivenenes are now available for cobra and Russell's viper in India, for the viperidæ and colubridæ of Africa, for the more deadly snakes of South America and for the crotalinæ of the United States. In Australia there is a monovalent antivenene for the tiger snake. The dosage varies, but antivenene must always be given intravenously as early as possible, and in colubrine bite is effective up to approximately two-thirds of the death time (Acton and Knowles). No case is too ill to receive it and even the most severely paralysed cases may recover; such patients must be carefully watched, as paralysis may reappear and further injections be necessary. In viperine bites it is less effective, and must be given in full dosage at the earliest moment. Infiltration of the tissues with antivenene in the vicinity of the bite may be useful (FitzSimmons). *General Measures.*—Patients must be kept warm and at rest. Black coffee and sal volatile may be given early, and injections of cortin, adrenaline or pituitary (posterior lobe) extract and of reconstituted plasma, followed by isotonic dextrose (5 per cent.), administered for circulatory shock. Nikethamide (coramine) has value as a respiratory and circulatory stimulant. Artificial respiration may prolong life, and it is important in cases with pharyngeal paresis to swab out the throat and keep the head low when the patient vomits; food should be withheld, and, if necessary, fluid given through a stomach-tube.

POISONOUS FISHES

In tropical waters casualties from poisonous fish are not infrequent. The effects of jelly-fish stings vary with different species; many are harmless, others produce local features such as urticaria, œdema, marked itching, burning and erythema, sometimes followed by vesicular dermatitis or actual sloughing and ulceration. Systemic symptoms may follow rapidly and include lachrymation, coryza, muscular pains, constriction of the chest, dyspnœa and cardiovascular shock. Deaths have been reported.

Fish of the genus *Muræna* bite with their powerful, grooved teeth down which poison from the venom sac enters the tissues; many harmful species are known, and their venom may have a depressant action on both the cardiac and nervous systems.

In other fish, such as the sting-rays, there are barbs in the dorsal fin or elsewhere connected with poison glands and these may produce not only severe inflammation locally, but neurotoxic features. Tetanus organisms may simultaneously be inoculated. Certain species of *Trachinus*, such as *T. draco* found in the Mediterranean, and of *Scorpæna*, such as *S. scropha* inhabiting tropical waters, are particularly dangerous, causing excruciating pain and local irritation, œdema, paralysis of the part, collapse, dyspnœa, delirium and even death within 24 hours. Septic infection may follow. Local treatment as for snake bite should be adopted. Infiltration of the tissues with procaine hydrochloride (novocaine) (2 per cent.) is often advisable for relief of pain, and morphine also may prove necessary.,

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SECTION V

DISEASES DUE TO PHYSICAL AND CHEMICAL AGENTS

CAISSON DISEASE

Synonyms.—Compressed Air Illness; Divers' Paralysis.

Definition.—Caisson disease is the name given to a series of phenomena which may result in any living animal upon return to a normal atmospheric pressure after exposure to an air pressure which must exceed 18lb. to the square inch above mean atmospheric pressure. These phenomena occur the more frequently and severely the greater the air pressure, and in direct proportion to the length of time of exposure to the high air pressure, and the more rapid the return to a normal atmospheric pressure. They are caused by the saturation of the living tissues with nitrogen at high atmospheric pressure which, on too rapid return to lower atmospheric pressures, boils within the tissues, and this liberation of bubbles of nitrogen causes tissue disruption and destruction on the one hand, and gas emboli on the other. The major capacity of fat to hold nitrogen in solution causes the liberation of nitrogen bubbles to occur most readily in the fatty tissues, and this occurs more easily in those parts of the body where the blood supply is less abundant, and therefore the rapid return of the excess of nitrogen to the atmosphere by solution in the blood stream less easy. For these reasons the white matter of the nervous system, composed as it is of fatty substance, and particularly those parts of it which are less liberally supplied with blood, such as the white matter of the lower dorsal spinal cord, is the most common site of gas liberation. The joints and also their surrounding structures, which are lowly vascularised, are also common sites of the lesions, as are also the subcutaneous tissues of fat subjects, on account of the high solubility of nitrogen in the fat.

These phenomena occur only upon decompression, and are always preventable if adequate means be adopted (1) to limit the time of exposure to very high atmospheric pressures, so that high degrees of tissue saturation with nitrogen shall not occur, and (2) to regulate the return to normal atmospheric pressure by graduated decompression, in such a way as to prevent boiling of nitrogen in the tissues. They are curable, after they have appeared, by immediate recompression followed by very gradual decompression. Exposure of the living animal to very high atmospheric pressures may be associated with most serious and usually fatal results, which occur before decompression, and which are due to over-saturation of the tissues with oxygen, death resulting from oxygen poisoning.

Ætiology.—This disease made its appearance in the middle of the nine-

teenth century, when the invention of Siebe's diving dress and of subaqueous chambers made it possible for subaquatic engineering and marine salvage to be performed under high atmospheric pressures. The men work in a pressure of air, which just exceeds the hydrostatic pressure of that depth of water which extends from the working position to the surface, and the pressure is produced and maintained by pumps and regulating apparatus. Workmen reach the working face of the caisson by passing from the normal atmosphere through a series of chambers with airtight doors, in which the air pressure is raised by rapid stages, until the high pressure of the working face is reached. They leave through the same chambers, the air pressure being lowered for some space of time in each as they pass through. This process is termed " compression " and " decompression," or " locking in and out." The diver is compressed as he slowly descends by an increasing air pressure from his pump, and is decompressed as he ascends much more slowly, this compression being regulated by an automatic valve in his helmet which retains the air pressure until it exceeds that of the water pressure outside. Caissons are worked under a much lower pressure than that at which divers can work ; but the working shifts are much longer, whereas the diver at great depths remains down only a very short time. Roughly speaking, each 33 feet of water produces a pressure of 15lb. to the square inch (5½ fathoms). Caissons are usually worked at a pressure of below 35 lb. and in 6- to 8-hourly shifts, but they have been successfully worked at a pressure of 45 lb. with 2-hourly shifts, and at 50 lb. with 1-hourly shifts. Divers frequently work at 20 fathoms (53 lb.), and the record depth and pressure reached has been 210 feet (95 lb.).

During compression no trouble is experienced beyond discomfort in the ears and rarely perforation of the membrane tympani, from disparity of air pressure in the middle ear. This the workmen avoid by opening the Eustachian tubes with an act of swallowing or yawning ; but it must be remembered that no person suffering from Eustachian catarrh should be allowed to enter the air locks. Under high atmospheric pressures combustion proceeds more readily, a candle when lighted burns away furiously, and a pipe bursts into flame with each draw. The workmen find that they can work more easily and with less fatigue.

The symptoms of the disease become manifest upon return to a lower atmospheric pressure, and directly in proportion to the suddenness of return to such pressure. If the return to a normal atmospheric pressure from a high and prolonged pressure be sudden, there may be a liberal escape of bubbles of nitrogen gas in the blood and in the tissues. The presence of the nitrogen may sometimes be felt as gas crackling underneath the skin or subcutaneous emphysema.

When the return to a normal atmospheric pressure is more gradual, the nitrogen may have time to escape from the blood and from most of the tissues by diffusion through the lungs, but in those tissues which are relatively less vascular, and from which, for that reason, interchange of gases by means of the blood stream is slow, or in these tissues in which nitrogen is especially soluble, such as the fats and myelin of the nervous system, the nitrogen is liable to escape in the form of bubbles, and to the mechanical effects upon the tissues in which the boiling of the nitrogen occurs, the symptoms of caisson disease are due.

That part of the nervous system which is least vascular, namely the four lower dorsal segments of the spinal cord, is the most common region for the lesions to occur, while the joints and peripheral nerve trunks are often affected.

Massive escape of gas may occur into the blood stream, and the heart has been found distended with gas after death in rapidly fatal cases. A similar escape of gas into the intestines may produce severe and even fatal abdominal distension. It is doubtless one of the causes of the abdominal pain, nausea and vomiting which are common symptoms of compressed air sickness.

The liberation of these gases, and therefore the occurrence of the compressed air disease, depends directly upon these factors—(1) the amount of pressure to which the living animal is exposed; (2) the length of time of exposure to the high pressure; and (3) the rapidity with which a return is made from the high pressure to normal atmospheric pressure. For example, the malady never occurs after short exposures, such as 15 minutes at a pressure of 45 lb., or 2 minutes at a pressure of 75 lb., even though decompression be as rapid as possible, for these periods are too short to allow of nitrogen saturation of the tissues. It is for this reason that compressed air sickness is so much less common in divers, who for the most part work for very short times only at high pressures, and so much more common in caisson workers, who work for many hours at a stretch at a pressure of from 30 to 40 lb.

There is one other factor which must be carefully borne in mind, and that is the amount of fat present in the body, which, from its nitrogen dissolving qualities, greatly increases the tendency to nitrogen boiling within the tissues if it be present in large amount. It has been shown experimentally that fat animals succumb to the disease while lean ones escape, and experience has shown the necessity of excluding fat workmen on account of their liability to the malady.

The disease is obviously always preventable, firstly by shortening the periods of exposure according to the height of the pressure so as to obviate nitrogen saturation; and secondly by arranging that such a graduated and prolonged return to normal pressure be made, as will prevent any possibility of nitrogen boiling, the slow return to normal pressure allowing of the nitrogen desaturation of the tissues without bubble formation.

It is quite safe, and does not produce any ill effects whatever for a man to breathe pure oxygen for as many as 6 hours at a time. This has been proved by the use of the Siebe-Gorman life-saving dress for rescue work from choke damp in mines. Beyond a certain limit of pressure, however, oxygen becomes poisonous. Highly compressed air causes rapid toxic effects in proportion to the partial pressure of the oxygen. It tends to cause direct death of the tissues. At lower partial pressures it has a convulsant effect, and at still lower pressures produces congestion of the tissues and especially of the lungs, which may present consolidation and all the signs of acute pneumonia, however slowly and carefully decompression has been accomplished. The limit of safety so far as oxygen poisoning is concerned is 10 atmospheres, or 300 feet of water. Neither divers nor caisson workers ever work at anything like so high a pressure.

The essential feature on post-mortem examination is the presence of bubbles of nitrogen in the tissues or bulky collections of nitrogen within the

organs, as in the heart or in the intestines, and the results of the associated tissue disruption and air emboli. When it is considered that the mass of blood constitutes about 5 per cent. of that of the whole body, and that the capacity of the tissues in a thin subject is thirty-five times that of the blood, the ratio being much higher in a fat subject, since fat will dissolve five times as much nitrogen as will any other tissue, the presence of bubbles in the tissues, and especially in the fatty tissues, will readily be understood.

The bubbles form first in the venous blood and in the fatty tissues, where they grow by accretion and cause tearing of the tissues, while air emboli and subsequent necrosis are common. Hundreds of bubbles have been counted in the spinal cord, and these are much more numerous in the white than in the grey matter. Collections of nitrogen may be found in the subcutaneous tissues, and may cause palpable crackling. Bubbles of gas are not uncommonly found in the liver cells. Occasionally similar lesions are found in the brain or in the eye, and in fact may occur in any of the tissues. In every fatal case which has been adequately examined patches of necrosis in the dorsal region of the spinal cord, with the usual secondary degenerations, have been found.

Symptoms.—The symptoms may be first manifest during the process of decompression, when the latter is rapid, and from a high pressure. More often the signs of the malady appear soon after a normal pressure is reached, while not infrequently they do not present themselves until an hour or more has elapsed. In slight cases headache, giddiness, diplopia and faintness may occur, and these symptoms pass off soon and leave no trouble. Severe and important symptoms occur in the following order of frequency: (1) pain in the extremities or trunk, commonly called by the workmen "the bends" from the position in which the painful limbs are held; (2) pain in the epigastrium, sometimes accompanied by nausea, vomiting and abdominal distension; (3) paraplegic paralysis which usually involves motor, sensory and sphincter functions, and extends as high as the ninth dorsal segmental level; (4) headache, vertigo and coma; (5) sudden death; (6) hemiplegia or monoplegia of cerebral origin.

The pain in the limbs is of a neuralgic character and is referred to the joints, which are kept in the semiflexed position, any attempt to straighten them causing great pain. The pain may come on gradually, or suddenly, and may be slight and transient, or severe and persistent. It is often intolerable. The knees, ankles and hips are the most frequently affected; but sometimes the joints of the upper extremities, or of the back and especially of the lumbar region, may be affected. Epigastric pain is common, and unless quickly relieved by recompression is followed by nausea and vomiting.

The paraplegia usually has its upper limit in the lower dorsal, but it may reach the cervical region and involve the arms. It comes on rapidly, and involves motor, sensory and sphincter functions. It may be of any degree of severity from a slight and transient effect to a complete and permanent loss of the functions of the spinal cord. The paraplegia occurs with increasing frequency and completeness in proportion to the degree of pressure and the length of exposure to its influence. It occurred in 61 per cent. of 119 cases in the St. Louis bridge caissons, which were worked at plus 50 lb. of pressure, and among these there were 14 deaths. There is no general relation between the pain and the paralysis, as either may occur without the

other, and it seems, therefore, that the pain is due to a peripheral lesion and not to the lesions of the spinal cord. It is an interesting fact that the peripheral pains may persist in severe degree, even when there is total loss of pain sensibility from the spinal cord lesions.

Course and Prognosis.—The duration of the attack may vary within very wide limits. The severity of the initial symptoms, and the immediate application of appropriate treatment, are the all-important modifying factors in the prognosis. The attack may last for a few hours only, or it may continue for days. The paralysis may recover in a few days, or it may last for months and may never recover. Death occurs only in cases which have severe initial symptoms, and except when occasioned by complications such as cystitis and bed-sores it usually takes place shortly after the attack.

Treatment.—PROPHYLACTIC.—Since the malady is due entirely to nitrogen saturation of the tissues, and the subsequent escape from solution of this gas into the tissues during a too rapid return to normal pressures, it follows that the malady can always be prevented by adopting suitable period lengths for compression. In the first place, the malady never arises from compressions below plus 18 lb. to the square inch, or roughly 40 feet of water, and those who work at such a pressure may do so for long hours and return to a normal pressure rapidly, and without any risk. At higher pressures the working shifts must be shortened as the pressure gets higher. The shifts should be not longer than 6 to 8 hours at a pressure of 30 to 35 lb., or 3 atmospheres; 2 to 3 hours at a pressure of 45 lb., and 1 hour only at a pressure of 50 lb. At higher pressures than this, which are only encountered by divers, a few minutes' exposure is allowed only.

Compressed air sickness never occurs if the return to the normal atmospheric pressure be sufficiently slow. Animals can be exposed to very high pressures, short of those causing oxygen poisoning, with impunity, provided they be decompressed slowly enough. This decompression is carried out in the case of the diver by raising him to various levels in stages, and letting him remain at each stage a longer and a longer period as the surface is approached. In the case of caisson workers a series of air-locked chambers is provided in which the air pressure is lowered in stages, the men remaining longer and longer at each stage as they approach the normal pressure. The important fact in connection with decompression is that the absolute pressure can always be halved forthwith without any risk. In the first air lock on leaving the working face of a caisson, for example, the pressure is at once reduced to one-half that of the working face, and in the remaining air locks the pressure is reduced by stages until zero is reached.

Leonard Hill has shown experimentally that it is always safe to lower the pressure to plus 20 lb. by gradual decompression during the space of 10 minutes, then to wait at that pressure for 2 hours, and then bring the pressure to zero by gradual reduction in 10 minutes. The Admiralty rules for divers require that a diver working, say at 140 feet shall be first raised straightaway to a depth of 50 feet where he waits 10 minutes, then to 40 feet for 10 minutes, 30 feet for 20 minutes, 20 feet for 30 minutes, 10 feet for 35 minutes, and then he leaves the water abruptly.

The difficulty and danger is the tendency on the part of the workers to curtail these weary waits, and get away from work as soon as possible. It is important that all fat subjects, and all those who have shown a susceptibility

to compressed air sickness, and all those not in absolutely sound bodily health, shall be excluded from working in highly compressed air.

CURATIVE.—It was early discovered by the caisson workers themselves that the only remedy for the malady was to re-enter the high-air pressure. A recompressing apparatus in the form of a medical air lock is now supplied at all caisson works, and on all ships engaged in deep salvage. On the appearance of any symptoms the worker is placed in the compressing room and the pressure is run up to the full pressure at which he has been working, when it is usual for the symptoms to ameliorate rapidly or disappear. After the recompression the decompression must be carried out very slowly, for the bubbles once formed in the tissues are not easy to get rid of, though they may be kept at a small size by the pressure. Cases apparently at the point of death with cyanosis and coma have many times been completely recovered in a few hours by recompression. When symptoms have appeared, the decompression should take at least 5 hours. Caisson workers and divers should sleep and live close to the medical air lock that they may be near aid during the first hours following decompression. The paralysis when once established is to be treated upon ordinary lines.

ANOXÆMIA

Definition.—A series of phenomena which result in the living animal from deficiency in oxygenation of the tissues in the absence of carbon dioxide retention.

Pathology.—The condition is directly referable to lack of oxygen and lowered internal respiration. Anoxæmia is divided into three classes, with widely differing causal mechanisms:

1. *Arterial anoxæmia.*—This is due to a deficiency in the oxygen content of the arterial blood, the oxygen-carrying power being normal and the carbon dioxide discharge unhindered. It is apt to appear whenever the oxygen content of the arterial blood falls below the normal limit of 94 per cent. of its total capacity, and it may or may not be associated with cyanosis. It is the usual result of breathing a rarefied atmosphere in which the partial pressure of oxygen is lowered, and in this connection is known as "mountain sickness" or "altitude sickness" when heights approaching 20,000 feet are reached. The characteristic phenomena can be produced at will by respiration within a partially exhausted chamber, and they can be obviated at high altitudes by adequate oxygen addition in respiration. Arterial anoxæmia is also present to some extent in those pulmonary diseases in which there is damage to the respiratory epithelium, obstruction to the air passages and when prolonged shallow breathing occurs, as in pulmonary œdema, emphysema and pneumonia, and in these conditions oxygen addition is valuable if its administration can be very prolonged.

2. *Stagnant or passive anoxæmia.*—This results when, on account of some fault in the circulatory mechanism, the passage of the blood through the tissues is too slow to provide for adequate oxygenation. It is the common happening in the circulatory failure of cardiac disease. There is here no fault with the oxygen content of the arterial blood. The oxygen saturation of the venous blood falls lower than 65 per cent. of the normal, and the

normal difference between the oxygen saturation of the arterial and of the venous blood, which is 20 to 30 per cent., is exceeded, and there is always cyanosis, which appears when the reduced hæmoglobin content reaches 40 per cent. of the total hæmoglobin. Since the arterial blood oxygen content is not at fault, oxygen administration is useless to relieve this condition.

3. *Anoxic anoxæmia.*—This results from a deficiency in the oxygen-carrying power of the blood, either by reason of deficient hæmoglobin content, as in the anæmias, or by fixation of some of a normal hæmoglobin content, as methhæmoglobin, sulphæmoglobin, or carbon monoxide hæmoglobin. In the anoxic varieties, cyanosis does not occur, however severe the anoxæmia, for the reason that cyanosis only appears when 40 per cent. of a normal hæmoglobin content exists as reduced hæmoglobin. Therefore, an anæmic patient with 50 per cent. hæmoglobin would require 90 per cent. of the total hæmoglobin present to be reduced for the appearance of cyanosis. Oxygen administration is of no avail in anoxic anoxæmia.

Altitude Sickness; Mountain Sickness.—There is considerable difference among individuals as regards liability to the appearance of symptoms at low atmospheric pressures, some suffering earlier and more than others. The immediate effect of exposure to such pressures is to cause rapid concentration of the blood and therefore a relative increase of the ratio of the hæmoglobin to the volume. A 10 per cent. rise in the hæmoglobin ratio may occur after 20 minutes' exposure. This is in part produced by the rôle of the spleen in acting as a reservoir for the erythrocytes, which are discharged rapidly into the general circulation under these circumstances. This serves as a compensation for the oxygen-want of the tissues, and its occurrence is associated with a disappearance or amelioration of the initial symptoms of oxygen-want. In those who remain at a bearable high altitude many weeks, some degree of acclimatisation occurs, and this is associated with hyperactivity of the blood-forming organs and a true erythræmia. The anoxæmia produces a hyperglycæmia, and there is at first an alkalæmia from increased ventilation, which subsequently lessens.

Symptoms.—*Mental effects* occur most importantly when rapid ascents to high altitudes are made in aviation, and consist of a gradually increasing dulling of perception, of which the subject is usually unaware. There is an increasing inaccuracy and lethargy of mental functions with a tendency to torpor and loss of memory. The skilled photographic observer takes eighteen photographs upon the same plate, the observer throws his valuable notes overboard, the pilot makes for a wrong destination or goes to sleep, and the fighting scout forgets to go into action. On return to land a muddled and confused memory of what has happened during the flight is all that remains. Lesser degrees of this condition have led to great errors in judgment, foolhardiness, apparent cowardice and irresponsibility in military aviation. So insensibly does this mental paralysis come on and so deep may be its effect before its presence is realised, that in Tissandier's balloon ascent in 1875, all three aeronauts, though provided with oxygen apparatus, were paralysed beyond movement before realising the necessity for using it, and two of them lost their lives. Diminution of auditory perception becomes so great at high altitudes that the aeroplane engine becomes almost inaudible.

Respiratory effects.—At an altitude of 12,000 feet, nose-breathing ceases, and above this height the breathing deepens into hyperpnœa, which may

be most distressful and may be periodic. The dyspnœa is greatly increased on exertion and is accompanied by cyanosis. Even such acts as talking and using a pressure pump may greatly increase the dyspnœa.

Muscular weakness.—Accompanying the mental lethargy is an increasing condition of muscular weakness. The slightest exertion is hard work. The machine is difficult to fly at very high altitudes, and the marksman shoots badly, and the mountaineer becomes incapable of taking exercise.

Other symptoms which may occur are—(1) headache, which may be very intense and which is very usually met with in prolonged exposure to high altitudes, as in mountain climbing; (2) spasmodic gulping accompanying the hyperpnœa; (3) fainting on exertion; (4) vomiting; and (5) hæmorrhage in the form of epistaxis, both of which are rare; and (6) frequency of micturition, which is common.

The mental effects are most conspicuous in aviators who had to make prolonged flights at very high altitudes during the War of 1914–1918 before the regular use of the oxygen apparatus. The dyspnœa, headache and muscular effects have been most troublesome in mountain ascents where exertion is unavoidable.

Death has occurred only in balloon ascents to gain a great altitude, and it occurs very rapidly, and is preceded by general muscular paralysis. Glaisher and Coxwell survived 29,000 feet by a lucky chance after complete paralysis of the limbs had set in. Sivel and Croce-Spinelli died at a height of 27,500 feet, while Tissandier, who was with them, survived. The after-effects of exposure to high altitudes have been well described by Birley, who, after observing many flight landings after high patrols during the War of 1914–1918, writes: "The gait of the men on landing is unsteady and laboured. Reports are laboriously made out (there being a general disagreement as to what was seen and done). Tempers are short, every one looks and feels tired, and the idea uppermost in the mind is to lie down and go to sleep. Severe frontal headache is common; it may persist until the following day and at times proves incapacitating. Appetites are poor and spirits are depressed. It is easy to understand that a repetition of this kind of work over any length of time was rapidly productive of deterioration of mental and physical well-being."

Remarkable individual tolerance to anoxæmia occurs in some subjects, but this tolerance tends to disappear with repeated long exposure. Physical fitness and training increase toleration up to a certain point, whereas unfitness and especially digestive disturbances lower tolerance, and the latter are apt to induce vomiting.

Treatment.—Since the symptoms are due solely to lack of oxygen they can be entirely avoided by the use of a portable apparatus to deliver the necessary oxygen by all those who have to encounter an altitude of over 15,000 feet. Professor Dreyer's apparatus is portable, compact and satisfactory, and its essential feature is the regulation of oxygen delivery by an aneroid controlled valve, so that the amount of oxygen delivered varies in inverse proportion to the barometric pressure of the atmosphere surrounding the instrument and consequently in direct proportion to the altitude.

When symptoms have developed, the immediate treatment requisite is the cessation of exertion, the provision of oxygen if available and a speedy return to a lower altitude.

SEA-SICKNESS AND ALLIED CONDITIONS

Definition.—A disorder of the central nervous system produced by an unaccustomed and irrelative stimulation of the afferent organs which subserve the orientation and sense of movement of the body in space, namely, the eyes, the labyrinths, the splanchnic sensorium and the common sensorium of skin and muscles. This stimulation may occur when the body as a whole is subject to continuous movement which does not allow of continuous correct ocular and vestibular correlation of self and external objects, as in train-sickness and dancing-sickness, and more especially when it is subject to alternating movements which destroy the correspondence between the afferent impressions reaching the nervous system from those organs, as in sea-sickness and swing-sickness. The symptoms of this disorder are expressed as a feeling of spatial insecurity and visual disorientation, vertigo, diplopia, headache, anorexia, nausea and vomiting, pallor, lowering of blood pressure and prostration.

Ætiology and Pathology.—Animals are as liable to the disorder as is man. Early infancy is immune from the affection, since the orienting mechanism has not attained physiological activity; and old age is relatively immune, probably from lessening irritability of the nervous system. Individual hypersusceptibility and individual immunity are very common, and the readiness with which toleration is acquired by training varies greatly in different people. An attack of sea-sickness resembles closely an attack of migraine, and again it resembles acute cerebellar irritation, and again the symptoms which follow chloroform and ether anæsthesia and alcohol poisoning, for the reason that in all these conditions it is the nervous mechanism of orientation which is especially disturbed. The subjects of migraine are almost invariably particularly bad sailors and train travellers, and the symptoms of their attacks of sea-sickness and train-sickness often take the pattern of the migrainous attack. The importance of the factor of ocular disorientation is well shown by the fact that "sea-sickness" may occur in a susceptible subject when he is stationary but when the objects around him move in undulatory fashion, as from the movements of the waves when he is upon a pier and when he witnesses sea movements as a stage effect.

The precautions which tend to obviate sea-sickness are those which tend to eliminate or lessen the essential factors in its production. A position amidships where the angular movements are least, a supine decubitus which most protects the semicircular canals from stimulation, and which removes the muscular sense element, and in a cabin which moves more or less with the body, and therefore produces little ocular disorientation, is the one best calculated to avert or lessen the disorder. A gyroscopic cabin which removes all the factors except the "lift" and "scend" element is said to obviate the disorder even in the most susceptible subject.

There are many adjuvant factors which are important but not essential, such as apprehension from previous experience, cold, expectant attention, the smell of the ship, dyspepsia and the presence of others suffering from sea-sickness.

Symptoms.—The initial symptoms are a loss of the usual feelings of well-

being, accompanied by a vague feeling of cephalic, ocular and epigastric discomfort. Salivation, gaping and yawning follow, with irregularity of respiration, flatulency, pallor of the face, and a sense of squeamishness, as though at any moment vomiting might occur.

In the fully developed attack it is convenient to divide the symptoms into two groups—cephalic and gastric; but though in different subjects one or the other group may dominate the aspect of the attack, yet few persons suffer from the one group of symptoms to the complete exclusion of the other. The cephalic group comprises ocular distress, diplopia, which may be severe though transient, giddiness, headache, depression, and mental despondency and apathy. These may persist for a very considerable time after the patient goes ashore.

The gastric symptoms consist of nausea, retching and vomiting, which are often most violent and distressing, the vomit ultimately consisting of a thin, bile-stained fluid. There is complete anorexia, and in severe cases nothing can be retained in the stomach. Constipation is often obstinate.

The general constitutional effects of prolonged sea-sickness may be very severe. There is a general condition of collapse. Alternate heats and chills, with frequent chattering of the teeth and shivering, pervade the system; the eyes are dull, and may be bloodshot from straining; the countenance becomes shrunken, pale and perhaps greenish, inexpressive and dejected. The cardiac action is depressed, the blood concentrated, the body desiccated, and little urine is passed. The pulse and respiration are quickened, the skin is cold and either dry or clammy, the tongue is moist and coated, and both the breath and the urine are likely to contain acetone bodies. Hebetude is always marked, and in severe cases the mind may be utterly indifferent to the surroundings and no consecutive train of thought can be pursued. There is a general feeling of bodily soreness and weariness and a sense of exhaustion.

Course and Prognosis.—The symptoms usually subside rapidly when the voyage or other movement causing the condition is over, but sometimes both the cephalic and gastric symptoms persist for a time, and the patient is "good for nothing" until he has had a night's sleep. In persons taking long sea voyages, the symptoms usually lessen in a few days, reaction sets in with a return of appetite, and convalescence is complete within a week, but symptoms are liable to return with an onset of rough seas. Some persons, on the other hand, never lose the symptoms until the voyage, however long, is over, and these may be reduced to a piteous condition of bodily weakness, from which subsequent convalescence is slow. Death appears never to have occurred even in the most severe condition of bodily depression and starvation from sea-sickness. Apart from the prolonged convalescence which may be required in severe and long-lasting cases, there seem to be no harmful results from sea-sickness. It has been held to have a salutary effect upon subsequent health since ancient times. In pregnant women it does not have any tendency to cause miscarriage.

Treatment.—To avoid sea-sickness a susceptible subject should, for a few days before taking to the sea, eat sparingly, avoid alcohol and over-fatigue, take regular exercise and carefully attend to any condition of dyspepsia and constipation, and partake of a good wholesome meal some two hours before going on board. He should secure a berth amidships, lie

supine with the head low, and keep warm. Some persons find a closed cabin insufferable, and are better on deck in the open air. The administration of bromides some hours before sailing is often of signal service, and this will often lessen the cephalic symptoms when an attack has developed. Chlorbutol, (chloretone) (grs. 5) and phenobarbitone (gardenal, luminal (gr. 1) are also very valuable, both as prophylactics, when they should be taken just before sailing, and as remedies during the attack. Combinations of bromides and chlorbutol are very useful, and there is at least one patent remedy, of which the basis is monobrom-camphor and chlorbutol, which is very efficacious.

During the attack it is essential to keep warm and as quiet as is possible, and avoid any source of further irritation of the organs of orientation; to quiet the irritation of the nervous system with bromides and chlorbutol; to secure sleep, to which end barbitone or adalin is very useful; to prevent acidosis and to see that the patient is fed. With severe and prolonged vomiting, anorexia and prostration it may be difficult to secure these ends. Swallowing food must be insisted on, and the administration of very small perfectly dry meals, such as cold chicken and biscuit, will often break the anorexia and vomiting. A severe case should always be brought into the open air on deck after four days in the cabin. Acidosis should be combated by the alkaline carbonates. Alcohol and aromatic carminatives are sometimes valuable.

JAMES COLLIER.
Revised by F. M. R. WALSHE.

ELECTRICAL INJURIES

Electrical injuries may be received from lightning-stroke, from accidental contact with high-tension conductors, or from judicial electrocution where this obtains.

The severity of the injuries sustained in any given case depends upon other factors than the voltage of the discharge received, and thus it is that fatal injuries may be received from currents of comparatively low voltage (120 volts), and survival may follow the reception of currents of higher potential. It is said that a current of 500 volts is commonly fatal, and that alternating currents are more dangerous than direct. Voltages of over 1000 are spoken of as "high tension." The quantity of the current is also of importance. A current of 100 amperes is dangerous, one of 500 is likely to be fatal. In judicial electrocution the victim is subjected to repeated discharges (4 to 8), each lasting some seconds (5 to 50), of alternately high and low potential (500 volts alternating with 2000).

Pathology.—In those who survive electrical injuries complete recovery is usual—though not invariable—and it is clear that the lesions found in the nervous system in fatal electrical injury can hardly obtain even in slight degree in non-fatal cases. We shall first describe the lesions found in fatal cases.

In death from lightning-stroke the head is invariably struck, and there is a localised effusion beneath the scalp, which may be differentiated from the effects of a blow by the absence of abrasion. The body surface shows burns of various forms—linear burns, arborescent burns, and severe localised

burns beneath any metal object which may have been carried in a pocket or worn on the person.

In the nervous system there are abnormal rents and fissures in the brain, the cerebro-spinal spaces are distended, the perivascular spaces enlarged, and the arteries at the base of the brain may show rupture of their muscular coats. In various situations the nerve cells show severe disruptive changes. In the past it has been assumed that these lesions are due to the passage of an electrical current through and over the body, but in a recent analysis of the circumstances of electrical injuries from the point of view of physical science Blake Pritchard has shown that this passage is inadequate to account for the nervous lesions, and that two factors are operative. These are the passage of current, and the charging of the body with electricity. It is the latter factor which alone is capable of producing the lesions found in the nervous system. The following brief summary is taken from Pritchard's account (*Lancet*, 1934, I. 1163).

If a man make contact with a conductor at high potential, or if he be struck by lightning, he will suddenly become highly charged with electricity. A current will pass through him only if he is in a position to lose this charge. If he is not insulated from earth the charge will pass rapidly through and over him, and will not accumulate upon him. This rapid passage will give rise to heating, electrolytic and mechanical effects, but these alone do not produce the lesions observed in fatal cases.

If he be more or less effectively insulated from earth, his body surface will become highly charged, and electrostatic forces will develop from the mechanical repulsion which is exerted between similarly charged particles or bodies. A charged body will be repelled from all similarly charged bodies, and all the constituent elements of the body which carry the charge will be repelled from one another. Thus it is that when more than one object is struck by lightning, they are flung apart; a man is flung several yards from a tree under which he has been standing; or two men simultaneously struck are flung away from each other; a parcel held by an individual struck is hurled out of his grasp, and also his clothes, belt and boots are burst and torn off him in fragments, and he may be stripped naked. Within his body the same disruptive forces are at work, and produce lesions in proportion to the rigidity and cohesion of the tissues. The charge upon his body surface will make each particle of the surface repel each other particle, the whole surface will tend to expand away from the body, and this sudden expansile force will pass inwards as a wave of decompression. In this way we may account for the characteristic disruptive lesions found in the brain.

It is probable, then, that the electrostatic effects play a determining part in the production of the nervous lesions, and that these in their turn are largely responsible for a fatal issue when this ensues.

The actual passage of the current has heating and electrolytic effects, and Pritchard has tried to assess the importance of these. In legal electrocution, where alternating currents are applied in the manner and of the strengths described earlier, it is possible to form a fairly precise estimate of the heating effects. The current probably passes chiefly in the body by the blood and cerebro-spinal fluid, as well, of course, as over the body surface, where it produces the characteristic burns. It is possible that currents of the orders used may cause a rise of temperature in the tissues

they traverse of as much as 60° C. In lightning-stroke, the rise is probably much less. The higher rise named is capable of severely damaging the nervous system, but not of producing the lesions seen in fatal cases. The electrolytic effects are probably negligible.

Another effect of the passage of current—as opposed to the charging of the body surface—is the violent and generalised cardio-vascular and skeletal muscle spasm found so constantly in the victims of electrical discharges. This spasm may persist for some time, and in fatal cases until death has ensued. The heart and muscular coats of the arteries are strongly contracted, the victim is pale and pulseless, and in non-fatal cases may so remain for as long as an hour while artificial respiration is being employed.

Symptoms.—Graphic accounts of the effects of lightning-stroke are given by H. A. Spence in his monograph, and are based upon an extensive experience in South Africa. When struck by lightning the individual may later have no recollection of the incident, but on the other hand may speak of receiving a tremendous blow on the head. Others have complained of intense visual or auditory sensations, of pain in the trunk and limbs, of giddiness, and so on. The subject is usually unconscious, pale and pulseless, and respiratory movements are suspended. Surface burns of varying severity and extent are seen, and examination of the scalp will reveal a localised swelling at or near the vertex, with no cutaneous abrasion. There may be powerful and generalised muscular spasm for a brief period and the limbs may be in flexion.

As respiration becomes re-established—either spontaneously or after artificial respiration—the subject may become restless and resistive, crying with the pain of muscular spasm. Later, he becomes drowsy, has headache, and for one or more days may not be fully alert.

This initial state of suspended animation and apparent death is common after lightning-stroke, but not so common, apparently, after accidental electrical injuries from contact with conductors. It may be necessary to carry out artificial respiration for as long as an hour before—in non-fatal cases—respiration becomes normally established.

After accidental electrical injury the degree of shock varies from individual to individual. It has been suggested that in sleep the injury is less severe than in the waking victim, but it is probable that the two main factors discussed earlier play a more important part in determining the severity of injury than matters of sleep, individual susceptibility, fatigue and old age, all of which have been thought to have some influence in this direction.

Recovery from the effects of electrical shock may, as we have seen, take several days, and in rare instances more or less permanent residual symptoms of a neurological kind may ensue. Thus, Spence records a case where memory remained defective, speech slow and gait unsteady, and one ear was permanently deaf. An immediate effect which has been described is profound weakness with sensory loss of the lower limbs, which may be blue and cold. This condition passes off gradually in the course of some hours. A progressive condition clinically resembling amyotrophic lateral sclerosis has been described by Panse as a rare sequel of electrical injury, and this factor has been invoked in connection with disseminated sclerosis and Parkinsonism when these have developed in the subjects of electrical injury. Attributions of this order should be received with caution. Of course, as after other injuries, traumatic neuroses may follow electrical shock.

Diagnosis.—Spence records instances in which the finding of a dead body has made it necessary to determine the cause of death. When this is due to lightning-stroke, the following signs are found. There is an effusion beneath the scalp without superficial abrasion, and streaks of "brushburn" will be found upon the body surface. The body will be more or less stripped of clothes. If a hat was worn, a hole will probably be found in it over the seat of the scalp lesion. Leather garments, boots and belts are burst. Of course, if the victim was hurled or flung down some other signs of injury caused in this way may be found.

Treatment.—When, as is commonly the case after lightning-stroke, the victim is unconscious, white and pulseless, artificial respiration must be undertaken at once, and persevered with for at least an hour before abandoning the patient. Even when respiration is first resumed, it may fail again and artificial respiration must be kept up until normal breathing movements are fully established. When consciousness is regained, the patient may complain of severe headache and of painful muscular cramp. The latter should be treated by massage. The usual restorative measures employed in severe shock may also be used, but the essence of treatment in severely shocked and unconscious patients is the carrying out of artificial respiration.

The superficial linear burns of lightning-stroke may smart if exposed to the air, and are best covered by ointment, but they usually heal without scarring. The deeper burns related to metallic objects carried by the victim, or to the points of entry and departure of the current in accidental injuries from contact with conductors, will sometimes require the ordinary treatment of burns according to their depth and extent.

The very rare residual neurological symptoms and disabilities may have to be dealt with according to their character and severity.

F. M. R. Walshe.

HEAT-STROKE AND THE EFFECTS OF HEAT

Under this heading are included those types of illness caused by exposure to a high atmospheric temperature. They are classified as—(1) heat exhaustion; (2) heat hyperpyrexia (heat-stroke or sun-stroke); (3) the gastric type of illness; and (4) the choleraic or gastro-intestinal type.

Ætiology.—*Exposure to high temperature.*—Cases commonly occur amongst those exposed to the sun in the hot seasons of a tropical climate; but the high temperature of the air in a dwelling, or the excessive heat to which stokers are exposed on board of ships, or, indeed, any prolonged exposure to a high atmospheric temperature, whatever its nature, may cause any of the types of heat-stroke. When the shade temperature reaches 110° F., danger occurs, and with each degree rise above this limit an increasingly larger number of cases results. The effect of heat exposure is cumulative in action, and it is a succession of hot days which is followed by a large number of cases of heat-stroke. A comparison by Willcox of the case incidence curves with the temperature curves in the Mesopotamian campaign indicated a delay of a few days in the rise of the former. An individual exposed to heat for one or more days may not be taken ill until the evening or early morning, when the temperature has fallen consider-

ably, the cumulative effect of the exposure gradually overcoming the body resistance. Since the temperature in the sun greatly exceeds that in the shade, exposure to the sun's rays is a very important exciting cause. In the hot seasons of tropical countries this danger is well known, and exposure to the sun is avoided as far as possible. It has not been shown that any rays of the sun other than the heat rays have a special significance in the causation of heat-stroke.

Climate.—Tropical climates in seasons when the shade temperature exceeds 110° are associated with the various forms of heat-stroke, and heat waves in any climate, if the temperature is sufficiently high, act as causes of illness. The absence of shade from the sun is an important factor, and heat-stroke is specially associated with hot climates of countries where flatness and absence of trees and vegetation are marked, as, for example, in Mesopotamia and the country round the Persian Gulf, and desert regions generally, as in the Sahara Desert in Africa. In countries where, during the hot season, there is little fall of the temperature at night, the danger from heat-stroke is increased.

Humidity of the atmosphere is an important predisposing factor. If this is high, heat loss is retarded, and there is greater liability to heat-stroke.

Stagnation of air.—Free currents of air promote the evaporation from the skin and protect by increasing heat loss. The great protective value of electric fans and punkahs in dwellings is due to this cause. It is important to remember, however, that when the temperature is very high, currents of hot air may do more harm than good, and for this reason, in tropical countries, houses provided with fans should be kept closed during the heat of the day, in order that the hot air may be excluded as far as possible. The "Kata" thermometer, introduced by Professor Leonard Hill, F.R.S., records the rate of heat loss from evaporation of a wet bulb, and is a valuable guide in estimating the dangers from heat-stroke in different situations, such as the wards of hospitals.

Dwellings.—Thick walls of non-conducting material, such as stone, brick, or dried mud are protective, and it is important that the roofs of dwellings should be thick, so as to keep out the heat from the sun's rays. A tent, even of double canvas walls and roofs, affords only poor protection.

Persons of any age are subject to heat-stroke if the exposure is sufficiently great. The case mortality is higher in those over 40. Race is a very important factor. The natives of tropical countries are rarely affected by heat-stroke, unless some complicating disease, such as malaria, is present. White races unaccustomed to tropical climates are specially susceptible to the effects of heat exposure. Exertion is an important predisposing cause. Heavy physical exertion in temperatures over 110° is very dangerous.

Predisposing diseases.—Any disease causing pyrexia, such as malaria, sand-fly fever, enteric and paratyphoid fever, typhus fever and small-pox, predisposes to heat-stroke.

Intercurrent diseases.—In a high percentage of cases the heat hyperpyrexia supervenes in the course of another disease, especially malaria. Cases of febrile disease may be suddenly complicated by hyperpyrexia if exposed to great heat, and special precautions are necessary to prevent this.

Pathology.—The symptoms of heat-stroke in its various forms all point

to an auto-intoxication. The effect of high temperature on the brain and central nervous system is to diminish its functional activity, and likewise the excretory organs, such as the liver and kidney, are undoubtedly impaired in their excretory power. In addition, owing to the effect of heat on the muscles and tissues of the body generally, there must be an increased production of toxic substances, due to protein katabolic changes. These factors all tend to produce a marked auto-intoxication, which explains many of the symptoms of heat-stroke. Indican is usually present in the urine in considerable excess, and is evidence of an auto-intoxication. Acetone and diacetic acid are not found in appreciable excess in the majority of cases, though in a small percentage they are present in moderate degree. The auto-intoxication cannot, therefore, be regarded as an acidosis. It has been shown by Dr. W. Cramer that beta-tetra-hydro-naphthylamine will cause hyperpyrexia in animals, and it is likely that substances having a similar action are produced as the result of the heat on the tissues. Suppression of sweating has been shown by Dr. K. G. Hearne to be an important factor in the hyperpyrexia cases, the paralysis of the sweat secretion by the intense heat leading to a rapid rise of body temperature. In hot climates, the administration of atropine may be followed by hyperpyrexia from a similar cause. Suppression of sweating does not explain the causation of the gastric and choleraic type of heat-stroke, nor of heat exhaustion. It has been stated that heat-stroke is due to a bacterial infection; but there is no recent evidence to support this view. In the Mesopotamian campaign a large number of blood examinations were made during life in cases of heat-stroke, but all gave a negative result.

Rigor mortis occurs early, and putrefactive changes set in within a few hours of death. Œdema and general hyperæmia of the brain and lepto-meninges occur, and the nerve cells in the grey matter show marked degenerative changes. Petechiæ occur in the skin and mucous membranes in severe cases. The right side of the heart is dilated, and venous congestion is marked in all the organs. Signs of intercurrent diseases, such as malaria and typhoid, may be present.

Prophylactic Treatment.—Adequate protective covering for the head by thick pith topees or good cork helmets is essential. Spinal pads for protection of the spinal cord are valuable. The clothing should be light and loose and not too thin. Hand-fans and umbrellas are of value. A large amount of water should be drunk by those exposed to great heat, as so much moisture is lost by the skin in regulating the body temperature. Salt (sodium chloride) should be taken freely with food, to compensate for the loss of sodium chloride by excessive sweat excretion. Alcohol should be avoided during the heat of the day. Constipation should be guarded against, as it predisposes to the effects of heat.

1. Heat Exhaustion

The onset is sudden, with weakness, giddiness, faintness and inability to walk. A mild pyrexia of 102° or 103° F. occurs, lasting 2 or 3 days. The pulse is rapid and weak, and some cardiac dilatation is usually evident. If early treatment is adopted, the symptoms quickly improve; otherwise, there is a great risk of the supervention of hyperpyrexia.

Curative Treatment.—This consists in removal from heat, rest in bed and the administration of aperients.

2. Heat Hyperpyrexia

The onset may be sudden, with rapid rise of temperature, coma and convulsions. In other cases, the onset is preceded by malaise, headache, restlessness and sometimes nausea or vomiting. Frequency of micturition and urethral pain may occur. The temperature is somewhat raised—to 100° or 102° F. or so—and the skin hot and dry. These premonitory symptoms may last for a few hours, sometimes as long as 48, when the temperature rises to 110° F. or more, and mental excitement and delirium supervene. Coma and stertorous breathing now occur, and the face is flushed and cyanosed, the conjunctivæ being congested. The pupils are commonly dilated in the early stages and contracted in the comatose condition. Parotitis may occur, and petechiæ of the skin may be present in severe cases.

Albumin is frequently present in the urine in small amount in acute cases. An excess of indican is usual, and in some cases acetone and diacetic acid occur. Fibrillary twitchings of muscles and convulsions usually result, and the breathing is frequently Cheyne-Stokes in character. Incontinence of urine and fæces occurs with the coma, and death rapidly results, unless the temperature is reduced. Marked cardiac dilatation, often associated with a systolic murmur, is present. Bronchitis and pulmonary congestion sometimes occur, and pulmonary œdema is a terminal event. In the acute stage the knee-jerk is almost always absent, and does not return until the symptoms have cleared up.

Defective articulation (anarthria) occasionally occurs as an after-symptom, and sometimes nystagmus, or squint, with diplopia has been observed. Multiple neuritis, with weakness and wasting of the extensor muscles of the legs, is a rare late complication. After the subsidence of the hyperpyrexia, a pyrexia up to 102° or 103° F. may persist for several days, and is due to the auto-intoxication present, no organism being found in the blood in the uncomplicated cases. For some weeks after the subsidence of the temperature there is great liability to a recurrence of heat hyperpyrexia, and the utmost care must be taken to avoid exposure to heat.

Sequelæ.—Cardiac dilatation may last for some days or weeks after an attack. There is a great susceptibility to heat for a long period after an attack, and headache may follow slight exposure, so that residence in a cool climate is advisable for some years afterwards. An abnormal mental condition, amounting in some cases to insanity, may result. Persistent nervous symptoms, the result of actual organic changes in the brain or cerebellum, may remain. The presence of the knee-jerks is a valuable prognostic sign; if they remain absent there is danger of a recurrence.

Curative Treatment.—The patient should be placed in cool surroundings and hydro-therapeutic measures immediately adopted. Spraying with ice-cooled water, the patient lying on a bed with a rush mattress, so that there is free circulation of air round the body, is the most convenient method. Ice should be applied to the back of the neck and head. Rectal injections of iced-cold water, to which about 1 per cent. of sodium chloride is added, are of value. Should the hyperpyrexia not quickly subside, or should it not

be readily controlled, an intramuscular or intravenous injection of a solution of quinine bihydrochloride, grs. 10 should be given. Blood film examinations should always be made immediately when hyperpyrexia occurs, and if these show a malarial infection the quinine treatment should be continued, daily injections being given for 3 or 4 days, and afterwards an oral course. Convulsions are best treated by a venesection of 10 to 20 ounces, and rectal injection of ice-cold water containing 120 grains of sodium chloride (common table salt) to the pint. In cases with convulsions it is not advisable to give intravenous saline after venesection, for the intravenous injection may cause recurrence of the convulsions. In some cases morphine hypodermically or inhalations of chloroform may be required. Cardiac failure should be treated by digitalin, strychnine, camphor in oil, nikethamide (coramine), adrenaline or pituitary extract hypodermically. Failure of respiration should be treated by artificial respiration, and oxygen bubbled through alcohol may be administered. Lumbar puncture is of value in the comatose condition, in order to relieve the excessive pressure in the cerebro-spinal fluid.

When the patient is able to swallow, as large quantities as are safely possible of physiological saline should be given. This may also be given by nasal tube.

Loss of sodium chloride is a marked feature of cases of illness due to the effects of heat. This should be administered in quantities of 12 to 20 grammes per day for several days.

3. The Gastric Type

In this insidious type of illness for several days the patient will suffer from restlessness and mental irritability, nausea and occasional vomiting. The face is flushed and the mouth temperature normal; but the rectal temperature may show a rise of a degree or two. The liver shows some enlargement, and the knee-jerks are lost. In many of these cases after 4 to 10 days' illness a sudden hyperpyrexia occurs, which is often fatal.

Curative Treatment.—This consists in keeping the patient at complete rest in bed and as cool as possible, free purgation, a lacto-vegetarian diet, and rectal injections of ice-cold water containing bicarbonate of soda, 60 grains and sodium chloride 120 grains to the pint, and the administration of 30 grains of sodium bicarbonate every 3 hours; by these means hyperpyrexia is avoided. Liquids should be taken freely by mouth, and sodium chloride in doses of 12 to 20 grammes daily should be given by mouth to replace the loss by sweating.

4. Gastro-Intestinal or Choleraic Type

In this form of illness the onset is sudden, and marked collapse is present. The temperature is raised to 100° or 102° F., and vomiting and diarrhœa occur. The face is pale, the skin clammy and the eyes sunken. The knee-jerks are lost. The stools are watery, and free from cholera organisms. Death usually occurs after a 3 or 4 days' illness.

Prognosis.—This is very grave.

Curative Treatment.—This consists in protection from heat, and the administration of normal saline subcutaneously or intravenously. The intra-

venous hypertonic saline treatment as advocated by Rogers, and described in detail under the article on Cholera (see page 121) should be given as soon as possible for the treatment of the collapse and loss of fluid. The administration of suitable cardiac stimulants hypodermically is advisable.

HEAT CRAMPS.—Attacks of heat cramps occasionally occur in persons who perform muscular exercises while exposed to high temperatures. The condition occurs in stokers on board ship, and in furnace workers. The muscular spasms occur in the calves, arms and sometimes the abdominal muscles, and are severe and very painful. They may last from 12 to 36 hours, and are followed by soreness and weakness. Deficiency of sodium chloride in the blood is the chief cause of the symptom. Doses of 10 to 20 grammes daily should be given well diluted with water or other beverage or food. Tablets of one gramme sodium chloride may be swallowed in doses up to 20 per day.

W. H. WILLCOX.

INJURIES FROM X-RAYS

Ætiology.—Within 3 months of the announcement by Röntgen of his discovery of X-rays in November, 1895, it became known that conjunctivitis could occur after some hours of exposure to irradiation. A year later erythema, swelling, and necrosis of the skin, alopecia, and chronic radiodermatitis were reported. In 1897 attention was directed to the acute constitutional symptoms. In 1902 a case of cancer was recorded following chronic ulceration caused by X-rays. The first death recognised as due to the action of X-rays occurred in 1914. In 1922 it was estimated that 100 radiologists had died from malignant disease due to their occupation. Deaths occurred among radiologists exposed to X-rays before the importance of adequate protection was realised, and unfortunately still occur.

So far nearly all the victims have been research workers, radiologists, laboratory assistants, technicians and nurses. Cases of industrial origin did not occur until later, because the use of X-rays in industry began later. Industrial workers, unlike professional workers, are often quite ignorant of the possible dangers of the apparatus used, so that industry is now, in respect to the use of radio-active substances, about where medical practice was in 1914. There is, however, no reason why the lamentable history of the pioneers in the medical field should be repeated. The human experiments have been made, the tragic results of carelessness demonstrated, and the measures necessary for adequate protection are known and available to anyone who cares to learn them.

X-rays may be used in industry for the detection of defects, cracks and blow-holes in castings, of defects in alloys from faulty mixture, of erosion in cables or gas cylinders, and of defects in reinforced concrete or in weldings. X-rays are also used to sort fresh eggs from stale, to reveal mineral adulterants in vegetable foods, and weevils in grain. For the examination of metals and all thick specimens very penetrating rays must be used.

Symptoms.—Injuries which follow a short single exposure, or perhaps several exposures, may vary enormously in intensity. In mild cases there is simply a transient reddening, lasting a few days and followed by scaling

and loss of hair. If the burn is deeper, blisters appear which may be serous or purulent, and the condition resembles that following a scald but is less acute and slower to heal. Sometimes the process, instead of disappearing in a few weeks, penetrates to the deeper layers of the skin and to the subcutaneous tissues, with the formation of a leathery slough, surrounded by a brawny indurated swelling with ill-defined limits. The process is exceedingly slow and obstinate, and has a tendency to progress and to resist treatment in a remarkable way. It is at times very painful.

In chronic X-ray dermatitis the changes in the hands begin round the base of the nails as a peculiar erythema and gradually increase. Transverse and longitudinal ridges appear on the nails, which become brittle, assume a characteristic dirty brown appearance, tend to separate from the matrix, and eventually thicken and form shapeless masses. The skin becomes uniformly red and atrophied ; small warts appear, increase in size and number and, when situated over the knuckles, crack and cause much pain. Later the dry thickened skin shows telangiectases, absence of hair, paronychia and ulcers which are slow to heal and prone to break down. The hair follicles and the sebaceous and sweat glands completely disappear in cases of long standing. The freedom of the palms of the hands may be due to the naturally thicker skin there, but the greater liability to exposure of the backs of the hands and fingers is probably the more important factor. The lesions are as a rule slowly progressive. Post-irradiation telangiectases, which have been regarded as compensatory for obliteration of the vessels in the corium, usually appear within 2 years, and sometimes in the absence of an initial erythema ; in some instances the interval between irradiation and the appearance of telangiectases is prolonged, even to 15 years. If exposure is continued the lesions may progress to involve the tendon sheaths and joints. There may be intense pain, of which the severity is out of proportion to the size of the lesions ; it is caused by the exposure of nerve-endings.

Squamous-celled carcinoma is almost always the form of malignant disease which has followed excessive X-ray exposure and long-continued X-ray dermatitis in man. Although most often seen in radiologists and manufacturers of X-ray apparatus, X-ray carcinoma may also occur in patients who have undergone treatment by X-irradiation. The interval between the onset of chronic X-ray dermatitis and the appearance of malignant disease varies from 3 to 27 years. The average of 35 cases was 7 years. The age incidence from 35 to 50 is comparatively early, that of ordinary carcinoma of the skin being between 55 and 58. The most frequent site of the growth, which is not uncommonly multiple, is on the backs of the hands and fingers, and the hand more exposed appears to be the one more severely affected, the left in radiologists and the right in those engaged in the manufacture of apparatus. Among radiologists carcinoma usually develops in an ulcer, less often in keratotic areas. The predominating symptom is pain, which may be constant and very severe, and has been ascribed to invasion of the terminations of nerves by the growth and to neuritis. Occasionally basal-celled carcinoma results from X-irradiation. In one case a basal-celled carcinoma of the scalp appeared 18 years after epilation for ringworm. A case has also been recorded of multiple basal-celled carcinomas on the trunk of a radiographer.

Constitutional symptoms only became prominent after the introduction of deep X-ray therapy, in which massive doses of deep penetrating rays were given. Severe constitutional symptoms may occur. They are nausea, uncontrollable vomiting, sometimes with hæmatemesis, diarrhœa, with the passage of blood, abdominal pain and distension, fever up to 104° F., restlessness, profound prostration, progressive cardiac failure, small rapid pulse and dyspnœa. When death has occurred it has usually taken place about the fourth day from the onset. Both animal experiments and necropsies of human victims show that the application of X-rays to the abdomen may result in necrosis of the intestinal mucosa. As long ago as 1905 unsuspected sterility was found in 18 persons who had for various periods been exposed to X-rays. The acute degenerative changes in the testes are followed by fibrous atrophy. Anæmia occurs in X-ray workers. After small doses of X-rays, the lymphocytes are first increased in number, then diminished. The red cells may also be increased at first, but anæmia sets in later and may become extreme. In patients who recover, the anæmia is slower to disappear than is the leucopenia. True aplastic anæmia does not occur.

Diagnosis.—The possibility of exposure to radium should always be excluded before attributing what appears to be aplastic anæmia in an X-ray worker to X-irradiation.

Treatment.—PROPHYLACTIC.—Within the first few months after their discovery it was found that X-rays were stopped more effectively by lead than by any other common metal. Hence lead for protection came into use very early. To-day lead, lead glass, lead rubber and lead bakelite are extensively used. Transparent lead glass windows in tube containers were first employed about 1900. At that time the need for protecting both operator and patient during radiographic exposure was very great, because low voltages were used, with consequent long exposure to a very soft and easily absorbed radiation. For example, to radiograph the spine required exposures up to 1 hour. That the radiologist was not more frequently affected by the scattered radiation of such exposures was due to the fact that during them he might retire to another room to see other patients. About 1903 there appeared a multitude of protective devices to be worn by the radiologist, including apron, jacket, gloves and goggles. This type of protection gradually reached its peak about 1914, when necessity threw caution to the winds, and the more elaborate devices gave place to means of protection which were built into the apparatus.

To-day there is international agreement as to the most effective methods of prevention. In Great Britain such methods have been widely adopted, and although they have no strictly legal recognition, powers of inspection and approval have been placed in the hands of the National Physical Laboratory. It is important that the industrial physician should plan measures for the protection of employees against the dangers of X-irradiation, for in large manufacturing establishments there are X-ray departments for diagnosis as extensive and as much used as the average hospital department. Here the problem may include protection of workers in neighbouring rooms, for unless walls and floors are very thick or are rendered impermeable by the use of lead, X-rays may pass through them and cause injury.

SYMPTOMATIC.—X-ray carcinoma should be treated either by diathermic coagulation under local anæsthesia, or by radium. Slight degrees of anæmia

recover on removal from exposure. In more severe degrees iron must be used, and when this fails blood transfusion is necessary.

INJURIES FROM RADIO-ACTIVE SUBSTANCES

Ætiology.—The gamma rays of radium appear to have a greater tendency than X-rays to cause aplastic anæmia; this impression is supported by the experimental evidence that the penetrative gamma rays of radium reach the bone marrow more readily than do X-rays. Three fatal cases of aplastic anæmia were reported in the London Radium Institute in 1920, one in a nurse and two in laboratory assistants. In 1925 the death of a chemical engineer working with radium and thorium-X was recorded.

The chief use of radium salts in industry has been in the manufacture of luminous paint for the figures of clocks and watches, and certain important parts of the machinery of aeroplanes. At two factories, one in New Jersey and the other in Connecticut, 38 deaths occurred among factory girls, chemists and physicists. The paint used contained insoluble radium sulphate, mesothorium and radiothorium. The girls affected introduced the paint into their mouths through the habit of pointing the brush between their lips and swallowed it for periods of from 1 to 4 or more years. The insoluble radio-active materials became deposited in the body to such an extent that even during life radio-active emanations could be detected in the expired air.

After death bone was found to be the tissue in which the materials had mainly accumulated. The anæmia resulted from the continuous bombardment of the hæmatogenous marrow by alpha particles, and it was found that these changes were quite different from those due to external irradiation with beta and gamma rays only. Radio-activity in the bones and teeth was demonstrated by autophotography. The bones when placed directly on photographic plates produced impressions in as short a period as 3 days. The total amount of radio-active material necessary to produce fatal results is extremely small. It is sufficient for 0·01 mg. to be distributed over the whole skeleton to produce a terrible death years after it has been ingested. Radium is thus the most deadly poison known; tetanus toxin previously held the record with a lethal dose of 0·22 mg.

Symptoms.—Dermatitis due to radium, isolated by the Curies in 1898, was reported in October 1900. Insufficiently protected tubes of radium salts kept in the waistcoat pocket for 6 hours produced reddening of the skin and within 10 days or so ulceration. Dermatitis has been reported in a number of persons engaged in making radium preparations, and less often in medical men. The ill-effects of ingestion of radio-active substances include severe anæmia, sometimes aplastic, necrosis of the jaw, spontaneous fractures and sarcoma of bone. The changes in the blood have been referred to as *anæmia radiotoxica*. The red cell count may drop below one million and the hæmoglobin below 20 per cent. Leucopenia, granulopenia and thrombopenia all occur. Purpura is followed by more serious bleeding, such as menorrhagia, hæmoptysis, hæmaturia and retinal hæmorrhages. Necrosis of the jaw occurs. It is similar to that produced by phosphorus, and is attributed to infection supervening upon changes in the bone. In certain cases necrosis of the jaw does not occur, but after a number of years generalised

changes in the bones develop with deformity and sometimes spontaneous fracture, a condition known as *radiation osteitis*. Bone sarcoma occurs in 25 per cent. of the cases of occupational mesothorium and radium poisoning.

Treatment.—Though medical practice is now almost safe so far as X-irradiation is concerned, matters are very different in the case of radium. There is no doubt that many people are affected by handling radium, chiefly by the gamma rays. Their penetrative powers are so great that it is not practicable to secure complete protection. In the case of persons who carry radium about the weight of lead they can bear to carry only partly protects them. Surgeons handling radium are also ill-protected. In the case of a man using 120 mg. of radium in the treatment of carcinoma of the cervix uteri, protection is very difficult as each time he has to handle the substance closely and carefully. It is obvious that ingestion or inhalation of radio-active materials in industry is highly dangerous, and that all occupations involving the handling of such substances should be strictly controlled and supervised. In the watch industry, outside New Jersey and Connecticut, the practice of pointing the brush with the lips is unknown, and no ill effects have been observed in other countries.

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ALCOHOLISM

Alcoholism is dealt with in this section mainly from the point of view of the physical effects. The subject may be conveniently divided into (1) acute alcoholism; (2) alcoholic coma; (3) dipsomania; and (4) chronic alcoholism. The section of Psychological Medicine (pp. 1836–1840) should also be consulted.

1. ACUTE ALCOHOLISM

Synonyms.—Acute Alcoholic Poisoning; Drunkenness.

Definition.—A person is said to suffer from acute alcoholism when as a result of alcohol he is unable to do with safety to himself or others that which he attempts.

Ætiology.—The effect of alcohol varies in different individuals, and depends not only on the amount taken but also on the physical state and mental stability of the patient.

Pathology.—Repeated sublethal doses cause no pathological changes in experimental animals. However, alcohol enhances the effects of other poisons and accelerates such degenerative processes as atheroma. Clinical observations on healthy human adults support these findings. It is a matter of common experience that post-alcoholic intestinal symptoms, malaise and headache, are more apt to occur when some other poison is taken at the same time. Examples are tobacco and the harsh acids of badly prepared wines. In alcoholic intoxication, the blood and urine alcohol reach a level between 0·1 and 0·3 per cent. The basal metabolism is raised, and there is great water loss from over-breathing, sweating, diuresis and sometimes vomiting. Alcohol depresses nervous activity. Reaction time is prolonged and perception dulled. The special senses become less acute, weakness of

accommodation and of ocular synergia occur with blurred vision and diplopia. The normal social inhibitions become dulled so that the animal tendencies escape repression, with consequent non-social or even anti-social behaviour. Indeed this lessening of inhibition is the end aimed at in taking alcohol, and allows a certain freedom and exhilaration in over-repressed persons. This escape from inhibition should not be regarded as an increase in general efficiency. In unstable persons, pathological mental tendencies may become uncovered, with resulting epileptic attacks either in the form of fits, or as "epileptic equivalents" such as mania a potu or automatism (see p. 1837).

Symptoms.—The clinical picture of drunkenness is well known. After sleeping the patient wakens with headache and the usual symptoms of a mild gastro-intestinal upset. As has been inferred before, there is little after-effect in the healthy person who drinks sensibly. People who have drunk unwisely or have taken too much tobacco will feel ill all the next day. They show the clinical picture of a mild melancholia with gloomy thoughts, poor volition and excessive irritability. Strong sensory stimuli are poorly tolerated. Mental concentration is poor, and there is marked lessening of general efficiency.

Diagnosis.—It is often impossible for an exact diagnosis to be made until the patient has been kept under observation, and this precaution should be taken where there is any doubt. No exact percentage of alcohol in the blood and urine can be fixed as the precise limit between sobriety and drunkenness for medico-legal purposes.

Prognosis.—Recovery usually takes place within 24 hours and can be hastened by appropriate treatment.

Treatment.—If the drunken person is seen before going to sleep, he should be given an emetic of warm sodium bicarbonate solution (60 grains to a pint) and subsequently encouraged to take a drink of water. The aim of this treatment is to remove any of the poison that remains in the stomach, to soothe the mucosa and to combat the dehydration. If the patient needs treatment and refuses it, apomorphine gr. $\frac{1}{20}$ or gr. $\frac{1}{10}$ hypodermically will induce vomiting within a few seconds and leave the patient amenable to subsequent treatment. He should then be put in a warm bed and allowed to sleep as long as possible. On waking a Seidlitz powder should be given and the patient encouraged to take plenty of fluid. This is usually acceptable in the form of tea. If tolerated, dextrose in some form should be given. When anorexia is marked, food should not be forced. If a great deal of alcohol has been taken, two grains of calomel can be given half an hour before the Seidlitz powder. If the patient has to get on with his work, 10 grains of calcium aspirin will improve his general feelings and combat the headache. Large doses of ordinary aspirin often irritate the stomach and should be avoided, as most of the symptoms of the next day are due to the gastro-intestinal upset. To give bitter alcoholic drinks as part of treatment is contrary to all medical principles and has no real therapeutic effect.

2. Alcoholic Coma

Synonyms.—Acute Alcoholic Poisoning; Wet Brain.

Ætiology.—Individual susceptibility varies so much and case histories are so falsified by prejudice and folklore that there are no reliable figures

of what constitutes a dangerous dose. Alcohol is much more dangerous in states of debility, whether such debility be the result of disease, exhaustion or hunger. Naturally beverages of high alcoholic content are more poisonous than those of low.

Pathology.—At post-mortem alcohol is present in all the body fluids. There is mucous catarrh of the stomach and evidence of right heart failure. The nervous system shows a moderate excess of cerebrospinal fluid and the superficial parts of the cortex are œdematous.

Symptoms.—These come on quickly. The euphoric exhilarated period is short, the patient becomes sleepy and soon passes into coma with stertor. Vomiting or even convulsions may occur during the early drowsy period, but neither of these symptoms is constant. In the coma, the patient lies in any position in which he is put, and is commonly found lying on his back. He is pale, collapsed and sweats profusely. In the early and middle stages he can be roused sufficiently to make a few disjointed remarks, and this has some diagnostic value. In these stages the pupils are dilated, the pulse full, the temperature subnormal, and the respirations deep. In the later stage the coma becomes dangerously deep, the pupils contract, the pulse weakens and the respirations are shallow. At all stages the limbs are flaccid, with diminished reflexes. In the early stages the plantar reflex is flexor, while in the later stages it cannot be elicited. Examination of the blood and urine show an alcohol content of 0·3 to 0·6 per cent.

Diagnosis.—It is of paramount importance to exclude cerebral trauma before making a final diagnosis of alcoholic coma. Sometimes the history of trauma is deliberately withheld by the person who has called the doctor. When there is a history of unconsciousness followed by a lucid interval and subsequent coma, this is good presumptive evidence of ruptured middle meningeal artery. The absence of such a history does not exclude this accident, as often the patient has taken alcohol, which implements the original concussion and does not allow the intermediate return of consciousness. Alcohol can precipitate other comas, notably diabetic coma, uræmic coma and epileptic coma. The urine must be examined in all cases, and when there is any doubt a lumbar puncture should be done. A careful general examination will reveal evidence of such conditions as renal disease or arterial degeneration, and may show scars on the tongue or elsewhere suggestive of epilepsy. Cerebral hæmorrhage or thrombosis must not be forgotten. Reference should be made to p. 1604 and elsewhere.

Prognosis.—With adequate treatment that is not too long delayed, this is good provided that the patient is otherwise healthy. The prognosis is unfavourable in those with cardiovascular disease, or when the acute attack occurs in the course of chronic alcoholism. Miosis is an unfavourable sign.

Treatment.—Treatment is necessary to combat shock and dehydration. Warm the patient, raise the limbs, and give fluids. The stomach should be washed out with one quart of a warm aqueous solution of sodium bicarbonate (60 grains to a pint), and a rectal drip of warm water should be started immediately. If there be evidence of heart failure with gross venous congestion, venesection should be done provided that the measures to combat shock and dehydration have been applied.

3. Dipsomania

Definition.—An intermittent compulsion to get drunk.

Pathology.—This is a compulsion neurosis.

Symptoms.—The periodicity varies in different individuals and in the same individual under differing stresses. Commonly it is about once a month. An irresistible desire to take large quantities of alcohol seizes the patient. Usually he begins drinking after work one day, takes a large amount, comes home with a bottle of spirits, and after drinking this becomes stuporose and has to be put to bed. The bouts tend to become more frequent. Usually no alcohol is taken between the attacks.

Prognosis.—A good deal of amelioration can be expected in expert hands; otherwise the outlook is not good.

Treatment.—The patient must be referred to a competent psychiatrist.

4. Chronic Alcoholism

Definition.—A patient is said to be a chronic alcoholic when he cannot carry on his ordinary life without alcohol.

Pathology.—This is primarily a mental disorder. The psycho-pathology is dealt with in the section on Psychological Medicine (pp. 1836–1840). Physically alcohol enhances degenerative tendencies, such as atheroma, and implements the toxicity of poisons; these effects are well seen in experimental animals. Gastro-intestinal catarrh occurs and results in deficient absorption of essential food elements. This is made worse because the patient prefers drinking to eating. In advanced cases achlorhydria is found. Bronchial catarrh and conjunctivitis are common, probably as a result of vitamin-A deficiency. Deficiency of vitamin B results in parenchymatous degeneration of nerves, and wasting of brain cells with chromatolysis. Ultimately the brain may be so wasted that the post-mortem appearance simulates that of G.P.I. Pachymeningitis hæmorrhagica is sometimes observed. The well-known susceptibility to pulmonary tuberculosis may be related to dietary deficiency. In the cardiovascular system atheroma and related degenerations are accelerated. However, it is a commonplace of pathology how little cardiovascular change there may be in an alcoholic subject. Gout is made much worse by alcohol, and osteoarthritis is common in alcoholics. The majority of persons with cirrhosis of the liver are heavy drinkers. No doubt some factor in addition to the alcohol is necessary to produce this condition, for it may be absent even in the worst chronic alcoholic. Alcohol is dangerous in diabetes, for it interferes with treatment and increases the tendency to complications.

Symptoms.—Typically the chronic alcoholic is a plethoric person with a plum-coloured complexion. The colour is most marked on the cheeks and nose. Its blue component is due to dilated small veins. After exposure to cold, the colour may darken to a deep mauve. The lips tremble, and there is a fairly coarse tremor of the hands. This tremor may affect the handwriting. The patient is fidgety, often wiping his mouth with his hand, fiddling with his tie, pulling at his ear or playing with his watch chain. He is restless in his chair, and often has tics involving the whole trunk or the head. He is often swift but superficial with his replies, and though his manner

is calculated to be disarming he is inclined to be irascible. He readily responds to the mood of the examiner. His eyes have an appearance that is variously described as glassy or watery. The conjunctivæ are red. His appetite is poor, and he has a preference for spicy and pungent foods. He rarely takes any breakfast, and does not feel himself until he has had a drink. On rising he clears his throat of much viscid mucus, which he usually refers to as "my catarrh." Often the hawking induces an attack of vomiting. Cases with much gastric catarrh vomit either on rising or at a fixed time afterwards. He is usually proud of the freedom of his bowels, but when careful inquiry is made it is found that he has diarrhœa. Night-rising once or twice is common. The majority of cases have attacks of paræsthesia in the limbs from time to time, and on examination the reflexes are found sluggish and the calves tender. In the presence of arterial degeneration a cerebral vascular accident may occur at any time, but more frequently the final illness is uræmia.

Neurological Complications.—Some degree of peripheral neuritis is common (see p. 1780). *Korsakoff's psychosis* may be present (see p. 1838). Sometimes in alcoholic neuritis the pupil is very sluggish to light. In such cases, if the neurological signs overshadow the mental, the condition is often referred to as *alcoholic pseudo-tabes*; if, on the other hand, the mental signs predominate over the physical, it may be called *alcoholic pseudo-paresis*. These terms are self-explanatory. *Acute hallucinosis* or the more serious *delirium tremens* are acute psychoses and are dealt with in the section of Psychological Medicine (see pp. 1837, 1838).

Prognosis.—(*a*) GENERAL.—As regards cure this is often bad. In many cases, however, suitable management leads to a good all round improvement. Intercurrent diseases, especially those of the respiratory system, are poorly tolerated. Pneumonia and tuberculosis have a much worse prognosis in these patients than in normal people. Anæsthetics are taken badly, and there is more likelihood of post-anæsthetic complications.

(*b*) NEUROLOGICAL.—This has been greatly altered for the better since the true nature of these complications has been understood, namely, that they are due to deficiency of vitamin B_1. Provided that no permanent damage has been done, cure can now be obtained of both the neuritis and the Korsakoff syndrome.

Treatment.—(*a*) OF THE CHRONIC ALCOHOLISM.—This is difficult, and usually disappointing in the hands of the general physician. The underlying causes are mental and these need the attention of experts. Should it be necessary to treat the patient in his own home without a psychiatrist the friends should be spoken to earnestly, and everyone in contact with the patient must be above suspicion because absolute withdrawal of alcohol is essential. Since the patient has been used to this nerve depressor, he may experience severe withdrawal symptoms and some simple sedative such as paraldehyde (min. 120) should be available. Where paraldehyde is not tolerated, soluble barbitone (medinal) (grs. viiss) is suitable. The patient's appetite will be poor, and may be encouraged by a simple stomachic before meals. After meals he should be given a sedative alkaline mixture, such as bism. carb. gr. 15, sodii bicarb. grs. 15, tr. bellad. min. 10, tr. card. co. min. 120, aq. menth. pip. ad min. 240. He should be handled sympathetically, and any outstanding domestic difficulties and worries resolved. Graduated doses

of strychnine are employed in many cases. Such treatment acts by suggestion. Better results will be obtained in these patients if at the beginning they are put to bed for a few weeks, and if the gastro-intestinal illness is treated intelligently. For psychological effect, the patient may be put on a rigid diet with all the quantities carefully prescribed and supervised. The form of the diet will depend on the circumstances, but it should be bland, well balanced, and rich in vitamins.

(*b*) NEUROLOGICAL.—Rest the affected parts, including the mind, and give large doses of vitamin B_1 (aneurine hydrochloride, thiamine hydrochloride). For the first two weeks, 6000 pigeon units (gr. 1/33 ; 1·8 mg.) should be given intramuscularly every alternate day, and thereafter, twice weekly. In addition, yeast extract (one drachm) should be given by mouth twice daily. After recovery the patient should continue to take vitamin B_1 indefinitely.

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LEAD POISONING

1. ACUTE LEAD POISONING

This is rare. It usually results from swallowing a large dose of a soluble lead compound, such as lead acetate, which is also known as sugar of lead, from its sweetish taste. It has occasionally occurred when white lead has been mistaken for chalk and when lead chromate has been used to colour cakes or confectionery.

Pathology.—There are the usual signs of acute gastro-enteritis, and the stomach may be covered with a whitish grey deposit. The wall of the stomach and duodenum is sometimes thickened and softened, and erosions may occur from the local action of the lead compound.

Symptoms.—An astringent metallic taste is at once experienced, followed by a feeling of constriction in the œsophagus. A burning sensation and pain are felt in the epigastrium, and vomiting occurs. The vomit contains opaque whitish material, due to the precipitated albuminate of lead and lead chloride, formed by the action of the lead salt on the gastric contents. Blood may also be present. Severe colicky pains occur in the abdomen, with rigidity of the abdominal muscles. Pressure on the abdomen gives relief, and the patient may bend forwards for this purpose, or lie on his abdomen. The tongue is coated, and the bowels are usually constipated ; but occasionally diarrhœa occurs. The stools are dark coloured, owing to the formation of lead sulphide. Prostration and collapse occur, if the abdominal symptoms are severe. There may be numbness or paræsthesia of the limbs, cramps in the legs, and partial suppression of urine. A blue line on the gums does not usually occur during the acute symptoms following a single dose of the poison.

The subacute form of poisoning follows the taking of repeated doses of a soluble lead compound. It may occur from repeated medicinal doses of lead acetate given to control diarrhœa. The symptoms of abdominal colic (lead colic) are pronounced, and the bowels are very constipated. The other symptoms of acute lead poisoning occur, but are less intense in character.

A blue line usually appears round the margin of the gums, owing to the formation of lead sulphide by the action of the decomposing food material around the teeth on the lead compounds in the gum tissue. If the teeth are frequently cleaned a blue line on the gums is less likely to be formed. If the symptoms are of long duration lead neuritis may result.

Diagnosis.—The diagnosis of acute or subacute lead poisoning can be confirmed by analysis of the vomit and fæces for lead during life, and after death by finding lead in the gastro-intestinal tract, liver, spleen and kidneys. Acute and subacute lead poisoning are rarely fatal.

Treatment.—If the case is seen within 3 hours of swallowing the poison, the stomach should be washed out with water. Sodium sulphate or magnesium sulphate in half-ounce doses, dissolved in half a tumblerful of warm water, should be given every 4 hours, until free purgation results, and this may be assisted by enemata, if necessary. The abdominal pain may be relieved by hot applications, repeated drinks of milk and large doses of calcium lactate, five grammes (75 grains) three times a day. In severe colic by the slow intravenous injection of 15 c.c. of a 20 per cent. solution of calcium gluconate, or of 10 c.c. of a 5 per cent. solution of calcium chloride, it is possible to relieve the pain by the time the injection is over. If necessary this treatment may be repeated in 2 hours. Should it not be available a hypodermic injection of gr. $\frac{1}{60}$ atropine sulphate and gr. $\frac{1}{4}$ morphine sulphate may be given. For some weeks saline aperients and a high calcium diet should be given. The diet should contain 3 pints of milk daily, including milk puddings, junket and ice cream, together with butter, cheese and eggs.

2. Chronic Lead Poisoning

Synonyms.—Plumbism; Saturnism.

Ætiology.—Apart from a few cases arising from accidental causes, chronic lead poisoning is of occupational origin. Lead is now encountered in more than 200 industries. In Great Britain there are more than 1500 workers in the lead industries and 150,000 painters. It has been known clinically for more than a hundred years that absorption of lead through the respiratory tract is very much more important than by the gastro-intestinal tract, and this view has since been amply confirmed by experiments on cats. In the prevention of dust and fumes great success has been secured from the application of preventive measures by the Factory Department of the Home Office. Idiosyncrasy is a factor in the development of lead poisoning, certain persons being more susceptible than others. Alcoholism also seems to be a predisposing cause. The sources from which lead is derived in chronic poisoning are very numerous, and they may be divided into 3 groups.

1. *Occupational risks.*—Men are exposed to danger in the smelting and tinning of metals, in vitreous enamelling, pottery glazing, shipbuilding, coach painting, plumbing and soldering, house painting, and in the manufacture of white lead, red lead, litharge, rubber, glass, cement, varnish, coloured pigments, linoleum and electric accumulators. Lead smelters are exposed to the fumes and dusts of furnaces and flues. Lead burners and chemical plumbers use oxy-acetylene, oxy-hydrogen, or oxy-coal-gas blowpipes in their work. The very high temperature of such flames constitutes

a much greater risk than that faced by the domestic plumber who uses a spirit blowlamp. Painters are exposed when they rub down interior surfaces which have been painted with lead paint. The use of a blowpipe for burning off old paint is not without risk. A painter nowadays is very rarely exposed in mixing paint from the dry material, because it comes to him already mixed in oil. There is some risk to compositors who handle type metal, and to gasfitters who use red and white lead. It frequently happens that changes in methods or the appearance of new industries provide new causes of lead poisoning. This was the case with ship-breaking following on the scrapping of warships after the War of 1914–1918. In this industry the volatilisation of lead from the paint and red lead stopping on the armour plating occurs in the heat of the oxy-acetylene blowpipe flames used for cutting purposes. The great increase in the use of wireless receiving apparatus and motor cars has led to a greater number of cases of lead poisoning in electric accumulator factories. Sometimes the converse is true, and lead poisoning is found to show a remarkable diminution in a given industry. Thus, the substitution of machine methods for hand labour has abolished the disease among file cutters. The recent fall in the incidence of poisoning in coach painting is largely due to the enormous development of spray painting of motor cars with leadless cellulose paints.

2. *Accidental causes.*—Drinking water, especially if it is soft, or contains traces of acid derived from peat or dead leaves, may dissolve lead from lead pipes or cisterns and so give rise to poisoning. Beer or cider drawn from casks through lead pipes may become heavily contaminated. Aerated waters delivered from syphons with pewter or lead valves may give rise to poisoning. The lead glaze on earthenware vessels may be dissolved by vinegar, lemon juice, cider or home-made wine. The cooking of food in vessels tinned with solder containing lead may cause lead poisoning, especially if vegetable acids are present. Tinned foods sometimes contain lead from solution of the solder used in the tinning process. The lead foil used for wrapping sweets or food may contaminate them. Cosmetics, hair-dyes, and snuff weighted with litharge all have given rise to cases. Children with perverted appetites may chew the paint off their cots or toys. In Queensland, Australia, where the dry climate leads to flaking of painted surfaces, children have been poisoned owing to the habit of licking the raindrops off the painted balconies and roofs after rain has fallen.

3. *Abortifacient uses of lead.*—Lead attacks the chorion epithelium, causing abortion in pregnant women. A like effect has been observed in animals in the proximity of lead works. Lead oleate plaster, known as diachylon, has been used in certain districts by pregnant women in order to cause miscarriage, the substance being swallowed in small portions rolled up in the form of a pill. To do this is very dangerous, for if miscarriage comes about death occurs later from lead poisoning. In consequence the sale of lead oleate has been restricted by placing it in Part I of the Poisons Schedule.

Pathology.—In chronic poisoning lead is stored in the skeleton, and under certain circumstances is released to attack (i) muscle, causing abdominal colic and lead palsy; (ii) the reticulated red cell, causing punctate basophilia (stippling) and anæmia; (iii) the chorion epithelium, causing abortion; and (iv) the brain, causing encephalopathy.

A good deal is known about the physico-chemical behaviour of lead in the animal body. It is probably transported in the blood plasma as the insoluble tertiary phosphate in the highly dispersed or colloidal form. At different stages of intoxication its distribution within the body varies somewhat. When absorption is slow it migrates to the skeleton, where about 95 per cent. is held without harm during the chronic stage of plumbism. If, however, large quantities of lead are being absorbed or are being liberated from the bones, lead is distributed throughout the tissues and the percentage in the bones is reduced. Under these conditions acute symptoms of poisoning occur. It has been shown that the total amount of lead stored in the skeleton in lead workers varies from 0·2 to 0·8 gramme. This deposition of lead suggests a mechanism similar to that involved in the deposition of calcium phosphate. Repeated observations have shown that under conditions which favour storage of calcium in the body, the excretion of stored lead diminishes; and that when conditions are unfavourable for retention of calcium the excretion of stored lead increases.

In studies of lead excretion it is to be noted that normal individuals with no occupational exposure to lead may pass lead in the fæces and urine. The mean lead excretion of a group of Cincinnati medical students was found to be 0·24 mg. for each 24 hours in the fæces and 0·08 mg. in the urine. The figures quoted represent the average excretion calculated for each 24 hours, and as such they form an approximate guide only. In toxicological analysis no satisfactory figures can be obtained unless specimens of stool and urine are collected for at least 3 days. A man working in a dusty lead industry, in addition to inhaling lead, may swallow repeated small amounts and pass lead unabsorbed in the fæces. The only proof of absorption, therefore, is to find lead in the urine. If specimens be taken some weeks after removal from exposure, the output may reach about 1 mg. for each 24 hours in the fæces and about 0·3 mg. in the urine. It seems doubtful whether renal excretion ever much exceeds this figure under any circumstances. Under effective treatment, however, the fæcal excretion may rise to about 2 mg. in each 24 hours. It is necessary to emphasise that the presence of lead in the excreta is not necessarily proof that a lead worker is suffering from lead poisoning. Many such workers are insusceptible and have never suffered from any of the toxic episodes.

Lead palsy begins in the muscles, and fatigue determines the site of paralysis. The chemical explanation offered is that in regions of muscular activity the excess lactic acid which diffuses from the fatigued muscle cells combines with the lead phosphate in the blood to form lead lactate. As this soluble lactate comes into contact with inorganic phosphate at the surface of the muscle cells the lead is re-precipitated as insoluble phosphate causing alterations in the surface permeability.

Studies of the blood in lead poisoning show that the stippled red cell arises from the reticulocyte, and that the attack occurs peripherally and not in the marrow. Blood films can be prepared showing all stages between stippled fragments and typical reticulum. Stippled cells are never found in the bone marrow in lead poisoning. The presence of punctate basophilia in the blood is not, of course, a specific sign of lead poisoning. It is seen in pernicious anæmia, in leukæmia, in the anæmias of carcinomatosis and in pneumonia in infants. Its occurrence in these various conditions

is relatively rare and slight as compared with the frequency and intensity of its appearance during plumbism. For this reason the demonstration of stippling of the red cells in the blood has come to be considered as almost definite evidence of absorption of lead. It is not an absolute indication of the severity of lead poisoning, but it often runs parallel to the state of health. If on examination of the films its presence is detected in a sufficiently large number of fields of the microscope, further exposure to lead in the patient concerned should be prevented immediately. Punctate counts are of value in the prophylaxis of plumbism among lead workers and are essential in the adequate hygienic control of lead processes.

Except in cases of encephalopathy, which are now very rare, chronic lead poisoning is not a direct cause of death. In 1854 Garrod pointed out that gout was quite common among lead workers in Great Britain, but there is nothing to show that the occurrence of these two conditions in one patient was other than fortuitous. Chronic lead poisoning produces no characteristic post-mortem changes. It perhaps accelerates arterial degeneration (arteriosclerosis). Chronic nephritis with renal insufficiency is a common cause of death in lead workers. The accompanying hypertension frequently leads to cerebral hæmorrhage at a comparatively early age.

Clinical History.—The past occupations of the patient should be inquired into, for latent lead poisoning is well known to occur. The present occupation is obviously of great importance and the exact details of the work he does should be elicited from the patient himself. Often a man's occupation does not at first sight suggest that he is exposed to compounds of lead. A man describing himself as a fitter may be exposed to dust or fumes of lead; this fact is only elicited in answer to a leading question. The occupation of a cooper becomes dangerous when the barrels worked upon have contained compounds of lead. Vitreous enamellers working, for example, on baths, sift a powder containing lead silicate on to the bath which has been heated in a furnace. They sometimes use a compressed-air apparatus which forces the enamel through a sieve. In the electric accumulator trade pasters fill the spaces in accumulator plates with a paste containing litharge and red lead. Colour manufacturers grind colours into a fine powder under edge runners with the necessary production of much dust. Amongst other things they grind lead chromate and red lead. A slate mason may construct storage tanks by fixing together slabs of slate with materials containing oxides of lead. A bullion refiner may use a process in which he adds lead to refinable silver in a furnace and taps off molten litharge. A rubber compounder adds oxides of lead to crude rubber in preparation for vulcanisation. A girl describing herself as a perambulator maker may be employed painting the body work of perambulators and then rubbing down the surface with dry sand-paper. An embroidery worker sometimes stencils materials by dabbing on the pattern commercial white lead instead of chalk.

Symptoms.—Individual opinion differs widely as to what is necessary for the definite diagnosis of lead poisoning. The diagnosis of intoxication as distinguished from absorption should be based upon evidence as to the presence of one or more of the toxic episodes. These are colic, palsy, anæmia, and encephalopathy. Constipation and slight stippling of red cells are insufficient without one of the toxic episodes to establish a diagnosis of poisoning. The urine should be collected for at least 3 days and examined

for lead, but a positive result is not proof that the patient is suffering from lead poisoning for he may be insusceptible.

Lead colic.—This is the most common and dramatic of the acute manifestations of plumbism. It is probably ten times as common as lead palsy. An acute attack of colic is usually preceded by several days of constipation. The pain is of a tearing or griping nature and of variable intensity. It is usually situated around or below the umbilicus, and the patient often indicates where it is by spreading both hands widely over the lower abdomen. While suffering from colic the patient is cold, pale, and often drenched with perspiration. He commonly bends over and may writhe about the bed in intense pain. Examination shows a scaphoid abdomen, held tense, but not showing any true rigidity. Vomiting quite frequently occurs at the onset of the pain.

Lead palsy.—This does not belong to the category of polyneuritis, either clinically or pathologically. It is in the first instance a muscle disease. Fatigue plays a most important part in determining the sites attacked. Where the muscle palsy is neglected the lead attacks the motor nerve fibres and ultimately the anterior horn cells of the spinal cord. (See also p. 1789.) Paralysis does not appear to be closely related to length of exposure. It may develop during the first month of work, or only after many years' exposure. The commonest form is the well-known wrist-drop which begins usually in the right hand and later becomes bilateral. The palsy first appears in the long extensors of the middle and ring fingers. It spreads to the other fingers, and then to the long extensors of the wrists. The supinator longus, and usually the long abductor of the thumb escape. The brachial type of paralysis involves the deltoid, biceps and supinator longus, but it is very rare for this to occur without wrist-drop. A third form of lead palsy in which progressive atrophy occurs of the thenar and hypothenar eminences, together with the interossei, used to be common in the left hand of file-cutters. In view of the theory that fatigue plays an important part in determining the site of lead paralysis, this observation is of great interest, for in their work file-cutters not only used particularly the muscles mentioned but placed the greatest strain upon the left hand. The substitution of machine methods for hand labour has abolished lead poisoning amongst file makers. Lead palsy rarely occurs in the lower limbs, but when it does so it affects the extensors of the toes, giving rise to foot-drop.

The lead line.—The lead line consists of fine granules of pigment arranged in the form of a very dark blue stippled line within the tissues of the gum about a millimetre from the border of the teeth. It is more marked round infected or dirty teeth, and is occasionally found on the mucosa of the cheek opposite such teeth. In spite of the fact that the pigment lies actually within the tissues and cannot be rubbed off, careful cleaning of the mouth and teeth is often found quickly to eliminate the line. Its clinical significance should be clearly recognised. Its intensity and size provide a rough guide to the duration and severity of exposure to lead.

The anæmia.—Secondary anæmia with basophil punctation (stippling) of the red cells is characteristic. It is usually mild, and it is rare to find less than 3 million red cells per c.mm. Because of the loss of circulating red cells there is compensatory regeneration of erythrocytes with a hig reticulocyte count.

Encephalopathy.—Most of the ancient writers speak of the frequent occurrence of convulsions in lead poisoning, but fortunately with the improvement of industrial conditions the incidence of lead encephalopathy has progressively decreased until to-day cases are very rarely seen. It is the most dramatic manifestation of lead poisoning, and is always of serious prognostic significance. In severe cases of plumbism the patient is dull, with poor memory, and inability to concentrate. The onset of encephalopathy is nevertheless sudden, usually with epileptiform convulsions. It may be divided into three groups—convulsive, comatose and delirious. The lymphocyte count in the cerebrospinal fluid may reach 100 per c.mm.

Diagnosis.—There is always a danger of wrongly attributing to lead poisoning any symptoms which may occur in persons exposed to lead. Acute appendicitis, chronic gastric or duodenal ulcer, and carcinoma of the stomach occur from time to time in lead workers. They must be carefully differentiated from colic. Equally a lead worker can suffer from pernicious anæmia or secondary anæmia due to piles, melæna or hæmatemesis. It is important to remember that lead poisoning has to be very severe indeed before the red cell count drops below 3 million. In industrial cases confusion is unlikely to occur in regard to the blue line. A similar phenomenon is commonly seen in patients under treatment with bismuth preparations given intramuscularly. The differential diagnosis of lead palsy should give rise to no difficulty, especially as the changes are entirely motor. In a case of peripheral neuritis in which there are motor, sensory and pigmentary changes the possibility of arsenic poisoning must be considered. Litigation hysteria is all too common in the lead worker. The manifestations include hysterical spasm of the hand and arm, weakness of various movements, including the flexors of the wrists and fingers, glove and stocking anæsthesia, complete hemi-anæsthesia and hysterical aphonia. Such symptoms are rarely alleviated until legal proceedings are completed.

Treatment.—PROPHYLACTIC.—The treatment of chronic lead poisoning is essentially preventive. Food and drink containing organic acids should not be stored in earthenware vessels glazed with lead. Supplies of soft water for drinking purposes when delivered through lead pipes should be artificially hardened by the addition of calcium salts. Lead pipes used to convey beer or cider from the cellar to the bar engine in public houses must be lined with tin. Children's toys and cots must never be painted with lead paint. The law must restrict the sale of lead oleate and forbid the addition of litharge to snuff in order to make it heavy.

In industry less than 100 cases of lead poisoning were notified in 1938 as compared with more than 1250 in 1889. In Great Britain preventive measures are carried out with such success that the majority of cases of lead poisoning are mild. It is unusual to-day to meet with a case either of severe colic or of extensive palsy, and encephalopathy has been abolished. The most important single measure of prophylaxis is the prevention of dust and fumes. In achieving this, great success has been secured from the application of the principle upon which Sir Thomas Legge always laid so much stress, namely, to apply methods entirely external to the workman—methods over which he himself can exercise no control. One such method is exhaust ventilation applied through hoods at the point of origin of dust or fumes. Benches, tools, floors and walls must be spotless, often at the expense of

the constant vigilance of several good foremen. No scrap lead nor dry white lead should be handled unless it has been thoroughly soaked with water from a hose. As far as possible mechanical means, such as cranes, rails, hoists, covered conveyors and hoppers, and automatic packing machinery must be substituted for hand carriage.

Fortunately about 50 per cent. of the white lead manufactured in Great Britain is never handled in the dry state. It is made by the stack process and leaves the stack in a wet state to be converted into an aqueous paste, mixed with linseed oil, and made into an oily paste in automatic closed-in machines without dry grinding. Since a white-lead worker may handle in the course of a day at least as much white lead as a painter handles in a year, the value of this wet pulping method will at once be realised. In the manufacture of litharge and red lead it is impracticable to use wet methods, and it is therefore necessary to use machinery designed to minimise dust. Since 1927 it has been illegal for a painter to rub down by dry methods any indoor structure previously treated with lead paint. A satisfactory damp rubbing down process has been introduced in which waxed sand-paper is repeatedly dipped in the vessel of water.

In addition to cleanliness in the workplaces, personal cleanliness is of the first importance. Cloak-rooms, washing-rooms, mess-rooms, baths, nail-brushes, towels and soap must be provided. The hands should always be washed before eating and the work-people urged to take a warm bath frequently. The bringing of food or drinks into the work-rooms should be forbidden, and so also should smoking at work. Medical examination of the workers exposed must be carried out periodically. At present there is no biological test by which to select workmen immune to the toxic effects of lead. Since they have been found unduly susceptible, it is necessary to forbid the employment of pregnant women and of all persons under 18 years of age in the potteries and other lead trades.

In the prevention of lead poisoning a diet of high calcium content plays its part. In lead works in Great Britain it has for many years been customary to provide the workmen free of cost with a glass of milk each morning. This is empirical treatment of considerable merit, anticipating as it did by many years the discovery that a high calcium intake assists the storage of lead in a harmless form in the bones. Workers should, in addition, take aperients regularly. Any worker who develops one of the toxic effects of lead has thereby proved his susceptibility, and ideally he should never again work in any department of a lead works.

CURATIVE.—Repeated observation has shown that with a high calcium diet lead excretion tends to diminish rapidly. This provides a means for controlling the storage of lead in the organism. To store lead in the bones so that it will not be free in the circulation to cause damage, it is only necessary to give a diet containing much calcium in the form of milk or calcium lactate. This produces a positive calcium balance which favours the storage of lead as a harmless deposit in the bones. In cases of lead poisoning showing toxic symptoms the diet should contain 3 pints of milk daily, including milk puddings, junket and ice-cream, together with butter, cheese and eggs. In the presence of acute symptoms it is important not to attempt elimination of lead, because so much is already circulating that it is safer temporarily to favour further storage. The first step should

then be to prescribe large quantities of calcium lactate, 5 grammes (75 grains) three times a day. When the calcium intake is sufficient most of the lead is stored in the bones, and the patient presents no symptoms.

Lead colic.—It is necessary to use local applications of heat, pressure and moisture. The bowels should be moved as early as possible by means of enemas of olive oil and warm water, and by the internal administration of magnesium sulphate along with belladonna and carminatives. Treatment by a high calcium diet usually brings relief within 2 days. The relief of lead colic by calcium therapy involves more than the mere tendency of calcium to favour storage of lead. There is evidently an anti-spasmodic action on involuntary muscle as well. The pain of lead colic is probably due to a contraction of the tonic ring in the intestine with marked peristalsis approaching this. A high calcium diet and the use of large doses of calcium lactate usually brings relief. In severe cases, by the slow intravenous injection of 15 c.c. of a 20 per cent. solution of calcium gluconate, or of 10 c.c. of a 5 per cent. solution of calcium chloride, it is possible to relieve the pain by the time the injection is over. The patient feels hot and flushed, and may vomit. The effect upon the pain is striking, and is superior to that of any other treatment. If necessary the injection may be repeated in 2 hours. Should such treatment not be available a hypodermic injection of $\frac{1}{60}$ grain atropine sulphate may be given.

Lead palsy.—During the development of lead palsy, a high calcium diet should be used to favour storage of lead. Massage, electrical treatment and strychnine are useful. In the early stages the hands, when affected by wrist-drop, should be supported on splints. The paralysed muscles may be stimulated by an induction coil, with or without a water bath, but overstimulation must be avoided since it induces fatigue, and so does harm.

Encephalopathy.—In Great Britain the Home Office regulations, by the control of dust and fumes, have abolished encephalopathy. In the few cases with which he has had to deal in the United States, Aub has had good results with a high calcium diet. Of six definite cases three occurred before the treatment was in use, and these all died. The other three were given large quantities of milk and calcium lactate and all promptly recovered.

Elimination of lead.—Experimental studies of the conditions favouring and hindering liberation of lead from the bones have contributed to the knowledge of the treatment of lead poisoning. In cats experimentally poisoned with lead, acute symptoms may develop during starvation and at necropsy lead is found distributed more generally through the body than is typical of the chronic condition. This suggests that during starvation acidosis sets lead free from the bones. The probable reason for this is the conversion of the tertiary phosphate of lead into the secondary phosphate which is exactly one hundred times more soluble. Hence the ingestion of acid as a method of treatment probably serves to liberate lead from the skeletal stores by converting it into a more soluble salt.

Acidosis may be produced by the use of phosphoric acid, but it is more satisfactory to give large doses of ammonium chloride. Chronic lead poisoning may be treated by the cautious administration of this substance in doses of 1 gramme (15 grains) given in a glass of water eight or ten times daily for 3 weeks at a time. Loss of appetite and headache signify the limit of tolerance to such treatment, and the dosage should be reduced if these

symptoms appear. In no case should ammonium chloride be used until a few weeks after the acute toxic episode has passed. A diet with a very low calcium content facilitates release of lead from the bones. In such a diet all milk, milk products, green vegetables and eggs are omitted. It may contain meat, liver, chicken, potato, peas, rice, tomato, banana, apple, lemon, tea, coffee, sugar, honey, salt and pepper. All bread must be prepared without milk. Butter fat must be substituted for butter. This is prepared by melting butter in hot water and skimming off the butter fat. In those places where the water supply is hard, vegetables should be cooked in distilled water and all drinks made up with it.

Various observations, particularly on animals, indicate that it is useless to attempt elimination of all the lead stored in the body. As this would doubtless require several years, it is probably desirable to eliminate only the most readily mobilised lead. In prolonged observations the results indicate that after a certain point elimination of lead becomes progressively more difficult. When this stage is reached it seems more practical to favour retention in the bones by maintenance of a positive calcium balance. Thus after 3 weeks' treatment by a low calcium diet and ammonium chloride, there should be a rest period of a week with normal diet and abundance of milk to correct the calcium deficiency. Treatment to accelerate elimination should then be re-instituted.

Potassium iodide has been employed by clinicians since 1844. It is not as effective as treatment by acidosis, but has the advantage of ease of administration. The dose should be increased from 5 grains three times a day to 15 grains three times a day. Its physiological effectiveness appears to diminish progressively after the first few days of treatment. Neither ammonium chloride nor potassium iodide should be used in the presence of nephritis or of toxic symptoms. Should any toxic episode appear during the use of ammonium chloride or potassium iodide, these drugs must be stopped and a high calcium diet at once used to favour the storage of lead. Occasionally cases of latent lead poisoning occur, that is to say, cases in which symptoms have been precipitated by various forms of treatment long after exposure to lead has ceased. Thus a lead line or wrist-drop may follow upon the use of potassium iodide as an expectorant.

It is necessary to emphasise the difference between the use of agents which assist excretion of lead and those assisting its storage. The acidosis method of lead elimination is so potent that its use during colic or any other toxic episode might prove fatal from the further mobilisation of lead at a time when the reverse procedure is essential. It is scarcely necessary to add that such treatment should never be used as an excuse for negligence in enforcing all the known measures for the prevention of exposure and absorption.

3. Tetra-ethyl Lead Poisoning

Tetra-ethyl lead is an organic lipoid-soluble compound, and is absorbed directly through the skin. It is added to petrol as an anti-knock substance in the proportion of 1 in 1400. In 1923, when it was first manufactured in the United States, 149 cases of encephalopathy occurred in men employed on the plant. Within 17 months 11 men died and 1 became insane. Much excitement and alarm was caused, and this led at first to the prohibition of

the manufacture. The men affected suffered from restlessness, talkativeness, ataxia, insomnia and delusions. There were no paralysis nor convulsions, but the condition terminated with violent mania, the patient shouting, leaping from bed, smashing furniture and acting as if in delirium tremens. By meticulous attention to detail it is possible to manufacture tetra-ethyl lead and to blend it with petrol without risk to the worker. Even so, ethyl petrol should not be used for cleansing the skin and to prevent this it is marked by a dye. There is no need for apprehension as to the possibility of the poisoning of garage workers by lead from the exhaust gases of motor cars.

DONALD HUNTER.

ARSENICAL POISONING

Arsenic is the most important of the irritant poisons, and owing to the almost tasteless property of many of its compounds and preparations it is perhaps the commonest poison used for homicidal purposes. At one time it had a reputation as a cosmetic, and was added to face powders and skin lotions. It is practically never used now for such purposes.

Occurrence.—White arsenic, i.e. arsenious acid, or arsenious anhydride, As_4O_6, is the most important of the compounds of arsenic. It occurs in the form of a white powder, or in lumps like glass or porcelain (vitreous arsenic). The powdered form resembles powdered sugar or flour, and when mixed with solid food is tasteless. It is slightly soluble in cold water, an ounce of cold water dissolving from a half to one grain. In boiling water it is twelve times more soluble, from 6 to 12 grains dissolving in an ounce. Alkaline solutions readily dissolve arsenic. If white arsenic is sold to the public the law requires that it should be mixed with soot or indigo to colour it. It is used in the composition of sheep dip, arsenical soap and rat poison.

Metallic arsenic is a black powder. It is very poisonous, and is used for killing flies. *Copper arsenite* (Scheele's green) is bright green in colour, and used to be employed for colouring wall-paper, toys, floorcloths and fabrics. Its use for such purposes has fortunately been abolished. *Arsenious sulphide*, or orpiment, is a yellow powder known as king's yellow. *Arsenic acid*, in the form of its potassium and sodium salts, which are white, crystalline and soluble in water, is used as a fly poison and in the manufacture of aniline dyes. Injurious effects, such as local skin eruptions, are sometimes caused by the action of the arsenical compound present in the dye of stockings. *Sodium arsenite*, in the form of solutions of arsenic in caustic soda, or in sodium carbonate, is commonly used for the preparation of fly-papers, weed-killer, preservative for wood and arsenical sprays for fruit trees. Weed-killer and some of the so-called preservatives for wood contain from 20 to 40 per cent. of arsenic in solution, and are intensely poisonous. Both weed-killer and the arsenic obtained from fly-papers have been used for homicidal purposes.

Arsenic in food.—Accidental contamination of food with arsenic, or its preparations, such as weed-killer, has occurred. Arsenical pigments have been used for colouring sweets and cakes, with fatal result. A serious outbreak occurred in 1900, owing to the contamination of commercial glucose by

arsenic. Sulphuric acid prepared from pyrites and containing a considerable amount of arsenic had been used in the process of the conversion of starch into commercial glucose, so that the latter became impregnated with arsenic. The use of the glucose in the manufacture of beer led to the outbreak of arsenical beer poisoning which occurred in Manchester and the North of England. A Royal Commission investigated the cause of this epidemic, and safeguarded the further occurrence of such poisoning. Limits of the amount of arsenic permitted in food-stuffs were fixed at $\frac{1}{100}$ gr. per gallon for liquids and per pound for solids.

Arseniuretted hydrogen, or arsine, is a very poisonous gas. It is produced when hydrogen is generated in the presence of a compound of arsenic, for example, in the action of mineral acids on impure metals, as occurs in metal pickling and in balloon filling.

Dimethylarsine is a poisonous gas produced by the action of moulds upon certain compounds of arsenic.

The *arsenobenzene* derivatives which are extensively used in the treatment of syphilis and other diseases, may give rise to fatal poisoning.

The varieties of arsenical poisoning are—(1) acute, (2) chronic, (3) arseniuretted hydrogen poisoning, (4) dimethylarsine poisoning, and (5) poisoning by arsenobenzene derivatives.

1. Acute Arsenical Poisoning

Pathology.—The stomach contents usually contain much mucus, which may be blood-stained. The signs of gastro-intestinal inflammation are present. The mucous membrane is swollen, red and congested, and petechiæ are usually well marked. The redness is most marked on the summits of the rugæ. When the arsenic has been taken in solid form, white or pigmented particles may be seen on the mucous membrane of the stomach. The duodenum is red and congested, and petechiæ may be present; there is usually marked yellow staining, due to altered bile. The small intestine may show similar signs to the duodenum, but these diminish on passing downwards. The liver, kidney and other organs may show cloudy swelling. In fatal cases the arsenic absorbed into the tissues has a preservative action, and tends to delay putrefaction.

Symptoms.—When the poison is taken by the mouth, if diluted well or mixed with food, no taste or pain in the mouth or throat is experienced. The symptoms begin within an hour if the stomach is empty; but may be delayed if the stomach is full, and if the poison is in the solid state there will be further delay. A burning pain occurs in the epigastric region, and nausea and vomiting usually follow. The vomit will contain any food present in the stomach, and there is often much mucus. Bile is usually present, and sometimes streaks of blood. As the poison is passed on to the intestine, abdominal pain, of a griping or colicky type, and usually diarrhœa occur. The stools are watery, and may contain flakes of mucus. The continued vomiting and diarrhœa cause exhaustion, faintness and collapse. Cramps in the legs may occur, but are not a constant symptom. In a severe case restlessness, stupor and coma develop, and death follows shortly. Death in an acute case may occur within 24 hours, or may be delayed for 3 days or more. When several repeated doses are taken, so that the symptoms are protracted over

several days, some of the symptoms of chronic arsenical poisoning may develop.

Fatal dose.—Two grains of arsenic have caused death in a woman, and this is accepted as a possible fatal dose.

Treatment.—The stomach should be washed out, and afterwards as an antidote freshly precipitated ferric hydroxide may be given. This is prepared by adding to half a tumblerful of water half an ounce of tincture of perchloride of iron and also sodium carbonate solution till the mixture is distinctly alkaline. Pain is relieved by the hypodermic injection of morphine. Demulcent drinks should be given, and the usual stimulant treatment for collapse.

2. Chronic Arsenical Poisoning

Symptoms.—The gastro-intestinal symptoms—nausea, abdominal pain, vomiting and diarrhœa—are not prominent, and even may be absent. The tongue is often covered with a silvery white fur. General malaise, anorexia and anæmia are usually present. Irritation of the throat and huskiness of the voice, due to the presence of pharyngitis and laryngitis, result. Conjunctivitis may occur, with redness and swelling of the eyelids. Skin affections, such as erythema, herpes, pigmentation, or erythromelalgia, are commonly to be noted.

If taken medicinally, or otherwise, over a long period, arsenic produces a finely mottled general brownish pigmentation of the skin. It affects principally the covered parts. The mucous membranes are not involved. Thickening of the epidermis of the soles and palms, and irregular thickening of the nails are present in long-standing cases. In some cases salivation is a marked feature, paroxysmal attacks of excessive secretion of saliva occurring. Symptoms of multiple neuritis are likely to develop, and these affect both the upper and lower extremities.

Long-continued poisoning causes anæmia, peripheral neuritis, progressive wasting and weakness, death resulting from exhaustion and cardiac failure, ascites and general œdema occurring towards the end. The urine, fæces, the distal portions of the hair and the nails contain arsenic, its detection serving to confirm the diagnosis during life. The tests for arsenic will be found in works on toxicology. It must be remembered that in cases of suspected arsenical poisoning the diagnosis can always be made with certainty by an analysis of the urine, vomit and fæces, and these should always be taken for examination, the tests being made by an expert toxicologist.

It is important to remember that acute arsenical poisoning, where a large dose is taken, may (if the patient recovers from the acute attack) be followed by symptoms of chronic arsenical poisoning. Severe peripheral neuritis may follow acute poisoning from a single dose of arsenic.

Treatment.—This consists in the prevention of the absorption of arsenic in any way, and eliminative and stimulant treatment.

3. Arseniuretted Hydrogen Poisoning

Ætiology.—Arseniuretted hydrogen is a poisonous gas which is not manufactured in industry but is evolved as an accidental by-product in

certain processes. The majority of cases have been due to the use of acids and metals contaminated with arsenic. The occupations concerned are the extraction of mineral ores, pickling and galvanising of metals, cleaning of acid tanks, the manufacture of hydrogen and its use in ballooning and the making and charging of accumulators. Poisoning may arise from the action of water upon metallic arsenides. Cases have also occurred when ferro-silicon, a substance used for hardening steel, has come in contact with water, when a mixture of arseniuretted and phosphoretted hydrogen is evolved.

Pathology.—The gas is inhaled and acts at once by hæmolysing the red cells within the vessels. Hæmolytic jaundice and anæmia follow. Death may occur from anuria if the renal tubules become blocked with hæmoglobin. Degenerative changes in the cells of the liver and kidneys, and numerous petechiæ on the mucous and serous membranes, are to be noted.

Symptoms.—Malaise, headache, dizziness, shivering and hæmoglobinuria occur within a few hours. Within 24 hours there is nausea, vomiting, and jaundice, and by the third day anæmia in which the red cell count may fall below 1,000,000 per c.mm. Delirium, stupor and coma precede death.

Diagnosis.—Mild cases are often mistaken for food poisoning. The sudden onset of hæmoglobinuria and jaundice at once suggests inquiry into a man's occupation.

Prognosis.—Mild cases quickly recover. The mortality rate is 30 per cent.

Treatment.—Workshops should be adequately ventilated and processes known to be risky should be forbidden in confined spaces. Sometimes a breathing apparatus suitable for use in irrespirable atmospheres must be employed. Such an apparatus consists of an oro-nasal mask with tube connection to the outer atmosphere. The wearer draws fresh air through the tube by his inspiratory efforts and expels the expired air through a valve in the mask.

4. Dimethylarsine Poisoning

The use of Scheele's green (cupric arsenite) in the preparation of artificial flowers and wall-papers has now only historical interest, because aniline colours have almost entirely taken the place of arsenic in these processes. The mould *Penicillium brevicaule* growing in the paste behind wall-papers in damp rooms liberated dimethylarsine. The same process may occur in damp houses where coke breeze containing arsenic forms a constituent of the plaster on the walls. The use of concrete blocks containing this substance and the deliberate addition of arsenious oxide to cements to increase their rates of hardening are clearly undesirable. The symptoms of poisoning are coryza, conjunctivitis, gastro-enteritis and tinglings in the extremities. Some cases are fatal.

5. Poisoning by Arsenobenzene Derivatives

Arsenobenzene derivatives, such as arsphenamine, neoarsphenamine, and sulpharsphenamine, are usually administered intravenously. After a full dose (0·6 g. arsphenamine, 0·9 g. neoarsphenamine) nausea, a slight rise of temperature, with perhaps vomiting and a little diarrhœa, may occur in the following 24 hours, after which the patient is quite well. Occasionally

severe vomiting and diarrhœa, with furred tongue, erythematous rash and acute gastro-intestinal symptoms, may follow. In such cases it is probable that there has been some decomposition in the solution administered, the symptoms resembling those of acute arsenical poisoning. This type of poisoning is rare. Arsphenamine and allied compounds, especially after the administration of successive doses, sometimes cause such damage to the liver that extensive necrosis occurs and toxic jaundice develops, which may be fatal.

When dangerous toxic symptoms occur after arsphenamine, they are usually of the following type: After an interval of 2 or 3 days, vomiting and restlessness, delirium, stupor, often with twitchings of muscles, convulsions and Cheyne-Stokes breathing, occur. Sometimes jaundice is observed. Coma develops, with suppression or urine, and death may occur within 48 hours. The symptoms are the result of impairment of the function of the liver and kidneys. The prognosis is very grave.

Treatment consists in the administration of alkalis by the mouth and bowel, and saline per rectum. Glucose, milk and fruit juices should be given freely.

In order to protect the liver, dextrose and calcium lactate may be given a few hours before administering arsphenamine compounds. It should also be borne in mind that if full doses are employed, a fortnight is required for the excretion of the drug, and that interval should elapse between the doses. Where submaximal doses are used, *e.g.* 0·4 g. arsphenamine or 0·6 g. neoarsphenamine, weekly injections are often administered, but after a few doses an interval of 3 or 4 weeks should be allowed to avoid a cumulative effect.

See also Toxic Effects of Arsphenamine Remedies, p. 210.

MERCURIAL POISONING

(1) Acute Mercurial Poisoning

This usually arises from the absorption of mercuric chloride, also known as corrosive sublimate ($HgCl_2$), which is largely used in medicine as a disinfectant or antiseptic. Biniodide of mercury has similar uses. Both are usually purchased in the form of tablets ready for solution in a required amount of water. Acute poisoning generally occurs from the taking of the poison by the mouth, but it may also arise from the use of mercuric compounds in solution as uterine or vaginal douches. Calomel (mercurous chloride), even if taken in large doses, does not give rise to the same degree of acute poisoning, owing to its insolubility. The writer has met with 2 cases in which over 100 grs. of calomel were taken with suicidal intent, and beyond some vomiting and diarrhœa, little harm resulted.

Symptoms.—If mercuric chloride is swallowed in tablet form there is risk of local corrosion and perforation of the stomach, with rapidly fatal result.

When taken in solution, or in tablet form with water, or on a full stomach, an acrid metallic taste is experienced, followed by a sense of constriction in the throat. A hot burning sensation occurs in the mouth and œsophagus. Acute abdominal pain and vomiting take place. The vomit contains much

slimy mucus and often blood. Diarrhœa and tenesmus occur. Collapse is associated with these early symptoms. The mouth and pharynx may show signs of local damage, such as white swollen patches, which may be followed by sloughing. Unless the poison is quickly removed by gastric lavage the dangerous sequelæ of absorption rapidly follow.

The two chief dangers of acute mercurial poisoning are: (1) suppression of urine and uræmia, due to the toxic action of the poison on the renal epithelium causing cloudy swelling, necrosis and loss of function; and (2) ulcerative colitis, the result of the action of the poison on the mucous membrane of the colon, whereby extensive necrosis and sloughing occur. Suppression of urine follows the absorption of the poison, and urine secretion may almost entirely cease. The cessation of renal secretion is followed by a rapid rise in the blood urea, and after 4 or 5 days dangerous symptoms of uræmia, vomiting, stupor, delirium, coma and convulsions set in, which are generally rapidly fatal. The ulcerative colitis begins about 24 hours after the intake of the poison, and is associated with profuse diarrhœa, and the passage of sloughs and shreds of necrotic mucous membrane and blood. The colitis may be caused as the result of absorption of the poison into the blood stream apart from its direct local action on the colon. Death may occur from exhaustion, and absorption of toxic products from the raw surface of the bowel.

Acute mercurial poisoning is always accompanied by a very severe stomatitis, which begins within a few hours. The breath is foul, the mucous membrane becomes ulcerated, the teeth may become loose and necrosis of the alveolus occur.

Five grains of mercuric chloride is a fatal dose for an adult, unless the poison is removed by gastric lavage within an hour or two.

Treatment.—Immediate gastric lavage should be employed. Afterwards, white of egg and milk should be given freely. The collapse, suppression of urine, ulcerative colitis and stomatitis are other symptoms treated by the appropriate methods for such conditions.

(2) Chronic Mercurial Poisoning

Ætiology.—This condition occurs chiefly amongst workers in the metal, or amongst those who are constantly brought into contact with compounds of mercury; for example, those engaged in mining and separation of the metal, *e.g.* at Almaden in Spain, at Idria in Austria, and at the mines in California, China, Peru and the Ural Mountains. Mirror makers, thermometer and barometer makers, and those engaged in the manufacture of chemical and electrical apparatus in which metallic mercury is used, are exposed to risk. Those engaged in the frequent handling or grinding of mercury compounds are sometimes attacked. It must be remembered that mercury is volatile at ordinary temperatures, and those working in ill-ventilated rooms where mercury is exposed are liable to attack. Cases have been recorded of chronic mercurial poisoning from the amalgam in tooth stoppings, and from sojourn in a respiration apparatus fitted with mercury air-valves. The nitrate of mercury is used in the felting of fur, and hatters' furriers are liable to chronic poisoning unless they are properly protected. The condition may result from the continued administration of calomel or blue pill, from

the inunction of mercury ointment, or from the prolonged use of mercurial vaginal douches.

Symptoms.—Dyspepsia, anæmia, general cachexia, with loss of weight and strength, occur. Sometimes a blue line is seen on the gums if the teeth are neglected. Stomatitis is one of the most constant symptoms; increased salivation and marked fetor of the breath occur, and are associated with tenderness of the gums and looseness of the teeth. Colitis, often of an ulcerative type, may result from chronic mercurial poisoning. It is a dangerous complication and difficult to treat. Skin rashes of an erythematous, eczematous or pustular type have occurred. Albuminuria is occasionally found. Glycosuria has been described, but it is rare. Tremor, affecting the muscles of the tongue and face, the arms and hands, and later the legs and trunk, occurs. It is of a fine type, but may be interrupted every few minutes by coarse shaking movements, known to the layman as the "hatters' shakes." The severe mental symptoms known as erethism have been rare since silver took the place of mercury in mirror making. The man affected is easily upset and embarrassed, loses all joy of life, and lives in constant fear of being dismissed. He has a sense of timidity and may lose self-control before strangers. He may be obliged to give up work because he can no longer take orders without losing his temper. Drowsiness by day, depression, loss of memory and insomnia may occur but under modern industrial conditions hallucinations, delusions and mania are rare.

Diagnosis.—This is made by the history and symptoms; but it should be confirmed by analytical tests. Mercury is excreted in small amounts in the fæces. The greatest care should be taken that no mercurial preparation is being administered medicinally during the test. The fæces are collected, and the organic matter destroyed by treatment with hydrochloric acid and potassium chlorate. The resulting solution is submitted to electrolysis, and the mercury present is deposited on a gold kathode, from which it may be dissolved and submitted to the usual chemical tests.

Treatment.—In the manufacture of clinical thermometers and in laboratories where mercury is handled extensively, the benches must be covered with a smooth and impervious surface sloping in such a way as to drain the mercury into a suitable receptacle at the lowest point. The walls and floors should be of impervious material, and the floor cleansed at the end of each day's work. Thermometers must not be filled without suitable exhaust-ventilation for the removal of mercury vapour. Overalls, mess-rooms, and washing facilities are provided. The mouth and pharynx are frequently rinsed with a mouth-wash, and the teeth cleaned with a soft toothbrush and a dentifrice. Periodical medical and dental examination can achieve a great deal, especially by emphasis on the proper hygiene of the mouth. Cavities in carious teeth are filled, sharp angles smoothed, and stumps and teeth irremediably decayed extracted. In the felt-hat trade the workshops must be well managed and spotlessly clean. Efficient exhaust-ventilation must be applied to remove the particles of fur and all vapours of mercury compounds at the source of origin. The failure of chemists to find an efficient substitute for mercuric nitrate in the felting of fur remains a blot upon modern industrial practice, for although the number of cases of poisoning in Great Britain is now negligible there are many elsewhere. Soviet Russia has had the courage to use potash in place of mercury, but this

produces felt of inferior quality. A workman affected by mercurial tremor must give up his work, and abstain from alcohol. Stomatitis should be treated by the use of the toothbrush, mouth washes and dental extractions when necessary. In cases of medicinal poisoning saline aperients should be given daily to promote the free elimination of mercury by the colon.

(3) Poisoning by Mercury Fulminate

Mercury fulminate is handled in explosives factories where detonators and percussion caps are made. In those processes where the fine dust of this substance falls upon the skin dermatitis follows. The susceptibility of some individuals is such that they cannot stand the dust for a day, whereas others only suffer in warm weather. As a rule the cases of "fulminate itch," as they are called in the trade, are slight. The face, eyelids, neck and forearms are attacked by erythema, accompanied by itching, swelling and œdema. Papules break out on the inflamed areas, and may become vesicles, bullæ and pustules. A pustular folliculitis commonly develops on the hairy parts of the skin. If the fulminate lodges in a crack or abrasion of the skin it may act as a corrosive, causing small painful necrotic lesions on the hands which last about a fortnight. The operatives call them "powder holes." Recovery takes place in from 1 to 2 weeks and is accompanied by desquamation. Inflammation of the conjunctivæ and mucous membranes of the nose and larynx may occur.

In the manufacture of mercury fulminate meticulous attention should be paid to detail in all matters of cleanliness in the entire plant. Where fumes are given off as the result of small explosions they must be removed by means of mechanical ventilation. All persons employed should be provided with well-fitting overalls, caps, indiarubber gloves, and if necessary respirators. Washing accommodation must be available close to the workroom, and a separate towel provided for each worker. The hands and arms are washed before meals and before leaving work in a 10 per cent. aqueous solution of sodium thiosulphate. A lanolin ointment is rubbed into the skin after washing. For the conjunctivitis a 2 per cent. solution of sodium thiosulphate as an eyewash has been beneficial.

(4) Poisoning by Organic Mercury Compounds

Fungicidal dusts containing organic mercury compounds are used extensively in agriculture to prevent certain smut diseases of cereals. For some years mercurial derivatives of the phenyl and tolyl series have been manufactured without any mishap worse than an occasional burn on the skin. Poisoning by inhalation of methyl mercury compounds leads to involvement of the nervous system in a unique way, salivation, stomatitis and erethism being absent. There is severe generalised ataxia, dysarthria and a gross constriction of the fields of vision, memory and intelligence being unaffected. In severe cases the patient remains crippled, and unable to stand or to speak intelligibly. The condition has been reproduced experimentally. Rats and monkeys were exposed to the vapour of methyl mercury iodide and they became grossly ataxic. Histological studies showed myelin degeneration in the peripheral nerves, posterior roots and dorsal columns.

In the manufacture of organic mercury compounds elaborate precautions must be taken to prevent contact with the skin or inhalation. The use of gloves and respirators is not enough. The whole process of manufacture, including the final packing of the dusts, must be carried out mechanically in closed apparatus. The farmer should be protected both by warnings that mercurial dressings are poisonous and by schemes whereby he can obtain from the seed merchant seed already dressed. The seed merchant must dress the seed in a completely closed apparatus. The ataxia and dysarthria of methyl mercury poisoning must be treated by re-educative movements, persuading the patient to walk on chalked lines. An expert in charge of a speech clinic with great patience and the use of a mirror should teach the workman to speak. With great perseverance in some cases he may be taught to use knife and fork, a pencil and even a typewriter.

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MANGANESE POISONING

Ætiology.—Manganese is used in the manufacture of dry batteries and in the pottery, soap and colour industries. Cases of poisoning have followed upon the inhalation of excessive amounts of dust in the grinding, sieving and packing of manganese ores, and in the manufacture of manganese steel in which the metal is first fused in the electric furnace.

Pathology.—Susceptible individuals are few. There is a similarity between this form of poisoning and progressive lenticular degeneration, except that in manganese poisoning the condition remains stationary or improves when exposure to manganese dust ceases. Histological studies on necropsy material have shown degenerative lesions of the nerve cells, particularly in the globus pallidus, the lenticular nucleus and the caudate nucleus. The fact that histological lesions have been found in the liver makes still closer the connection between poisoning by manganese and progressive lenticular degeneration. The condition has been reproduced experimentally in monkeys by administering manganese chloride by intraperitoneal injection. The animals developed choreic movements, passed into a state of rigidity, and finally developed tremor resembling paralysis agitans. Gross morbid changes were found in the lenticular nucleus and liver. The experiments afford an explanation of the symptoms in most of the cases described. The extrapyramidal motor system is clearly picked out by the poison, hence the rigidity, difficult gait, retropulsion, propulsion, mask-like facies, sleepiness, tremor, and uncontrollable laughter.

Symptoms.—The symptoms include languor and sleepiness, low monotonous voice, mask-like facies, involuntary movements varying in degree from a fine tremor of the hands to gross rhythmical movements of the arms, legs, trunk and head, cramps in the calves, retropulsion and propulsion, unsteady gait, and occasionally uncontrollable laughter or crying. There is no disability except in the nervous system.

Prognosis.—Although men seriously poisoned are life-long cripples, the condition is not lethal.

Treatment.—Manganese poisoning can be prevented by wearing res-

pirators wherever dusts or vapours are encountered. Personal hygiene is important, and the worker must wear protective clothing and gloves, since the occurrence of skin absorption is established. Local exhaust ventilation should be applied, both at the furnaces to remove fumes and at the packing and sieving apparatus to remove dust. These measures are attended with good results, for it has been found that when they were applied in one particular factory they removed all risk of poisoning encountered by the workers over a period of 6 years.

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CARBON MONOXIDE POISONING

Carbon Monoxide, or Carbonic Oxide (CO), is a very poisonous gas. If present in the air breathed in an amount equal to 0·2 per cent. it is capable of destroying life; while an atmosphere containing 0·05 per cent. of carbon monoxide gives rise to definite symptoms of poisoning.

Ætiology and Pathology.—When carbon is burnt in a limited supply of oxygen, carbon monoxide is produced in varying amount. *Domestic poisoning:* Charcoal fires and braziers give rise to considerable amounts of CO. Certain types of water heaters and slow combustion stoves are common sources of production of the gas, which may give rise to poisoning if the ventilating flues are inadequate. In lime kilns there is evolution of CO_2 and CO. The exhaust fumes from motor-cars and petrol-burning engines contain approximately 6 per cent. of carbon monoxide. The commonest source of carbon monoxide poisoning is from coal gas which is used for illuminating or heating purposes. Coal gas contains normally a percentage of from 4 to 10 per cent. carbon monoxide, and it often approximates to the latter figure. It is a common cause of death either from accidental leakage of pipes or from purposive exposure due to turned-on taps. Carbon monoxide occurs in the smoke and fumes from fires with inadequate chimney ventilation. It is important to remember that the products of combustion of gas stoves and gas fires contain an appreciable amount of carbon monoxide. The flues from these are often quite inadequate completely to carry away the products of combustion, in which case the gas stoves and gas fires, when used, give rise to the addition of carbon monoxide to the air of dwellings and so are a source of ill-health or chronic CO poisoning. *Industrial poisoning*: This occurs from the fumes from blast furnaces, in iron smelting, and in blasting operations in mines. In coal mines the explosions from coal dust, or inflammable gases, lead to the production of carbon monoxide (after-damp). *Water gas* is prepared by passing steam over red-hot coke, and contains upwards of 30 per cent. CO. It is used for heating purposes, and is sometimes added to coal gas before its distribution. It is very poisonous and, owing to its slight smell, is very dangerous unless mixed with odorous gases. *Producer gas* is prepared by passing a mixture of steam and air over red-hot coke in retorts. It is used for heating the coal retorts for the preparation of coal gas. Producer gas is a mixture of carbon monoxide, hydrogen and nitrogen, and is similar in composition and properties to water gas, and may contain as much as 30 per cent. of carbon monoxide. Industrial dangers

also arise from leakages in the plant and from the process of charging the producer-gas retorts.

Action of carbon monoxide.—Carbon monoxide has 220 times the affinity for hæmoglobin that oxygen has. If respired, it will, therefore, more or less completely displace the oxygen from its combination with the hæmoglobin of the red cells. This prevents oxygen being carried in requisite amount by the red cells to the tissues of the body, which thus become deprived of the oxygen necessary for their vital functions. The extent to which the hæmoglobin is saturated with carbon monoxide depends upon the percentage of the latter in the air breathed. When the hæmoglobin becomes one-third saturated with carbon monoxide, definite symptoms of poisoning occur, and when the saturation exceeds 50 per cent. there is grave danger of a fatal issue. It is important to note that carbon monoxide is a tissue poison. It does not act simply as an oxygen depriver to the tissues, but undoubtedly has in addition a narcotic action upon them. This is best illustrated by considering the serious symptoms of narcosis (muscular paralysis and loss of consciousness) which occur in a person in whom 50 per cent. saturation of the hæmoglobin with carbon monoxide exists. These symptoms far exceed in gravity those of a person possessing only 50 per cent. of hæmoglobin as the result of anæmia from disease or hæmorrhage. Carbon monoxide acts as a tissue poison especially to the nervous system, but there is evidence to show that it acts on all the tissues of the body, notably the cardiac muscle, and may cause degenerative changes in them.

Post-mortem appearances.—The external appearances are characteristic, the cheeks and lips and post-mortem stains appearing cherry-pink in colour. On opening the body, the blood, muscles and internal organs have a characteristic cherry-pink colour. The lungs may show areas of consolidation due to broncho-pneumonia. Small hæmorrhages may be visible, and œdema is common. The brain shows congestion and œdema, and small punctiform hæmorrhages may be found in the cortex and basal ganglia. The heart may show degeneration of the cardiac muscle and punctiform hæmorrhages beneath the pericardium. In some cases of carbon monoxide poisoning putrefaction is much delayed.

Symptoms.—The onset of carbon monoxide poisoning is usually very insidious, since the gas is odourless and any smell of an atmosphere containing it is due to the presence of other gases or vapours having a characteristic odour. Also the gas may be respired freely without any irritation to the air passages. Premonitory symptoms are giddiness, ataxic gait, a swimming sensation, headache or a sensation of heaviness or constriction in the head, noises in the ears, and a feeling of oppression in the chest. Sometimes nausea and vomiting occur. The onset is, however, often sudden, and this is likely to be so when the percentage of carbon monoxide is relatively high. In these cases, the first symptoms may be sudden collapse, with loss of consciousness, and this is associated with complete loss of power of the muscular system. In subacute cases the symptoms may resemble those of acute alcoholic poisoning. An analysis of the blood would at once reveal the exact diagnosis.

Cardio-vascular symptoms, such as violent beating of the heart and throbbing of the blood vessels, occur. The blood pressure rises at first, and the pulse is full and may not be increased in frequency. Muscular weak-

ness and drowsiness quickly supervene in severe cases, and the patient falls unconscious. In the condition of coma the blood pressure falls and the pulse becomes rapid and small. The conjunctivæ become hyperæmic and the eyes have a staring appearance, the pupils being partially dilated, and do not react to light. The complexion has a cherry-red appearance. Froth may be present on the lips. The breathing is stertorous. The temperature is usually subnormal in the early stages of coma, but is sometimes raised above the normal in the later stages. There is relaxation of the sphincters in severe cases. Broncho-pneumonia may develop if the coma is prolonged for more than a few hours. When the state of coma lasts only for an hour or two, the recovery may be rapid. It is very important to remember that though the muscular power recovers quickly, the tissues of the body have been submitted to a serious acute toxæmia. In all cases where coma has occurred, careful after-treatment is essential, since thereby the occurrence of after-effects such as weakness or paralysis, or mental disorder, may be avoided.

Diagnosis.—In all cases, at the earliest opportunity, a specimen of blood should be obtained for analysis. About 10 c.c. are removed from a convenient vein of the arm, and placed in a small test-tube so as almost to fill it, and a cork inserted. This can then be sent to the laboratory for analysis. It should not be shaken or exposed to the air. The carbon monoxide present in the blood is most conveniently estimated by means of Hartridge's reversion spectroscope. The percentage of carbon monoxide present is of value not only for diagnosis but for prognosis.

It may be remarked that a record of the blood analysis in cases of carbon monoxide poisoning would be of great interest and value for research purposes.

Treatment.—Elimination of the carbon monoxide is best effected by the ventilation of the lungs with pure air and oxygen.

Immediate removal of the patient to an uncontaminated atmosphere is the first step. Onlookers should not be allowed near the patient. If removed to a room, the windows and doors should be widely open and a free current of air encouraged. Complete rest is absolutely necessary, and attempts to keep the patient on the move should be forbidden. The patient should be lying flat, and all constricting clothing round the neck and chest should be loosened or removed. Care should be taken that the air passages are free, and any froth or saliva wiped away from the mouth or nose. If necessary, the tongue should be pulled forwards with tongue forceps. In some cases, especially if convulsions have occurred, a gag may be required to keep the mouth open. Warmth of the body is important, and blankets and hot-water bottles should be used.

Artificial respiration is of great value, as this enables oxygen to reach the alveoli of the lung. The method most suitable is Sylvester's, for this permits of free access of fresh air to the air passages and is more convenient for the administration of oxygen. The upper extremities are moved upwards to a fully extended position above the head and kept there for two seconds, they are then lowered to the sides of the chest and firmly pressed against the ribs for about two seconds, the double movements being repeated about fifteen times per minute. Oxygen and 5 per cent. carbon dioxide should be administered without delay. For its efficient administration a cylinder,

with a suitable regulating valve tap, and a B.L.B. mask are required. If no cylinder containing the mixture be available a sparklet bulb containing CO_2 may be used in conjunction with an oxygen cylinder. A special metal perforator with tube attached is available for the purpose of perforating the sparklet and admitting the carbon dioxide at a desired rate by means of a rubber tube. The rubber tube is placed under the oxygen mouthpiece, so that the mixture of oxygen and carbon dioxide can be conveniently administered. This method of administration is easily and conveniently effected and is entirely free from any risk. When the respiration of the patient has become normal, pure oxygen should be administered for about 3 hours, with short intervals for feeding. This will be of value in getting rid of the carbon monoxide from the blood of the patient.

Atropine sulphate, gr. $\frac{1}{100}$, may be given hypodermically, and repeated, if required. In severe cases it may be necessary to treat collapse by means of subcutaneous normal saline (1 pint), or possibly blood transfusion.

After-Treatment.—In mild cases, where coma only lasts a short time, it is important that the patient should be kept completely at rest in bed and under medical supervision for a few days. In severe cases, where coma has been prolonged for several hours, complete rest in bed under medical supervision for 2 or 3 weeks or more will be required, since otherwise there is a danger of after-complications. A certain proportion of cases that have been severely poisoned develop confusional insanity. Prognosis for life is then good, but the mental prognosis is poor.

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POISONING BY COAL-TAR DERIVATIVES

The coal-tar derivatives are so numerous and complex that it is difficult for the toxicologist to keep pace with the chemists who produce them. The following compounds will be discussed: benzene, mononitrobenzene, dinitrobenzene, phenylenediamine, trinitrotoluene, dinitrophenol and aniline. It is sometimes possible to predict from the chemical composition of the simpler members of the group what their physiological action is likely to be. Addition of a nitro- or nitroso-group usually produces a more toxic compound, but it does not follow that toxicity will continue to increase as more nitro-groups are added. Thus, 1–2–4 dinitrophenol is toxic, whereas trinitrophenol is practically harmless. The position of the substituent groups in the benzene ring has a great effect on the toxic action. Thus, the toxic properties of 1–2–4 dinitrophenol are not shared by any of the other isomers. When a nitro-compound is reduced to an amine, as when nitrobenzene is reduced to aniline or nitrotoluene to a toluidine, the toxic characteristics remain much the same, but the intensity of the action is lessened. Sulphonation renders a compound non-toxic; as soon as aniline is sulphonated it ceases to give trouble. The entrance of chlorine into an aromatic compound does not increase the toxicity, as it does in the case of an aliphatic compound. In fact, chlorbenzene is less toxic than benzene.

1. Benzene

Coal-tar benzene or benzole is obtained as a by-product from the distillation of tar in the manufacture of coal gas. It is the most interesting of the industrial solvents, and with the exception of tetrachlorethane the most dangerous. It must not be confused with benzine, which is unfortunately pronounced in the same way. Benzine is derived from the distillation of petroleum and is non-toxic. Coal-tar benzene has two fields of application in industry: (1) where it is handled in large quantities in closed mechanical systems, as in the distillation of coal-tar, the blending of motor fuel and in chemical industry; and (2) where it is used as a solvent, as in the rubber industry, artificial leather manufacture, the dyeing and cleaning industry, the manufacture of paints, varnishes, celluloid, artificial manure and glue.

Acute benzene poisoning usually occurs as the result of the breaking of distilling apparatus, or in the cleaning of tanks. In slight cases there is giddiness, and a stage of excitement; in severe cases these symptoms may be followed by convulsions, coma and death. Benzene sinks into the metal of tanks. It is therefore necessary to forbid men to enter such tanks until they have been washed clean and exposed to the open air for many days. Even then a workman lowered into such a tank must be equipped with body belt, life-line and breathing apparatus communicating with a hose to the exterior. In the stage of excitement the victim may shriek, sing madly and fight with the rescuer, who, on account of his greater exertions, runs more risk than the rescued.

Chronic benzene poisoning has always been very rare in Great Britain. Speaking for the whole world, however, it was at one time the most important industrial poison after lead. Benzene poisoning may begin with giddiness, nausea, anorexia, weakness and nervousness. These symptoms are followed by progressive anæmia, with hæmorrhagic manifestations, such as bleeding gums, epistaxis, menorrhagia, purpura and visceral and retinal hæmorrhages. Ulcers or gangrenous patches on the lips, fauces and pharynx are common. Although poisoning may occur only after many years' exposure there have been fatalities after a few weeks' exposure. The victims of industrial poisoning often constitute a small minority of the workers; a single susceptible individual may contract fatal poisoning in an environment which does not give rise even to mild poisoning in others. The factors responsible for the great variations in susceptibility are largely unknown, but in general women, especially young women, are more susceptible than men. Changes in the blood may begin from 2 days to 1 month after the first exposure, according to the amount absorbed, and they may progress or even develop after exposure has ceased. Acclimatisation to the vapour of benzene does not seem to occur, and it is doubtful whether any concentration greater than zero is safe over a long period of time.

The bone marrow is attacked, and it may be aplastic, normal, hyperplastic or leukæmic, the corresponding changes being reflected in the peripheral blood. In the early stages of poisoning there may be little or no evidence of damage to the red cells but only purpura with leukopenia and granulopenia. The total leucocyte count may fall to a very low level; in fact, the white cells may almost disappear. A count of one thousand per c.mm. is common. In some cases the granular leucocytes fall as low as

10 per cent. The bleeding time may be increased to half an hour, with a corresponding drop in the platelets. The red cell count may fall as low as three-quarters of a million per c.mm. Splenomegaly may appear in protracted cases of poisoning. Myeloid leukæmia, confirmed by post-mortem examination, has been found in several cases. Necropsy usually shows aplasia of the bone marrow. Hæmorrhages may be found in the skin, pericardium, pleura, alimentary tract, meninges, bladder and uterus. Gangrenous stomatitis and even necrosis of the gastric mucosa have been recorded. Benzene cannot be discovered in the body after death.

Benzene is so toxic that its substitution wherever possible by other solvents which are harmless is in preventive treatment the method of first choice. In all processes involving the presence of benzene the value of frequent periodical medical examination, including examination of the blood, has been proved by experience. The more complete and effective the prevention of the escape of vapours into the workrooms and the more efficient the daily supervision of the ventilating apparatus, the less is the necessity for periodical medical examination.

In acute benzene poisoning the usual methods of resuscitation are used: rest, warmth, artificial respiration, administration of oxygen and carbon dioxide mixture, and injection of coramine as a respiratory stimulant. The patient should be prevented from returning to work too early.

Cases of chronic benzene poisoning must be treated by repeated blood transfusions and it must be remembered that the toxic influence may persist even after removal from exposure. The results of treatment are so poor as to convince all who have studied the subject that the use of benzene in industry must be ruthlessly suppressed, except where the process used is entirely enclosed. Fortunately in Great Britain it has been possible to do this.

2. Mono-nitrobenzene

Mono-nitrobenzene (oil of mirbane; artificial oil of bitter almonds) is used in the manufacture of aniline, in perfumery and as a flavouring agent, being the chief substitute for oil of bitter almonds. It is sometimes taken as an abortifacient, and on several occasions 15–25 drops have proved fatal, especially if the poison is taken with alcohol. The stomach should be washed out repeatedly with water until the returned fluid no longer smells of nitrobenzene. Purgatives should be given. In factories death has taken place from absorption through the skin, where the oil has been spilled on the clothing. The victim of such an accident should be stripped promptly of his clothes, sponged with weak acetic acid or vinegar, and provided with a shower bath and clean clothes. The symptoms vary according to the acuteness of the poisoning. Pallor appears, quickly followed by lividity. Unconsciousness occurs with great rapidity, perhaps in 20 minutes. The patient is generally deeply cyanosed, and the blood is dark and viscid, and will sooner or later show the spectrum of methæmoglobin. Death occurs in coma, or recovery takes place after a variable period of unconsciousness. However, nausea and vomiting may begin again after a few days, and toxic jaundice appear. The blood picture is that of anæmia with granular degeneration of the red cells (stippling), and sometimes the presence of nucleated red cells. In severe anæmia a blood transfusion may be considered.

3. Dinitrobenzene

Dinitrobenzene is used in the manufacture of dyes, and is itself an important explosive. It is a solid, and in consequence poisoning develops less rapidly and is less severe than in the case of mono-nitrobenzene. Poisoning occurs amongst men who either shovel or melt dinitrobenzene. In a mild case there is a sense of pressure in the head, which increases to a violent throbbing headache, giddiness and dyspnœa. In severe cases the face is deeply cyanosed; the lips, tongue and ears are deeply purple; and there are nausea, sometimes vomiting, abdominal pain, a staggering gait and extreme weakness. An attack rarely occurs during work; the man is usually overcome some hours after he has left the plant. Cyanosis occurs, and is accompanied by anæmia with marked stippling of the red cells. Methæmoglobin, hæmatoporphyrin, hæmoglobin, and even albumin have been found in the urine. The smoky colour of the urine may be noticed by the men themselves soon after their first contact with nitrobenzene or aniline. Only very rarely does toxic jaundice occur. It is well known in industry that cases of poisoning are more frequent in hot weather than during the colder seasons of the year. Lack of care and unclean habits are predisposing causes. Those who do not change their working clothes on returning home may sit before the fire and absorb the poison from the evaporation of crystals or from the material in solution on their clothing. Absorption from the alimentary canal is more rapid if the stomach is empty, and it is therefore desirable that men should take a meal before they work. Alcohol undoubtedly favours absorption, and several instances are on record in which poisoning has supervened after indulgence in ordinary amounts.

4. Phenylenediamine

Phenylenediamine is used for two similar purposes; for dyeing hair black and as a dye for furs. It is well known that it may cause dermatitis and sometimes asthma in susceptible persons. Its systemic effects are much rarer and have received less attention. Hairdressers handling the dye have suffered from attacks of weakness and vomiting, with intense violet cyanosis of the lips and face. In unusually susceptible individuals toxic jaundice has occurred, followed by death from hepatic insufficiency after about 6 months. At necropsy the liver is small and shows the changes of subacute atrophy with regeneration nodules. Persons handling the dye should wear rubber gloves. Avoidance of exposure removes the cyanosis completely.

5. Trinitrotoluene

Trinitrotoluene is handled mainly in the filling of shells. The first symptoms of poisoning are drowsiness, headache, nausea, loss of appetite, epigastric pain, vomiting and giddiness. There is some cyanosis of the lips, followed by dyspnœa with marked drowsiness and staggering gait. Dermatitis in the form of a diffuse erythema sometimes occurs on the dorsal surfaces of the wrists, and on the face and neck. The symptoms come on gradually after several days' or weeks' work, or they appear on a hot day

after a few hours' work and cause collapse. If cyanosis occurs in one in ten of the workers, toxic jaundice probably affects one in five hundred. The greatest incidence of jaundice is in the third month of employment. Premonitory symptoms, such as drowsiness, giddiness, depression, and dark urine are sometimes present, but the onset is often quite sudden. Sometimes a latent interval occurs between removal from exposure and the onset of jaundice. The prognosis is always uncertain, but grave symptoms of hepatic insufficiency sometimes appear rapidly. The mortality is 25 per cent. The morbid appearances are those of yellow and red necrosis of the liver, with great reduction in its size and weight. The necrosis of the liver cells is associated with infiltration and subsequent fibrosis resembling ordinary portal cirrhosis. Aplastic anæmia sometimes occurs among trinitrotoluene workers, but its incidence is very small. The latency of the blood changes is even longer than the latency of the jaundice, for it is found that anæmia can develop as long as 9 months after exposure to trinitrotoluene has ceased. The anæmia is usually, if not always, fatal. At necropsy fatty marrow is found throughout all bones. There is an excess of iron pigment in the liver, and multiple hæmorrhages are found in the tissues. The skin is the main channel of absorption. Experience in industry goes to show that when a poison is absorbed by this route the application of preventive measures is most difficult; trinitrotoluene is no exception. By the end of the War of 1914–1918 the risk of poisoning had been greatly diminished, not by any single precaution but by the combination of several, of which alternation of employment, periodical medical examination, ventilation and clean working conditions were the chief. Success was not achieved until mechanical means were substituted for the hand filling of shells, combined with measures of cleanliness which were so precise as to prevent the contamination of the outside of the shell by trinitrotoluene.

6. Dinitrophenol

It is the 1–2–4 isomer of dinitrophenol which has toxic properties. These were revealed in the War of 1914–1918, especially in French shell-filling factories. The illness begins with lassitude, and the worker may notice yellow patches on the covered parts of the skin due to excretion in the sweat of dinitrophenol. Tremor, excitement and intense thirst follow, and the face may be slightly cyanosed. In severe cases orthopnœa, hyperpyrexia and convulsions set in, and death occurs in a condition resembling uræmia. The urine is of an orange yellow colour, and gives a diazo reaction, which serves both quantitatively and qualitatively to determine the amount of the poison absorbed, and so to give a clear indication as to when suspension and transference to other work are necessary. At necropsy no pathognomonic feature is found; there is no atrophy of the liver. The workmen must be provided with a complete set of underclothing and overalls into which they change from their working clothes, a separate cubicle being provided for each man. Well designed exhaust ventilation must be applied locally to take away the fumes in the melting of the compound and also in the filling of shells. Any dust that collects around the margin of the shell must be removed by a vacuum cleaner.

7. Aniline

Aniline is a colourless oily liquid which darkens on exposure to light or air. It is handled in the manufacture of dyes, in the dyeing and cloth-pressing industries, in the extraction of resin and in the rubber industry. Aniline poisoning arises usually from inhalation, but absorption through the skin and less frequently inhalation of dusts of aniline compounds may cause it. Care must be taken to change the clothes at once whenever they are splashed with aniline. Men must avoid entering chambers filled with its vapour. The symptoms of aniline poisoning are similar in all respects to those of nitrobenzene poisoning. The convenient term *anilism* may be used to cover the symptoms produced by most of the nitro- and amino-derivatives of benzene.

In *acute aniline poisoning* there is headache, weakness, difficulty in breathing, cyanosis, loss of power in the limbs and giddiness. In severe cases the cyanosis is more intense and prostration occurs with a cold moist skin, small pulse, air hunger and even death in coma. When recovery occurs it is often gradual and may be accompanied by increased frequency of micturition. In *chronic poisoning* the workers show slight cyanosis, secondary anæmia, and sometimes sleeplessness, headache, giddiness and abdominal discomfort. In hot weather practically all the men exposed to aniline and similar compounds in a dye works show cyanosis.

The manufacture of nitrobenzene, and the reduction of nitrobenzene and nitrotoluene to aniline and toluidine must take place in closed vessels. Even so, escape of small quantities of aniline into the atmosphere is very difficult to prevent unless ample ventilation is provided. Therefore in addition to the technical regulations there must be insistence on cleanliness of the workrooms, personal cleanliness on the part of the workers and provision of baths and changes of clothing. Contact with aniline and nitrobenzene, especially on the skin, and also the spilling and splashing of these fluids must be carefully avoided. All workers must be strictly instructed as to the symptoms of nitrobenzene and aniline poisoning, and the right steps to take if poisoned. Regular medical inspection of workmen is desirable.

Workers, and especially those newly employed, must be under supervision in order that assistance may be rendered them on the first signs of poisoning. Medical assistance should be within easy reach. Systematic instruction should be given in first-aid methods, and in the use of apparatus for oxygen and carbon dioxide inhalation. The possibility of skin absorption must always be borne in mind. A victim whose skin or clothing has been splashed with aniline may turn blue in the face and begin to stagger. Someone may take him out to the fresh air or administer oxygen, when what he needs most is to have his clothes stripped off and be given a bath. Workers entering stills and similar chambers should always be equipped with breathing apparatus and a supply of oxygen. Other aids, such as safety belts which are held by helpers, involve certain risks, especially as the rescuer is easily induced to spring to the assistance of his unfortunate mate without the necessary breathing equipment. The frequency of such accidents calls urgently for the use of breathing apparatus.

POISONING BY CHLORINATED HYDROCARBONS

The rapid growth of the moulded plastics and cellulose lacquer industries has led to the extensive use of many new solvents, most of which were little more than chemical curiosities before about 1925. Amongst these are the chlorinated hydrocarbons which have flooded the market largely because the alkali industry requires an outlet for its by-product chlorine. The various members of the group are useful as refrigerants, as degreasers of metals, fire-extinguishers, cleansers of textiles, solvents for rubber and thinners of cellulose lacquers. They are non-inflammable, non-combustible, and non-explosive, but they are far from harmless in their effects on the human body. The action of carbon tetrachloride has been extensively studied because of its use in hookworm therapy. Tetrachlorethane dramatically attracted attention in the War of 1914–1918, and a mass poisoning from leaking refrigerators in Chicago has led to an increase in knowledge of the action of methyl chloride. Trichlorethylene has been studied because of its extensive use in dry cleaning.

1. Methyl Chloride

Men working in chemical plants or employed upon making, installing or repairing refrigerators may be exposed to methyl chloride. Symptoms of poisoning include giddiness, weakness of extremities, nausea, vomiting, restlessness, followed by somnolence, and then by dimness of vision, which may not clear up until 14 days after removal from exposure. Later there is some rise of temperature, pulse, and respiratory rate, usually with oliguria and occasionally with suppression lasting up to 48 hours. Evidence of acute nephritis is found in about half the cases. Anæmia may be found, the red cells dropping as low as 3 million per c.mm., and the hæmoglobin as low as 50 per cent. The death-rate is as high as 35 per cent.

2. Carbon Tetrachloride

Carbon tetrachloride is used in industry as a solvent for fats and rubber, for dry cleaning, for cleaning oil from machinery, and under the name pyrene as a fire extinguisher. Acute and sometimes fatal poisoning has occurred from the anæsthetic effects of carbon tetrachloride used as a dry shampoo for the hair. Men exposed to the vapour sprayed from pyrene fire extinguishers in confined spaces have suffered from oliguria and jaundice. In animal experiments carbon tetrachloride has been shown to cause necrosis of the liver. In man it may attack both liver and kidneys, but in most clinical histories so far published the symptoms of renal injury overshadow those of hepatic injury. The early stages of the illness are characterised by persistent headache, nausea, vomiting, diarrhœa and tenderness over the liver. Such symptoms are often followed by oliguria, suppression of urine and uræmia. The blood urea may rise to 300 mg. per 100 c.c. and the patient, though practically moribund, may suddenly develop polyuria and recover even after almost complete anuria lasting 10 days. When the liver is attacked recovery may follow an attack of jaundice lasting as long as 2 months.

In the treatment of cases rendered unconscious by acute poisoning, it is important that the patient should not be placed upon the floor of the room where the accident occurred, for the vapour is five times denser than air and therefore accumulates on the floor. Chronic poisoning should be treated by glucose drinks, together with large doses of calcium lactate up to 15 grammes a day. If necessary calcium gluconate may be given by intramuscular injection.

3. Tetrachlorethane

Tetrachlorethane is the most dangerous of all the chlorinated hydrocarbons, being nine times as toxic as carbon tetrachloride. It is a very good solvent for cellulose acetate, which, being non-inflammable, is used for purposes for which cellulose nitrate (celluloid) is not adapted. Cellulose acetate was the chief constituent of the dope used as a waterproof coating for the wings of aeroplanes in the War of 1914–1918, and it is now used to make non-inflammable cinema film. The symptoms of poisoning are general malaise, loss of appetite, nausea, headache and constipation. After several days or even weeks, jaundice develops and vomiting is then likely to become more marked. In fatal cases necrosis of the liver is found in the form of acute red and yellow atrophy. In one case the liver weighed only 19 oz. The blood changes in mild poisoning consist of an increase of large mononuclear cells up to 40 per cent., with a slight elevation of the white count. Blood counts have been taken in order to detect early poisoning. Elaborate exhaust ventilation in factories and workshops fails to prevent toxic jaundice. It is therefore necessary to use a harmless solvent, such as amyl acetate in place of tetrachlorethane.

4. Trichlorethylene

Trichlorethylene is a non-inflammable solvent employed extensively in dry cleaning. It has assumed an important place in the list of fat and rubber solvents, displacing to some extent carbon tetrachloride. Trichlorethylene has a powerful narcotic effect. The workman affected is usually found unconscious on the floor, and if there has been prolonged exposure to a large dose the effects may be fatal. Chronic exposure has been held responsible for paralysis of the sensory fibres of the fifth nerve, and also for retrobulbar neuritis followed by optic atrophy. An indirect form of injury to the eye sometimes occurs when a foreign body lodges in the cornea and produces ulceration. The workman is not aware of the presence of the irritant substance, because the cornea has been rendered insensitive. Apparently trichlorethylene is not so likely to attack the liver as tetrachlorethane. Toxic jaundice and albuminuria have only rarely been recorded. Dry cleaning establishments employing trichlorethylene should be provided with efficient exhaust ventilation. When solutions containing trichlorethylene are applied to the interior of closed vats the men should work in pairs, relieving each other frequently. The man in the enclosed space should be provided with a lifebelt and also with an apparatus through which he can breathe air from outside.

Donald Hunter.

ACKEE POISONING

Synonym.—Vomiting sickness of Jamaica.

Definition.—A frequently fatal disease, especially affecting children in the West Indies, characterised by vomiting and nervous symptoms due to eating the unripe ackee fruit.

Ætiology.—Ackee fruit grows on the tree *Blighia sapida* (Sapindaceæ) in the West Indies and West Coast of Africa. The mature fruit is quite harmless, but when eaten in an immature state before the fruit opens, it proves a deadly poison, especially if soup be made from it or other ingredients like rice be boiled in ackee water. The poison is contained in the arilli of the unripe fruit.

Pathology.—Intense fatty changes are found constantly in the liver and to a lesser degree in the kidneys, heart and cortical brain-cells. Hyperæmia of the meninges and other organs occurs, also hæmorrhages in the viscera.

Symptoms.—The patient, who is generally a child and quite well, suddenly commences vomiting some 2 hours after a meal containing unripe ackee fruit and complains of nausea and abdominal discomfort. After 3 or 4 hours of sickness a calm interval ensues, followed by nervous symptoms, including cerebral vomiting, twitching of muscles, convulsions and coma.

Prognosis.—Once nervous symptoms supervene the condition is invariably fatal, the average duration being 12 to 14 hours.

Treatment.—Prevention consists in discarding the immature unopen fruit and in not utilising the water in which ackee fruit is boiled as soup. Alcohol precipitates the poison, and the immediate administration of rum or ether and ammonia as advocated by Scott has reduced the mortality in school children from 90 to 27 per cent.

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FOOD POISONING

Food poisoning occurs when, in mistake for a wholesome food, some article is eaten which is of itself normally poisonous, or rendered poisonous by contamination from outside sources. The former is called Endogenous Food Poisoning, while the latter, which is the ordinary form of food poisoning, is spoken of as Exogenous.

Endogenous Food Poisoning.—The following are examples:

(1) *Poisonous fungi* are sometimes eaten in mistake for edible mushrooms, and dangerous or even fatal results may follow, owing to the presence in them of poisonous substances. Unfortunately there are no simple tests by which the layman may distinguish the poisonous from the harmless species. Experiments in eating new or unfamiliar varieties should never be undertaken.

(*a*) *Amanita phalloides.*—This contains the deadly substance, phallin or amanita toxin. The susceptibility of children is greater than that of adults. The ingestion even of part of a plant may result in poisoning and

the mortality rate is high. After a prodromal period of 4 to 24 hours, acute abdominal pain, vomiting and diarrhœa occur. The vomit and stools may contain blood and mucus. Anuria may occur. Short periods of remission may follow, but usually within a day or two jaundice, cyanosis, and coldness of the extremities develop. In fatal cases coma supervenes. When poisoning is less severe, the symptoms abate in about a week and the patient is well within 4 weeks.

(*b*) *Amanita muscaria.*—This contains muscarine. After a small dose the patient becomes mildly excited, and the fungus is used by Siberian peasants to induce drunkenness. After larger doses the first symptoms appear within 2 to 6 hours. They are salivation, sweating, retching, vomiting and diarrhœa. Giddiness, confusion and hallucinations rapidly follow, and the pupils become contracted and fail to react to light or on accommodation. Amaurosis and diplopia may occur. Although the symptoms are violent the mortality rate is low. In all cases of mild poisoning the prognosis is good.

(2) *Poisonous fish.*—Certain fish, such as those of the species Tetrodon, found in Japanese waters, are normally poisonous, and the same applies to mussels when grown under unhealthy conditions. The symptoms caused by these poisonous foods are those of acute gastro-enteritis, with marked nervous disturbance and collapse.

(3) *Poisonous parts of plants* may be eaten in mistake for foods; for example aconite root for horse radish, or deadly nightshade berries for edible fruit.

Potato Poisoning.—Under certain conditions potatoes may contain a dangerous amount of the poisonous alkaloid solanine. This is produced by the growth of certain forms of bacteria in the tubers, which is likely to occur if, owing to improper storage, sprouting of the potatoes has taken place. The symptoms of solanine poisoning are those of acute gastro-enteritis, associated with nervous prostration and collapse, resembling those caused by poisonous fungi.

In some countries certain harmful vegetables are more or less habitually used as foods. [See (4) and (5).]

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4. Lathyrism—

Definition.—A disease of limited geographical distribution, characterised by spastic spinal paralysis, and caused by poisoning with peas of a vetch of the genus *Lathyrus*.

Ætiology.—The disease, formerly met with in Italy, has been reported from India, especially North Behar and the United Provinces, Algiers, France, Persia, etc. Three species of *Lathyrus* may be associated with poisoning in man: (1) *Lathyrus sativus*, known in India as Khesari dal; (2) *Lathyrus cicera*, the dwarf chick-pea found in France, Italy and Algeria; and (3) *Lathyrus clymenum*, found in Spain, North Africa and the Levant. It is solely confined to countries where different kinds of chick-pea are used for food, but the causative principle is unknown. Young people are specially liable, and men are more affected than women. It occurs as an epidemic amongst the poorest classes in times of great scarcity, when bread is made from a mixture of pea and wheat flour. It may also be eaten as porridge,

or the peas may be boiled with oil and then consumed. Formerly it was attributed to the grain of *Lathyrus sativus* (Khesari dal), but in India, Howard, Anderson and Simonsen failed to demonstrate any poisonous principle. They succeeded in isolating two toxic alkaloid-like bases, vicine and divicine from *Vicia sativa* (akta), an allied vetch, the seeds of which were a common contaminant of Khesari dal and produced symptoms of lathyrism when fed to ducks. It has also been suggested that an absence of vitamin A in the diet may be a contributory factor.

Pathology.—A chronic sclerosis is found in the spinal cord involving the posterior and lateral columns. Possibly a toxic spasm of the arteries of the cord, followed by thrombosis, is the basis of the condition.

Symptoms.—The onset may be insidious with backache, burning pains and weakness of the legs, or it may be sudden, as when after a hard day's work in the rain the patient wakes up with stiff, weak and trembling legs, which feel heavy to lift. These symptoms increase rapidly, and in 10 days walking may be impossible without the aid of a stick. Both legs are usually affected simultaneously, first the calves, then the thighs. Gradually a peculiar gait develops, the patient laboriously progressing by means of a two-handed staff; "the leg bearing the weight of the body is bent at the knee and trembles, while the advancing limb dragged wearily forward and strongly abducted, is planted unsteadily directly in front of its fellow, the toes reaching the ground first." When lying on the back, spasm of the adductors ceases and the thighs can be separated. There is little or no atrophy or loss of muscular tone, the knee-jerks are increased and ankle clonus is marked. Sensation is normal. Incontinence of urine and fæces and possibly loss of sexual power follow involvement of the lumbar enlargement, but the upper extremities are rarely implicated.

Diagnosis.—The occurrence of multiple cases simultaneously and the history of eating chick-peas as food confirm the diagnosis.

Prognosis.—This depends on the stage at which the case is diagnosed: if early, great improvement follows treatment, but in later cases when the cord has become permanently damaged spasticity persists.

Treatment.—Varieties of chick-pea must be avoided as human food, and their abolition stamps out the disease. Avoidance of damp and wet ameliorate the symptoms. A generous diet rich in vitamin A should be given. Massage and electricity are indicated.

5. Atriplicism—

Definition.—A disease associated with local œdema, disturbances of sensibility, and vaso-motor and trophic disorders.

Ætiology.—It occurs in North China. Females are oftener attacked than males; no age is exempt. The condition is due to poisoning with *Atriplex littoralis* (Chenopodiaceæ). Poor people and beggars eat the young shoots, either raw in salads, or in bread.

Pathology.—There are no records of post-mortem examinations with proper histological examinations.

Symptoms.—The onset is sudden, occurring quickly after the ingestion of the plant. First, there is tingling of the fingers, then the backs of the fingers, hands, and later the forearms begin to swell; finally, the face is similarly affected, with violent itching. There may be anæsthesia of the

forefingers and thumbs. Heat sensation is increased. Scratching may cause an ecchymotic condition of some areas, from which eventually the skin is shed in patches, and ulcers may follow.

Diagnosis.—It may be mistaken for Raynaud's disease or erythromelalgia.

Prognosis.—The swellings last for a week or so, but the general health is not affected. The ulcers often become chronic.

Treatment.—All that is required is to avoid eating the plant. Salines, gastro-intestinal disinfectants and, later, tonics may be employed.

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Exogenous Food Poisoning.—The contamination may be due to bacteria, or to fungi, or to chemical substances.

A. *Contamination by Bacteria.*

(1) The commonest type of food poisoning is that caused by contamination with Salmonella and other organisms. It is described under the heading "Bacterial food poisoning" (see p. 394).

(2) Specific diseases may be caused by the accidental contamination of food with the specific pathogenic organisms. Thus typhoid or paratyphoid fevers may be caused by milk or oysters containing the specific bacilli; scarlet fever or diphtheria by infection of milk with the specific organism; cholera by the contamination of foods or water with cholera germs, amœbic dysentery by contamination with the specific amœbæ or their cysts, and bacillary dysentery by infection of food with its specific bacilli.

A very common cause of these forms of food poisoning is the handling of food by persons known as "carriers," who are apparently healthy but harbour in their bodies the specific germs of a particular disease, their excreta containing large numbers of the pathogenic organism, so that it is an easy matter for the infection of a food-borne disease to be conveyed by the hands of a "carrier" who is engaged in any way in the handling of food; cooks or milkmen frequently spread infection in this manner. The course of the disease is exactly similar to that described under the diseases in question.

(3) Diseases in animals communicable to man may arise from the consumption of food derived from a diseased animal. Thus the flesh of an animal which has died from anthrax may give rise to this disease in man. Tuberculosis of the mammary glands in the cow will cause the presence of tubercle bacilli in milk, the consumption of which may give rise to human tuberculosis. The flesh of animals suffering from actinomycosis may cause this disease in man. Parasitic diseases, such as trichinosis and tapeworm infections, arise from the consumption of the flesh of animals suffering from these infections. These types of food poisoning are fully described under the diseases in question.

(4) Specific organisms may produce in food highly poisonous toxins, the ingestion of which causes acute and perhaps fatal illness. An instance of this is Botulism (see p. 401).

B. *Contamination by Fungi.*

Ergotism.—The grains of cereals attacked by the ergot fungus (*Claviceps purpurea*) are poisonous, and if consumed give rise to a series of symptoms

known as ergotism. Two types of this condition are known—(*a*) *The gangrenous type.* The onset is with numbness beginning in the extremities, and in the course of a few days gangrene appears in the fingers, toes and sometimes the lobes of the ears and tip of the nose. There is agonising pain which penetrates the affected limb like fire—hence the name, centuries old, *St. Anthony's fire.* Later there is complete anæsthesia in the affected part which becomes livid and then black. (*b*) *The nervous type.* The illness begins with numbness of the hands and feet and twitchings of the muscles of fingers and toes extending to the arms, knees, shoulders, hips and ultimately to the whole body. Severe giddiness, fits, blindness, deafness, delirium and stupidity passing on to dementia are also known. Histological examination shows that the dorsal columns are particularly involved.

C. *Contamination by Chemical Substances.*

Chemical poisons may accidently contaminate foods and give rise to the special symptoms of that kind of poisoning. Examples of this are :

Metallic poisoning resulting from contamination of tinned foods by poisonous metals derived from the container. This is a rare form of poisoning, and is only likely to occur when the contents of the tin are liquid, such as fruit juice, liquefied jelly or soups. If the tin is sound, and care is taken in the canning and in the soldering process, so that the solder does not come in contact with the contents of the tin, the risk of poisoning is negligible. Cases of poisoning have occasionally occurred from the solution of lead, derived from the solder, coming in contact with the contents of the tin. The symptoms of metallic poisoning are described elsewhere.

Arsenical poisoning from the contamination of commercial glucose during its manufacture is described under arsenical poisoning.

Drinking water may be contaminated by lead and give rise to chronic poisoning.

Food preservatives, such as boric acid, formalin, and salicylic acid, if added to foods, may give rise to illness from their toxic effects. The addition of food preservatives to milk is for this reason prohibited by law in this country.

BACTERIAL FOOD POISONING

Synonym.—Ptomaine Poisoning.

This is the form of poisoning caused by the contamination of food with Salmonella and other organisms. The resulting symptoms are caused by the bacterial toxins produced in the food by its contamination. There may also be an actual bacterial infection, should the organisms not be killed in the process of cooking. Since bacterial contamination finds a most suitable culture medium in foods rich in protein, this type of food poisoning usually follows the consumption of meat, fish or milk—especially meat.

It was formerly thought that food poisoning was caused by the presence in food of poisonous alkaloidal substances called ptomaines, produced by putrefactive changes. Neurine and mydaleine are examples of such. It is now known that ptomaines are very rarely, if ever, the cause of food poisoning, but that the usual cause is bacterial contamination of food. It is possible that in the consumption of food highly advanced in putrefaction,

such as high game, ptomaines may play a part in the causation of toxic symptoms, but cases of this kind are uncommon.

Ætiology.—*Predisposing causes.*—Contaminated food has a much more serious effect on persons suffering from pre-existing gastro-intestinal disease. Thus the presence of colitis or enteritis greatly increases the susceptibility of the patient to bacterial food poisoning, and the resulting symptoms are likely to be more severe than in a person previously healthy. Dysentery or post-dysenteric colitis has a like effect. Starvation or malnutrition increases the susceptibility to bacterial food poisoning, and emptiness of the stomach at the time of taking of contaminated food is likely to lead to the earlier onset and greater severity of the symptoms produced. The above considerations help to explain the remarkable fact that sometimes when several persons partake of the same unwholesome food some may suffer from serious symptoms of food poisoning, while others may have only very slight symptoms, or even be unaffected. Young children are much more susceptible. In hot climates bacterial food contamination is likely to be followed by a very rapid development of bacterial poisons. Dust, flies, dirt and insanitary conditions generally are likely to favour the contamination of food with the bacteria of food poisoning. Careful storage of food in refrigerators where it can be kept free from contamination, is most important.

Meat poisoning may be due to contamination of the flesh during the cutting-up process by the butcher, or the meat may be contaminated either in the process of cooking or afterwards, owing to lack of care in storage.

Sausages.—Many epidemics of poisoning have occurred from infected sausages. This can be readily understood, since the process of mincing, which the meat undergoes, renders it liable to contamination. Moreover, in sausages it is easy for unwholesome meat to be used, with little possibility of detection. The fact that sausages are made with raw or only partly cooked meat, and that they are frequently eaten merely smoked, with little or no cooking, still further adds to the risk.

Tinned meat.—This has been frequently the cause of food poisoning. The meat may be contaminated by Salmonella organisms before tinning, and though the process of canning, by the heat applied, may kill the microbes, yet the toxins may not be destroyed, and these will give rise to symptoms of poisoning when the food is eaten. During the War of 1914–1918 tinned meat was consumed in enormous quantities by our troops. Very few cases of food poisoning from tinned meats were recorded, and in those cases where investigations were made the cause of the poisoning was traced to infection of the food after the tins had been opened. Usually the food had been handled by a cook who was a " carrier " of food poisoning organisms. At the present time so much care is taken in the selection of the meat and in the whole process of canning that tinned meat from a reliable source can be regarded as one of the safest foods.

Fish.—Numerous epidemics of food poisoning have been due to eating fish. These have been traced to the contamination of the fish with bacteria of the type already described, and the resulting symptoms have been similar in character. Cooking the fish—boiling or frying—may not entirely destroy the toxins present.

Shellfish.—These are sometimes grown in waters contaminated by sewage containing typhoid and Salmonella bacilli. Mussels, oysters, lobsters,

crabs, etc., have frequently caused severe attacks of food poisoning, and commonly the shellfish appeared perfectly fresh, with no objectionable taste or smell. Under the Ministry of Agriculture and Fisheries in this country special researches have been successfully carried out on the purification of shellfish for human consumption, particularly in the case of oysters and mussels. These shellfish, if obtained from accredited sources of supply under government supervision, can at the present time be guaranteed as free from pathogenic infection, and regular tests are made to ensure the safety of the shellfish put on the market.

Tinned fish.—This, like tinned meat, may give rise to poisoning from the contamination of the food by bacteria before canning. It is important to remember that tinned fish, even if wholesome at the time the tins are opened, is very liable to bacterial contamination. It should never be kept, but should be eaten on the day of opening.

Vegetables and fruit.—These may, if contaminated by bacteria of the type described, give rise to the disease. Since, however, the bacteria find vegetables an unsuitable medium for growth, outbreaks of food poisoning from vegetables are uncommon.

Milk.—Milk has on several occasions been the cause of outbreaks of food poisoning, and both Salmonella organisms and staphylococci have been found present in the affected milk. If milk is infected with the microbes, all that is necessary is a suitable temperature for their growth, and it speedily becomes a dangerous article of food. It is readily understood, therefore, that these cases are of much commoner occurrence in the warm weather of summer. Carriers of Salmonella organisms are a common cause of outbreaks due to milk or cream. Milk and cream may be contaminated with pathogenic organisms, and give rise to epidemics, *e.g.* typhoid and paratyphoid fever, from polluted water or from carriers handling the milk. In a similar manner outbreaks of tonsillitis and scarlet fever may result from carrier infections.

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Donald Hunter.

Bacteriology.—Following work by Savage in this country, and by Jordan in America, bacterial food poisoning came to be regarded as synonymous with infection by food-borne Salmonella bacilli. This group of bacilli, like typhoid and dysentery bacilli fail to ferment lactose, but differ by fermenting glucose, mannite and dulcite with the formation of gas.

In the first decade of the century the best-known bacilli of this group were the paratyphoid and enteritidis bacilli, but in 1912 Bainbridge, in the Milroy Lectures, differentiated *Bact. enteritidis aertrycke* from *Bact. paratyphosus* B, and established the fact that *Bact. aertrycke* was a much more important cause of acute epidemic food poisoning than *Bact. paratyphosus* B. By absorption methods of agglutination he showed that the two bacilli were separate entities, although their sugar reactions were identical. *Bact. aertrycke* was subsequently identified with *Bact. typhi-murium*, by which name it is now known. The result of Bainbridge's work was to establish the fact that with few exceptions epidemic food poisoning is caused by *Bact. typhi-murium* or *Bact. enteritidis* (B. Gaertner). Thus Scott, during the years 1923–34, investigated 186 outbreaks of food poisoning in this country. No less than

110 of these were caused by *Bact. typhi-murium*, while 19 were due to *Bact. enteritidis*, 16 to *Bact. thompson*, 13 to *Bact. newport*, and 8 to *Bact. cholera-suis* and its variety *Bact. cholera-suis var. kunzendorf*.

Many of these bacilli are well known as causing infections in animals, and though the consumption of meat from "emergency slaughtered" animals is rare in this country, in Germany, on the other hand, it is common, as is also the consumption of uncooked or partially-cooked meat. Thus Meyer, in 1929, reporting on the incidence of Salmonella food poisoning in Germany following the consumption of meat and meat products during the years 1923–28, alludes to 493 outbreaks, with 14,567 cases and 133 deaths; while Savage and White, from January 1921 to October 1923, reported 86 outbreaks in this country, with 2300 cases and 24 deaths.

Failure to recover bacilli of the Salmonella group from some cases of bacterial food-poisoning led Savage to suggest that some cases were caused by the ingestion of the products of previously existing bacilli, which had been killed in the preparatory processes, usually canning. This involved the existence of specific exotoxins in connection with the various bacilli involved, which, be it noted, were not limited to the Salmonella group. The symptoms of this "toxin" type of food poisoning tended to come on with less delay than was observed with infections with members of the Salmonella group, and the vehicle tended to be of the canned type, whereas the "infective" type was usually associated with more recently prepared foods. Moreover, in 1930 Dack and Jordan announced the discovery of cases of staphylococcal food poisoning. Since then many cases have been reported. Most of these have followed the consumption of milk products, though some have been traced to gravy, canned meat, pressed beef or fish. No one type of staphylococcus has been involved; indeed, very few strains of staphylococci appear to have this property of toxin formation. That a preformed toxin is involved seems certain, in that the opportunity for the multiplication of the staphylococci before the consumption of the food is an antecedent necessity. The toxin is resistant to heat to such an extent that it is not completely destroyed by boiling for 30 minutes. It has very little effect on ordinary laboratory animals. Other cases of this type of "Toxin" food poisoning have occurred, due to such organisms as coliform bacilli in milk, and streptococci in fish, etc. Scott has suggested that about one-third of the reported outbreaks of food poisoning in this country are the result of staphylococcal intoxication, and Topley and Wilson suggest that another third may be due to other species of bacteria.

The general method of investigating outbreaks of food poisoning is described in a memorandum by the Ministry of Health (1935).

Chronic food poisoning differs from the epidemic type in that it is met with in individuals with no relationship, or no recent relationship, to epidemics of food poisoning. It is usually diagnosed in the laboratory, though a history of recurrent attacks of diarrhœa, or even of gastro-enteritis, perhaps over a number of years, and possibly dating from a typhoid-like illness may suggest to the clinician the presence of a member of the food-poisoning group of bacilli. Such infections are not infrequently met with in cases of colitis or "intestinal toxæmia," or may be disclosed in the routine examination of the intestinal contents, in which no intestinal symptoms exist. Such examination may disclose the presence of non-lactose-fermenting bacilli, and

exploitation thereof by way of vaccine therapy may strengthen the hypothetical connection between the infection and clinical condition.

The variety of bacilli thus found in connection with chronic food poisoning is much larger than is the case with acute epidemic food poisoning, which, as shown above, tends to be confined to few types, viz. *Bact. typhi-murium* and *Bact. enteritidis*. A condensed table of the chief sugar reactions and characteristics of these non-lactose-fermenting bacilli follows:

	Lactose.	Glucose.	Mannite.	Dulcite.	Saccharose.	Indole.	Motility.	
Bact. typhosus . .	—	A	A	--	--	—	+	Described by Eberth in 1880. Cultivated by Saffrey in 1884.
B. shigæ	—	A	—	--	—	—	—	Shiga, 1898. Kause, 1900.
B. flexneri . . .	--	A	A	-	—	+	—	Flexner, 1900. Strong, 1900.
B. sonnei. . . .	A late	A —	A	A late	--	--	--	Sonne, 1915.
B. paratyphosus A. .	—	+	+	+	-	—	+	Definitely classified by agglutination.
B. paratyphosus B. .	—	+	+	+	—	—	+	Can only be differentiated one from the other by absorption or complement deviation tests. The common agglutination reaction differentiates them from the other members of the group.
B. aertrycke . . . (Now known as *B. typhimurium*.)	--	+	+	+	—	—	+	
B. gaertner . . .	—	+	+	+	—	—	+	Definitely classified by agglutination.
B. asiaticus . . .	--	+	+	—	+	+	—	The only non-motile member of the group.
B. of epidemic jaundice	—	+	+	—	—	+	+	
B. moryan . . .	—	+	—	—	—	+	+	
B. pyocyaneus . .	—	—	—	—	--	—	+	Usually shows characteristic pigment formation.
B. fæcalis alkaligenes	—	—	--	—	—	—	—	Fine growth resembling that of typhoid.

(+) indicates formation of acid and gas in sugar tubes, or formation of indole, or active motility, respectively.

(—) indicates the converse, respectively.

(A) indicates formation of acid, without gas, respectively.

The group of Salmonella bacteria typified by *B. paratyphosus* A and B, *B. typhi-murium* and *B. gaertner* constitute upwards of sixty named varieties of bacilli. Their ultimate classification depends upon the composition of their antigens—flagellar and somatic—indeed, their antigenic analysis.

The ultimate classification of any particular intestinal bacillus must rest upon specific serum agglutinations, antigen analyses and absorption tests. Such tests have differentiated from 60 to 70 varieties of bacilli in the "Salmonella" group alone.

The foregoing bacilli are the common abnormal bacteria found in epidemic and chronic food poisoning. The list is not to be taken as in any way exhaustive. There are, for instance, bacilli giving the sugar reactions of the paratyphoids which do not agglutinate with the specific sera of the members noted above, nor yet with a mixed Salmonella serum as issued by the Oxford laboratory, and yet which are controlled by an autogenous vaccine. There is more than one variety of Morgan's bacillus, and Castellani has described a *Bact. pseudo-asiaticus*, which ferments dulcite, specimens of which are occasionally found in the human stool in this country. Again there appears to be a group of "late-lactose-fermenting" bacilli, which give the reactions of the Salmonella group, and after a lapse of perhaps 48 hours lactose is fermented. Finally, there is a group which gives acid fermentation of glucose, mannite and dulcite, without gas, many of which are promptly controlled by the use of an autogenous vaccine.

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Pathology.—The *post-mortem signs* are those of an acute gastro-enteritis, with evidence of a general bacterial infection or toxæmia. When diarrhœa has been very severe, the tissues of the body may be shrunken from drainage of fluid. Rigor mortis sets in early. The stomach may show some redness from congestion, and, especially where vomiting has been severe, there may be small submucous hæmorrhages. Much mucus is generally present, but the stomach contents are free from blood. The inflammatory signs in the small intestines are usually more marked than in the stomach, which is an important distinction from chemical irritant poisoning, such as that caused by arsenic. The mucous membrane is swollen and congested, and the lymphoid follicles and Peyer's patches often show marked swelling and congestion. The signs are often more marked in the ileum than in the upper part of the small intestine. The mucous membrane of the large intestine may be swollen and congested, and the lymphoid follicles much enlarged. The contents are liquid and may contain much mucus. Small submucous hæmorrhages may occur in any part of the intestinal tract. The spleen is congested and soft, and in cases where infection with living bacteria has occurred, it may be enlarged. The liver and kidneys may show cloudy swelling or fatty degenerative changes. It is important to remember that in fatal cases of food poisoning the macroscopic morbid changes found post mortem may be very slight. Cultures made from the blood in the heart, from the spleen, and from the intestinal contents may reveal the presence of food-poisoning organisms.

Symptoms.—*Latent period.*—The period which elapses between partaking of the contaminated food and the onset of symptoms may vary from a few hours to 3 or 4 days. Usually, however, the latent period is short, from 2 to

6 hours being common. The greater the amount of preformed bacterial toxins in the food, the earlier will be the appearance of symptoms. The latent period is influenced by other conditions. Thus, if the poisonous food is taken on an empty stomach, the symptoms will come earlier. Again, if the infected food is taken alone, the symptoms will occur earlier than if it is taken with a considerable amount of other wholesome food.

The symptoms are of sudden onset, and in some cases a rigor may usher in the attack. The symptoms are usually those of gastro-enteritis, namely, furred tongue, severe abdominal pain and a rise of temperature, and often vomiting and purging. The stools are liquid and very offensive, and sometimes contain mucus and blood. In severe cases there may be cramps in the calves of the legs, and collapse with heart weakness, and the patient may become cold and blue owing to the feeble circulation consequent on a state of extreme collapse. In some cases rashes appear of the type of "erythema," and in severe cases "purpura." Often the severe cases present the symptoms of bacterial infection of the blood (septicæmia) and such complications as pneumonia or toxic jaundice are then likely to occur. In some attacks of food poisoning, especially those due to contaminated fish, the toxins appear to act especially on the blood vessels, producing rashes with considerable swelling of the skin (erythema and urticaria), which are associated with fever and a furred tongue, though there may be but little or no diarrhœa and vomiting. In these cases, idiosyncrasy or allergy may play an important part.

Diagnosis.—The diagnosis is usually clear, from the sudden onset of typical symptoms a short period after taking contaminated food. A specimen of the stool should be taken for bacteriological examination in order to determine the presence of organisms of the Salmonella group, etc. A sample of blood should be taken for agglutination tests with organisms of the food-poisoning group, and the blood agglutination tests should be repeated after an interval of a few days, when a rise in the agglutination titre would be expected. It cannot be too strongly emphasised that the symptoms of bacterial food poisoning are almost identical with those of poisoning by arsenic or antimony or other chemical irritant poison. An analysis of the vomit, fæces and urine for arsenic and irritant chemical poisons at once renders the diagnosis clear.

Course and Prognosis.—In mild cases, the symptoms clear up in a few days and the patient is completely restored to health. Where there is an actual infection with living pathogenic organisms the illness may run a course similar to that of typhoid fever. Severe cases may present symptoms so acute as to resemble true cholera, and in these the prognosis is grave.

Complications and Sequelæ.—An attack of bacterial food poisoning may be complicated by the development of a specific disease, such as enteric or paratyphoid fever, owing to the living organisms of this disease being also present in the contaminated food. After an attack of bacterial food poisoning there is sometimes left a latent bacterial intestinal infection so that the patient, in addition to being a "carrier" of disease, is liable to recurring attacks of enteritis from slight causes.

Treatment.—PROPHYLACTIC.—The importance of this has been already indicated above. The greatest care should be taken in the avoidance of articles of food likely to be contaminated, and the efficient cooking of food

whereby any living bacteria present are destroyed is a great safeguard. After cooking, rigid care should be taken in the storage of food to prevent contamination.

General treatment.—Rest in bed is essential. The diet should consist of liquids, such as water, albumin water, dextrose 5 per cent. solution in normal saline, chicken broth or whey. *Milk* is often best avoided ; peptonised milk or citrated milk (2 grains of sodium citrate to the ounce of milk) diluted with an equal quantity of water may be given. The feeds should consist of 3 or 4 ounces of liquid every 2 hours, and to these 1 or 2 teaspoonfuls of brandy may be added with advantage. As the symptoms improve, the dietary is gradually increased. Hot applications to the abdomen are advisable. Where there is much pain and diarrhœa without collapse, the hypodermic injection of morphine is advisable. This may be given with advantage with atropine, *e.g.* morphine hydrochlor. gr. $\frac{1}{6}$, atropine sulph. gr. $\frac{1}{100}$. Colon irrigations with 2 pints of normal saline are of value in cases with diarrhœa and slight collapse. In cases with choleraic symptoms and marked collapse, subcutaneous or intravenous injections of normal or hypertonic saline should be given. (See Article on Treatment of Cholera, p. 120.) A mixture of bismuth and soda with hydrocyanic acid is of value in relieving the gastric irritation, and to control the diarrhœa bismuth salicylate in 10 or 15 grain doses is useful.

The treatment of a case of food poisoning should be accompanied by periodical bacteriological investigations of the stools, and a case cannot be regarded as cured until three successive bacteriological examinations made at intervals of 2 or 3 days have shown freedom from infection with the pathogenic organisms of the disease.

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BOTULISM

Synonyms.—Sausage poisoning, Allantiasis.

Definition.—A rare, but very fatal form of poisoning due to the effect on the nervous system of the toxins of the *Bacillus botulinus*. Botulism belongs to the food-poisoning class of disease, but differs from the old conception of ptomaine poisoning, in which the actual poison was supposed to be altered food product, on the one hand, and from the bacterial food poisonings, in which an actual infection is transmitted, on the other hand. Ptomaine poisoning has now only historic interest, and the bacterial food poisonings fall into the group of infections known as enterica, in which a period of incubation is involved, and more or less symptoms of gastro-enteritis occur. Botulism depends upon the ingestion of a certain minute quantity of preformed toxin, and in no way upon the introduction of the bacillus or spores thereof.

Bacteriology.—*B. botulinus* is a large gram-positive bacillus, 4–9 μ long by 0·9 1·2 μ broad. It stains well with ordinary dyes, but tends to lose Gram's stain if care be not taken. It possesses flagella, and is slightly motile. It forms terminal or sub-terminal spores, especially, in the case of most strains, at a temperature between 20° and 25° C. Likewise the optimum temperature of growth for most strains is between 20° and 30°. The bacillus is a strict anaerobe, and will only grow in slightly alkaline or neutral media.

In deep stab culture growth occurs as a thin whitish streak, not reaching to the surface; later the medium is cracked by the abundant formation of gas. With strict anaerobiosis the organism grows well on the ordinary media. Gelatine is liquefied. There are two types, A and B. They are readily separated by the fact that chickens are susceptible to type A only. Three different strains are named. They are the Boise (type A), the Nevin (type B), and the Memphis (type A). Type A is more common on the Pacific Coast of America, while type B is more common in the Eastern States, and in Europe. The strains differ in their behaviour to heat. Most strains are killed by boiling, but the Boise strain can survive boiling for an hour, and consequently steam pressures are necessary to sterilise adequately food products contaminated therewith. The toxins of the various strains all seem to be destroyed by temperatures slightly less than 80° C., the Boise strain toxin being destroyed by 10 minutes at 73° C. The toxicity of the toxin can be so high that 0·0001 c.c. of the filtrate of a culture grown at 35° C. proved lethal to a guinea-pig of 350 g. The Boise strain also differs from the others in that it grows best at or about body temperature, and has a characteristic odour.

Symptoms.—There being no incubation period, there are no symptoms prior to the onset of the dizziness and diplopia that constitute the first signs of the involvement of the cranial nerves. Occasionally there are some abdominal pains, accompanied by vomiting, and there is some weight in the suggestion that the vomiting denotes an unusually heavy dose of toxin, for vomiting usually presages a fatal termination. Other cranial nerves are gradually affected, the larynx becomes involved and speech may be lost, and later respiration and the heart's action become affected, by reason of the involvement of the spinal accessory and vagus. Consciousness is not lost. Obstinate constipation is the rule, in sharp contrast to the diarrhœa usually associated with enterica. Botulism differs from encephalitis lethargica in that there is an entire absence of the somnolent state characteristic of the latter condition, while the absence of fever differentiates it from anterior poliomyelitis.

Prognosis.—This is very grave, the mortality being more than 50 per cent. In some outbreaks, for instance that of Loch Maree, every case proved fatal. Death may take place in 36 hours, or may be delayed for a week.

Treatment.—Antitoxin given experimentally with toxin prevents the fatal effect of the latter. In practice, antitoxin treatment will only be available for use in the later or less severe cases of an outbreak. Measures to promote elimination of toxin are called for, but are handicapped by the obstinate constipation. Alcohol appears to have a distinct effect in "denaturing" the toxin, and may, therefore, be given freely, partly for this effect and partly for stimulation. Strychnine should also be given. Ether anæsthesia is said to delay fixation of toxin by the tissues, and if so it might be usefully employed while antitoxin was being procured. Some relief from the mental distress due to the absence of unconsciousness would also accrue.

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SECTION VI

DISEASES OF METABOLISM

BASAL METABOLISM

By basal metabolism is meant the metabolism of an individual when he is lying down in as complete a condition of rest as possible, and has taken no food for 14 hours—the post-absorptive state.

Basal metabolism is increased by the intake of food, and the amount and nature of the food determines the amount of its increase. Exercise also increases metabolism, and considerably so. In order to obtain an accurate estimate, certain precautions are therefore necessary. It is customary to prescribe a light evening meal some 14 hours before the test, and to make the subject lie down, with the muscles in complete relaxation, for half an hour. The actual estimation may be performed in two ways, namely, by the direct method and by the indirect method, the latter being easier but not so accurate. In the direct method, the air which is breathed out under the standard conditions is collected in a Douglas bag for 10 minutes and the total volume measured. The amounts of carbon dioxide and oxygen present are estimated by means of a Haldane gas analysis apparatus. By this means the Respiratory Quotient (R.Q.), *i.e.* the ratio of the volume of carbon dioxide given out to the volume of oxygen taken in, and the amount of oxygen used may be determined with great accuracy. In the indirect method, the subject breathes oxygen which is in a closed system for 10 minutes. The carbon dioxide formed is absorbed with soda lime, and the oxygen which has been used is calculated from the amount of gas which has disappeared from the system. The surface area of the body in square metres is then estimated from the weight and height of the patient by means of the nomograph (Fig. 7). The amount of oxygen which has been used by the patient is then expressed in terms of one square metre of body surface per minute. The next step may be done in one of two ways. (1) The amount of oxygen per square metre of body surface is compared with the amount of oxygen which an average subject of the same age and sex consumes (see Table I.). (2) The number of heat calories which the oxygen would give when burnt under standard conditions is ascertained from the tables of oxygen values, and this result is compared with the calories per square metre of body surface which an average subject of the same age and sex would consume (see Table II.). The final result in either method is expressed as plus or minus x per cent. as compared with the average values in the case of normal people.

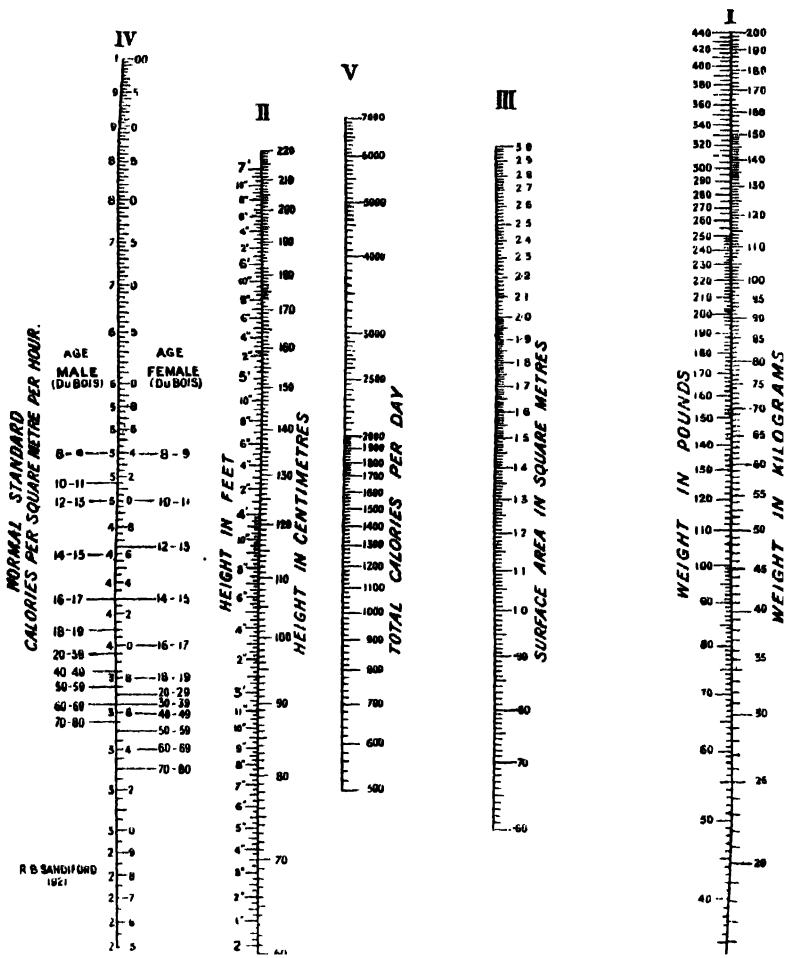


FIG 7.—BOOTHBY AND SANDIFORD'S NOMOGRAPH.

The weight in pounds or kilogrammes is shown on Scale I. The height in inches and centimetres is shown on Scale II. The surface area in square metres is shown on Scale III. The normal standard calories per square metre of body surface per hour are shown on Scale IV. The total calories per diem are shown on Scale V.

Directions.—Keep the chart flat. Use a flexible ruler with a straight edge, or a strip of stiff paper, such as a postcard. (A) Locate the position of the weight and height on Scales I. and II. respectively. Apply the straight edge of the ruler, and note where it cuts Scale III. Read the figure on Scale III., which will give the surface area of the body in square metres. (B) Locate the surface area on Scale III., and the normal standard calories per square metre per hour for the age and sex of the subject on Scale IV. Apply the straight edge of the ruler, and see where it cuts Scale V. Read this figure, which gives the total basal calories per 24 hours.

Large scale nomographs may be obtained from W. B Saunders Co., West Washington Square, Philadelphia, U.S.A., or from H. N. Elmer, 1641 Monadnock Buildings, Chicago, U.S.A.

It is accepted that the subject is normal if the figure lies within the limits of plus or minus 10 per cent. Important variations occur when the thyroid is affected. If the gland is atrophied or absent (myxœdema), the basal rate may be as low as minus 40 per cent.; while if it is overactive (exophthalmic goitre), the basal rate may be very high, varying from plus 15 to 20 per cent. to 100 per cent. or even more. In starvation and severe undernutrition, the basal rate will be below minus 10 per cent.

STANDARDS

TABLE I.—Average Amounts of Oxygen per min. per square metre of body surface (Du Bois).

Age.	Males.	Females.
	Cubic Centimetres of Oxygen	
12-13	172	—
14-16	159	148
16-18	148	138
18-20	142	131
20-30	136	128
30-40	136	126
40-50	133	124
50-60	129	121
60-70	126	117
70-80	122	114

TABLE II.—Average Calories per hour per square metre of body surface (Du Bois).

Age.	Males.	Females.
14-16	46·0	43·0
16-18	43·0	40·0
18-20	41·0	38·0
20-30	39·5	37·0
30-40	39·5	36·6
40-50	38·5	36·0
50-60	37·5	35·0
60-70	36·5	34·0
70-80	35·5	33·0

ACIDÆMIA, ALKALÆMIA, AND ALLIED CONDITIONS

Definitions.—*Acidæmia* signifies that there is an increase in the H-ion concentration of the blood. This may be due to an increase in the amount of CO_2 in the blood, or to an increase in the fixed acids of the blood. In the latter case, the acid unites with the bases and lowers the amount of CO_2 which can be carried in the blood. The name *acidosis* has been applied to this latter condition, but it has given rise to so much confusion that it is better to abandon the name altogether, and to speak of a decrease in the alkali reserve of the blood. *Alkalæmia* signifies that there is a decrease in the H-ion concentration of the blood. The name *alkalosis* has been used to describe the conditions in which there is an increase in the alkali reserve of the blood, but, for the same reason as for acidosis, it would be better to drop the name altogether, and to speak of an increase in the alkali reserve.

Physiology.—The reaction of a fluid is best expressed in terms of the concentration of the H ions. It is known that the H and OH ions react in accordance with the equation $(H)\times(OH)=(H_2O)$, and that the equilibrium reached obeys the law of mass action. This is expressed as follows: $\frac{(H)\times(OH)}{(H_2O)}=K$. The brackets signify concentrations and K is a constant, which is dependent on the temperature. Since the mass of the water is enormously greater than the mass of (H) and (OH) ions, (H_2O) may be regarded as a constant, and the equation may be written in a simpler form $(H)\times(OH)=K$. The constant K is called the dissociation constant of

water, and at 15° C. has the value of $10^{-14.14}$. If a solution is neutral, the concentration of H and OH ions will be equal, *i.e.* $(H) = (OH) = 10^{-7.07}$, since $(H) \times (OH) = 10^{-14.14}$. An acid solution has a greater concentration of H ions than OH ions, and it follows from the equation that an increase in the concentration of the H ions results in a decrease in OH ions, since K is a constant. It is inconvenient to express (H) as a negative and fractional power of 10, and Sörensen has introduced a notation which avoids this difficulty. Since $(H) = 10^{-7.07}$, −7·07 is, by the definition of the term logarithm, the log. of the H-ion concentration of water. Sörensen disregarded the negative sign and called the numeral 7·07 the *p*H value of water. It follows from this that as the *p*H value of a fluid increases, the H-ion concentration and, therefore, the acidity diminishes, because a large negative number is actually smaller than a small negative number. If a fluid has *p* H = 7·07 it is neutral, like water; if it has *p*H = 1 it has the acidity of decinormal hydrochloric acid; while if *p*H = 13·2 it has the alkalinity of decinormal caustic soda. Normal blood has a *p*H which is slightly alkaline, and lies between 7·34 and 7·47 by the Hydrogen Electrode Method and 7·64 and 7·72 by the Indicator Method. The figures for the Hydrogen Electrode Method will be used in this article.

It is very easy to change the reaction of a fluid like water, which only contains H and OH ions. Blood, however, is a very complex fluid, since it contains salts of weak acids, such as the acid and alkaline phosphates, and sodium bicarbonate, which, together with the hæmoglobin and proteins, act as "buffers" and prevent the reaction of the blood being easily changed. Further, other regulating mechanisms are at work, since urea can be split up into carbon dioxide and ammonia; the former can be excreted by the lungs, while the latter can be used to neutralise an acid. The kidney can excrete acid or alkaline salts which may be in excess, and thus help to keep the reaction of the blood constant. Much attention has been paid to the regulation of the blood by means of the sodium bicarbonate and carbon dioxide. In this process, the respiratory centre plays a very important rôle, since, if it is damaged in disease or by drugs, such as morphine, the regulating mechanism is upset. When a fluid contains only weak acids and their salts, the H-ion concentration varies according to the equation $(H) = \frac{(H_2CO_3)}{BHCO_3)} \times K$, when K is a constant, and the brackets signify concentrations. If there is an increase in the H-ions of the blood, there must be an increase in the size of the fraction $\frac{(H_2CO_3)}{(NaHCO_3)}$, since the value of K does not alter. The increase can be made in two ways, namely, either by decreasing the amount of $NaHCO_3$, or by increasing the H_2CO_3. If, on the other hand, the H-ion concentratiom is decreased, K can be kept constant, either by increasing the amount of $NaHCO_3$, or by decreasing the H_2CO_3. The amount of $NaHCO_3$ present in the blood is termed the alkali reserve. This is estimated by measuring the CO_2 present in the blood or plasma which has been exposed to CO_2 at a pressure of 40 mm. of Hg. (Van Slyke's method). The figure for normal blood lies between 40 and 55 vols. per 100 c.c., while that for plasma, which is the one usually estimated, is 55–70 vols. per 100 c.c. of blood. The estimation of the CO_2 in the alveolar air is also of assistance, since in health the CO_2 is present at the same tension in the blood and alveolar air. When the alkali reserve is reduced, there will

also be a decrease in the percentage of CO_2 in the alveolar air, from the usual figure of 5 per cent., which will keep the fraction $\frac{(H_2CO_3)}{(NaHCO_3)}$ constant, and so prevent any change in the *p*H. This will necessitate an increase in the volume of the respiration, as the same amount of CO_2 will be excreted under similar conditions of exercise and food. The increased depth of respiration is seen in the " air hunger " of diabetic coma.

Acidæmia.—This may be due to :

(1) A considerable increase in the H_2CO_3 of the blood together with a smaller increase in the alkali reserve. This occurs in morphine poisoning, since the respiratory centre is depressed and thus rendered insensitive to a small concentration of H_2CO_3.

(2) An increase in the H_2CO_3 of the blood, with little or no change in the alkali reserve. This occurs in emphysema, bronchitis, asthma and other causes of bronchial obstruction, in which there is difficulty in getting rid of the CO_2 from the blood.

(3) A decrease in the alkali reserve, with little or no change in the H_2CO_3. This condition may be due to many causes. The simplest are the administration of acids and acid salts, such as calcium chloride and ammonium chloride. In uræmia the condition is the result of the inability of the kidney to excrete acid salts. In diabetic coma and in the carbohydrate starvation which is found in cyclic vomiting, pernicious vomiting of pregnancy, and the vomiting due to chloroform or ether anæsthesia, the resulting ketosis is responsible for the acidæmia. It is believed that the enolic group $\begin{vmatrix} COH \\ CH \end{vmatrix}$ of aceto-acetic acid stimulates the respiratory centre. Acidæmia of this type is also met with in gastro-enteritis. In all these conditions there is an increase in the depth of the respiration, most marked in diabetic coma (air hunger), but may be very striking in the other conditions. The *p*H of the blood may rise to 7·25 or 7·3, and the alkali reserve may fall to 30 or 25 vols. of CO_2 per 100 c.c. ; and the percentage of CO_2 in the alveolar air may be reduced to 2 or 1·5 per cent. If the vomiting is very severe and the ketosis slight the patient will develop an alkalosis.

Alkalæmia.—This is the opposite of acidæmia, and may be due to :

(1) A considerable increase in the alkali reserve, with little or no increase in the H_2CO_3 of the blood. This may be the result of the administration of large doses of alkali, as in the treatment of gastric ulcer. The symptoms in this case are loss of appetite, severe headache, irritability, restlessness and tetany. The condition may also arise if a patient suffers from severe vomiting, without ketosis, as in pyloric obstruction or high intestinal obstruction, and in young children with hypertrophic pyloric stenosis. In such the symptoms are due to the loss of the hydrochloric acid and sodium chloride present in the vomit, which outweighs the tendency towards acidæmia produced by the ketosis, and has most effect when, for some reason, ketosis has not occurred. In all these conditions the kidneys may fail to excrete urea and other substances, and the patient may die of uræmia, although the organs are not obviously diseased. The alkali reserve is high, and may be 80 or 90 vols. of CO_2 per 100 c.c. of blood, while the *p*H of the blood is less than 7·5.

(2) A decrease in the alkali reserve with a considerable decrease in the

H_2CO_3 of the blood occurs in people who live in high altitudes. They are often cyanosed because the blood is anoxæmic. If an individual ascends quickly, he will at first suffer from dyspnœa as well as cyanosis. The lack of oxygen causes deeper respiration, and more carbon dioxide is washed out of the blood. In the attempt to compensate for this change, the kidney excretes less acid and more ammonia, and the urine becomes alkaline. The loss of alkali causes a decrease in the alkali reserve, and at first suggests that an acidæmia exists, but the fall in the *p*H is conclusive proof that the loss of CO_2 is greater than that of alkali $\frac{(H_2CO_3)}{(BHCO_3)}$. As the patient becomes acclimatised, the *p*H gradually rises to normal, although the cyanosis still exists.

Diagnosis.—This can only be made with certainty by employing the more accurate methods for determining (1) the H-ion concentration of the blood (Hastings and Sendroy), (2) the alkali reserve of the blood (van Slyke), (3) the alveolar CO_2 (Haldane and Priestley, Hasselbach, Fridericia), (4) the reaction of the freshly passed urine, (5) the amount of accto-acetic acid and ammonia in the urine, and (6) the amount of sodium bicarbonate which is necessary to make the urine alkaline. (In health a dose of 5 g. is sufficient to make the urine alkaline for a short while.)

Prognosis.—This depends almost entirely on the nature of the disease causing the condition.

Treatment.—This should be directed to removing the cause of the condition. The treatment of the ketosis which occurs in diabetes is described on p. 427. In acidæmia, sodium bicarbonate, ʒi (4 g.) 4-hourly, should be given together with dextrose 1 oz. (25 g.) 4-hourly, with an abundance of water; in severe cases it is better to give 600 c.c. of a mixture of 2 per cent. sodium bicarbonate and 10 per cent. dextrose intravenously. The treatment should, if possible, be controlled by estimations of the alkali reserve. Small doses of insulin, 10 to 20 units, may be of assistance. The bowels should be kept well open.

In alkalæmia, all alkalis should be stopped and acid sodium phosphate, gr. 30 (2 g.) 4-hourly, should be prescribed, besides sugar and water, as in acidæmia; in severe cases it is better to give 600 c.c. of a mixture of 10 per cent. dextrose intravenously. Here also treatment should, if possible, be controlled by estimations of the alkali reserve.

DIABETES MELLITUS

Diabetes mellitus is a disease in which the metabolism of carbohydrates, together with that of proteins and fats, is disturbed. The obvious signs of this are the presence of sugar and acetone bodies in the urine.

Ætiology.—(*a*) Predisposing Causes.—Diabetes is more common among Jews than Gentiles, and in Frankfurt 31·5 per cent. of the cases were of Jewish descent. It is also very common in a mild form among the natives of India and Ceylon. Heredity undoubtedly plays some part, as many members of a family may be affected. This can partly be explained as being due to the same excesses of diet, especially when the disease develops late in life. But this cannot explain all the cases, especially those which occur among the

younger members of the family. The familial form is sometimes very mild, but may be very severe. Joslin obtained a history of heredity in 13 per cent. of his cases. The inheritance of diabetes is probably a recessive characteristic. On this hypothesis, if two diabetics marry 100 per cent. of the children should develop diabetes, but so far only 8 out of 32 children, or 25 per cent., have done so; if a diabetic marries someone whose near relations have diabetes, 40 per cent. of the children should develop the disease, but only 48 out of 475 children, or 10 per cent., have been affected; and if two people whose near relations have diabetes marry, 16 per cent. of the children should become diabetic, but only 98 out of 2309 children, or 2.4 per cent., have had the disease. The discrepancy between the anticipated and observed figures is due to the short period in which the patients have been observed, as many of them may develop the disease in old age. (White and Pincus.) Cases of diabetes in husband and wife occur occasionally, but this is probably due to similarity of living and not to contagion. The disease is more common among males than females. It is commoner between the ages of 40 and 60; these two decades contained 48 per cent. of Joslin's cases, while only 7 per cent. of the cases occurred between the ages of 20 and 40, and 4 per cent. were under 20.

(*b*) Exciting Causes.—The disease is often present among elderly people who (1) take an excess of carbohydrate foods and sugar, (2) are considerably overweight, (3) have a blood pressure which is considerably raised, and (4) are subject to great anxieties. But the exciting cause of the acute disease which is seen in young people is quite unknown.

Pathology.—The blood normally contains sugar, and the amount varies in health between 80 and 120 mg. per 100 c.c. The total amount of sugar in the blood of a man weighing 65 kilos, or 10 st. 3 lb., would be 4 to 6 g. assuming that the total volume of the blood is $\frac{1}{13}$th of the body-weight, *i.e.* 5000 c.c. The percentage amount of sugar in the blood remains fairly constant, so long as no food is eaten. A dose of 50 g. of dextrose will cause a rise in the blood sugar in the arterial blood, from 100 to 150 to 180 mg. per 100 c.c. The change may be evident in 10 minutes, and usually reaches its maximum in 30 minutes. The sugar returns to its original level in a variable time—60, 90, 120 minutes, depending on the individual (Fig. 8). The sugar in the venous blood, after a carbohydrate meal, is about 20 mg. less than that in the arterial blood. Provided that the blood sugar does not exceed 180 to 200 mg. per 100 c.c. in the arterial blood, no sugar is excreted in the urine; but this again is a variable factor, as some people pass sugar at a considerably lower level than 180 mg. per 100 c.c., whereas others do not although the blood sugar rises to 250 to 300 mg. per 100 c.c. A carbohydrate meal produces a similar effect, but the rise is usually slower and more sustained. Protein does not cause any rise in the blood sugar of healthy people, but it does so in diabetic patients.

Some of the sugar which is eaten is burnt at once as the respiratory quotient approaches 1 after the dose of sugar, but the greater part of it must be stored, either in the liver or muscles. A healthy adult can usually eat 100 to 200 g. of pure dextrose without causing any glycosuria, but the individual variations are great.

In the mild cases of diabetes the blood sugar when fasting may be within

normal limits, but a dose of 50 g. of dextrose will raise the blood sugar from 120 mg. per 100 c.c. to above 200 mg. per 100 c.c. The maximum height may be reached in 1, 2 or 3 hours, and then the blood sugar returns slowly to its original level (Fig. 9). Sugar is excreted in the urine all the time the blood sugar is above the threshold of the kidney for the individual, which may be 180 mg. or 200 mg. per 100 c.c. In the more severe cases the blood sugar is always above the threshold, and sugar is excreted throughout the day. In these cases there is a decrease in the power of burning sugar, and the respiratory quotient does not approach 1 after a meal, and may be below 0·8. When the carbohydrate metabolism is seriously upset, proteins also cause a rise in the blood sugar, as 58 per cent. of the protein molecule is burnt as sugar. The thirst of which the patient complains is due to the excretion of the sugar, as apparently this cannot be excreted without a good deal of water.

When the sugar cannot be burnt properly, the metabolism of fat is also upset, and the fatty acids, aceto-acetic acid, β-oxybutyric acid, and acetone, are excreted in the urine. These are incomplete products of fat metabolism, and cannot be burnt completely in the absence of a certain amount of sugar metabolism. The amount of acetone excreted in the urine is very small; the aceto-acetic acid forms about 30 per cent. and β-oxybutyric acid 70 per cent. of the total acetone bodies if these are present in large amounts. This condition is now called ketosis, instead of acidosis, as usually there is no change in the H-ion concentration of the blood.

The amount of carbon dioxide in the alveolar air is usually over 5 per cent. in healthy persons, but it is reduced when ketosis is present (Beddard, Pembrey & Spriggs, Poulton). It may fall below 3 per cent., but this does not mean that the patient will pass into coma at once, but only that the condition is serious. If it falls below 2 per cent., the patient is usually comatose and is unlikely to recover unless insulin is injected in adequate amounts. The poisonous substance is probably aceto-acetic acid, acting not as an acid, but through the enolic group $\begin{matrix}|\\ COH\\ \|\\ CH\\ |\end{matrix}$. This acts on the respiratory centre (Hurtley and Trevan). The alkali reserve of the blood plasma is much reduced in severe cases and may fall from the normal 55 to 70 vols. per cent. to below 20 vols. per cent.

The sugar metabolism is controlled by the internal secretion of four glands, namely, that of the islands of Langerhans, this being opposed by the suprarenal gland, the thyroid gland, and the posterior lobe of the pituitary gland.

The islands of Langerhans.—The relation of the pancreas to the metabolism of sugar has been recognised ever since von Mering and Minkowski, in 1889, showed that complete removal of the gland caused glycosúria and death of the animal. If, in a dog, the remnant be $\frac{1}{8}$th to $\frac{1}{9}$th of the whole gland, mild diabetes occurs; if less than $\frac{1}{9}$th, severe diabetes results (Allen). The pancreas is made up of two glands:—(1) the acinous portion, which secretes the pancreatic juice through the pancreatic duct. It has no action on the

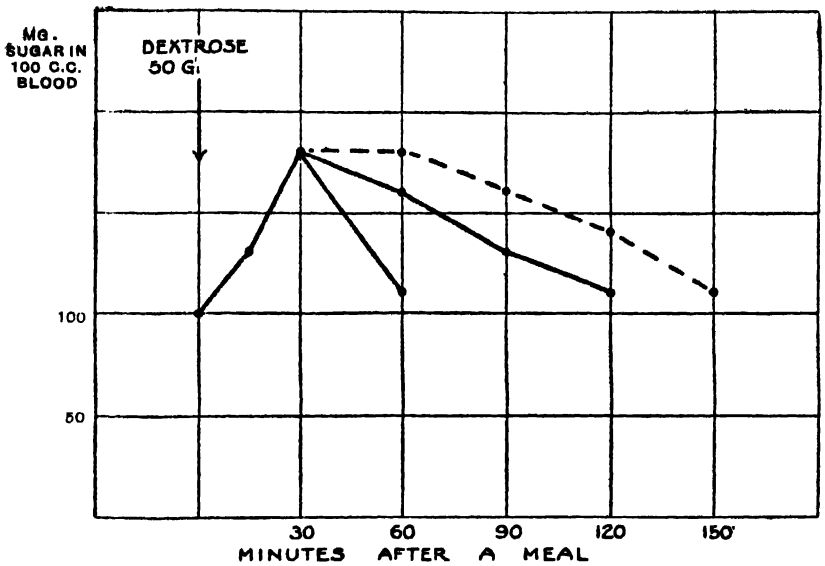


FIG. 8 —A normal curve.

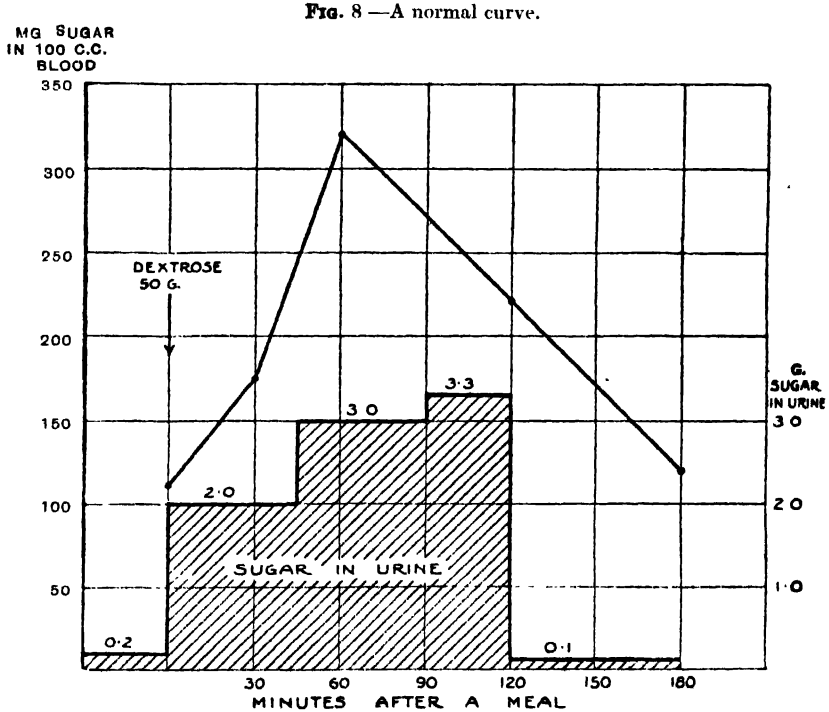


FIG. 9 —A mild diabetic curve.

sugar metabolism, since if it is entirely destroyed as a result of ligaturing the duct and replaced by fibrous tissue the sugar metabolism is quite unaffected so long as the islands of Langerhans are intact. (2) The islands, first described by Langerhans in 1869, are now recognised as definite entities, forming about $\frac{1}{100}$ part of the whole pancreas, and having an abundant blood supply. They contain three kinds of cells, called alpha, beta and gamma cells, which contain granules in their protoplasm as in the case of the gland cells of other organs. The alpha cells form about $\frac{1}{3}$rd, and the beta about $\frac{2}{3}$rds of the islands, while the gamma cells are few in number. The granules in the alpha cells stain differently from those in the beta and gamma cells, and these again stain differently from those in the acinous portion. Hence, if the tissues are fresh, the three kinds of cells in the islands can easily be distinguished from each other. When the surviving islands of a partially depancreatised dog are overworked by excessive sugar or carbohydrate feeding, only the beta cells are affected. The granules gradually disappear and a vacuole appears (hydrops of the cell). This process may continue until the cell finally consists of a large vacuole, with the nucleus flattened against one side, whilst all the granules have disappeared. Finally the cell breaks up and disappears. If the process is continued long enough the island will consist of alpha and gamma cells alone, and will be much smaller than usual. These experiments prove that it is the beta cells which control the sugar metabolism. The action of the alpha and gamma cells is unknown. The internal secretion of the beta cells had never been isolated until, in 1922, Banting, working with Best, succeeded in preparing an extract which had the power of lowering the blood sugar of a depancreatised dog, and of prolonging its life considerably. At first it was necessary to destroy the acinous portion of the pancreas by ligaturing the duct thirteen weeks before the extract was made, but now the extract is made from the fresh gland.

Properties of insulin.—The extract of the islands of Langerhans is called insulin. It has been prepared in crystalline form, and 1 mg. contains about 25 units. Its constitution is not known, but the molecule must be very complex since it contains 23–24 tyrosine groups as well as some sulphur atoms. It has considerable capacity for binding acids, for it forms salts with hydrochloric acid, and has a greater capacity for binding bases. It is destroyed by pepsin, trypsin and alkalis, and therefore cannot be absorbed from the alimentary canal. Insulin enables the blood sugar to be kept within normal limits, and the liver and muscle to contain plenty of glycogen, so that the respiratory quotient will be about 1·0 and the fat correctly burnt. If insufficient insulin is present, the blood sugar will be increased in amount; the liver and muscles will contain little glycogen, the respiratory quotient will be about 0·7; and the urine will contain sugar and also acetone bodies, as the fats cannot be correctly burnt under these conditions. If there is excess of insulin the blood sugar will be small in amount; the muscles will contain plenty of glycogen, but the liver will contain very little. The precise way in which insulin acts is not yet understood, as it has no action on dextrose outside the body.

The potency of insulin is estimated by its power to lower the blood sugar of a healthy fasting rabbit or mouse to a certain level. The amount of insulin which lowers the blood sugar of a healthy fasting rabbit weighing about 2 kg. to 45 mg. per 100 c.c. in 2 hours is termed 2 units, and this represents about 0·04 mg. of the pure product. All the insulin prepared in this country

has been carefully tested under the supervision of the Medical Research Council. It is dissolved in acid solution containing 0·5 per cent. of tricresol, and is of such a strength that 1 c.c. contains 20 units, 40 units (double strength), or 80 units (quadruple strength). It is put up in rubber-capped bottles, and does not deteriorate even in hot climates.

If too big a dose of insulin is given to a rabbit, the blood sugar will fall below 45 mg. per 100 c.c. and the animal may have convulsions and die. These symptoms can be relieved at once by the subcutaneous injection of 2 or 3 g. of sugar, unless the dose of insulin has been very large. Adrenaline, 1 in 1000, 0·3 c.c. (min. 5), or pituitary (posterior lobe) extract, 5 units

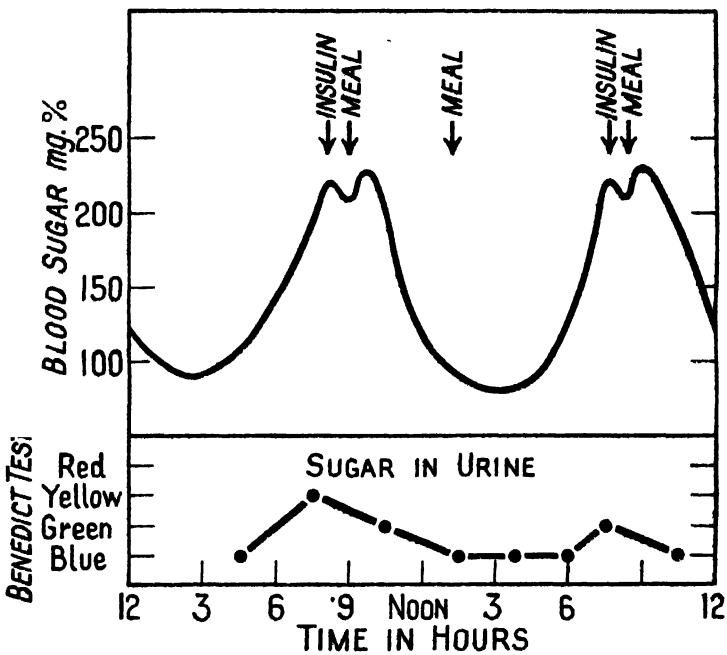


FIG. 10.—Figure showing the effect of a dose of insulin on the blood sugar and urine sugar of a diabetic patient.

(0·5 c.c.), will also relieve the symptoms at once. In human beings insulin acts in a similar manner, and if sufficient insulin is administered the blood sugar is always lowered. A dose of 5 to 10 units will lower the blood sugar of a healthy fasting adult of about 65 kilos to about 50 mg. per 100 c.c., but usually does not cause any symptoms of hypoglycæmia. Human beings, considering their much greater weight, are, therefore, much more sensitive to insulin than a rabbit.

When the blood sugar is raised, as in diabetes, the insulin causes a similar decrease in the blood sugar provided that a sufficient amount has been given. The extent to which the blood sugar is lowered varies in every patient and no definite law can be stated. The maximal decrease (Fig. 10) occurs about

nervous symptoms during life, there may be definite changes in the spinal cord, such as sclerosis of the posterior columns. There is no change in the sympathetic ganglia or in the pituitary gland. Atrophy or hypertrophy of the subcutaneous tissues may be seen at the site of the insulin injection.

LIPÆMIA.—In severe and advanced cases of diabetes the blood contains an excess of fat, either fatty acids or cholesterol. On separation of the corpuscles the plasma or serum has a pearly white appearance; this is always a sign of the severity of the disease, but patients have occasionally made fair recoveries of sugar tolerance. The retinal vessels in lipæmia are very striking objects. In the less severe cases, the arteries and veins have a salmon pink appearance throughout their course. In the more severe cases, the vessels at the periphery become creamy white in colour, although near the disk, they are still salmon pink. In the severe cases, the distinction between the arteries and veins is completely lost and the vessels resemble flat ribbons. The vision remains unaffected.

Symptoms.—The onset of the disease may be very acute and great thirst is complained of; the very day of onset of the thirst can sometimes be discovered. Some of these cases have died in coma, undiagnosed. Usually the onset of symptoms is insidious, with lassitude, loss of energy, or pruritus, thirst not being a prominent symptom. In the mild cases, especially among elderly people, the diagnosis is usually made either in the course of a routine examination, or by accident, *e.g.* because of the complaint of white spots on the clothes or boots. In severe cases, thirst is the most troublesome complaint, and this necessitates drinking a great deal of fluid and passing a great deal of urine. The pruritus also troubles the patients, especially as the usual situation for it is the penis in males and the vulva in females. Weakness is usually complained of, and sometimes a large appetite is a troublesome symptom. Constipation is usually present, and it dates from the onset of the thirst in the acute cases. The tongue does not present any changes in mild or treated cases, but in severe and untreated cases it is dry and red—the so-called "raw beef" tongue; this is only present when the patient is "desiccated," as a result of great polyuria. There is usually great loss of weight. In the severe cases, the volume of the urine may be 4, 6, 8 or even 10,000 c.c. per diem, but in the treated case it is usually less than 2000 c.c. The specific gravity of the urine in the untreated case may be 1040 or 1050, depending on the amount of sugar in the urine.

Complications.—(*a*) *Coma.*—Formerly this was a frequent termination of the disease, but now it should only be seen in: 1. The very acute and the undiagnosed cases. 2. The severe and untreated cases. 3. As a terminal event as a result of any acute infection. Out of 9 cases of coma, 7 showed definite signs of a severe disease, 1 became comatose 7 days after the onset of the thirst, and in 1 no cause for the coma was discovered (Graham). There are two main types, namely: (1) the hyperpnœa is well marked (air hunger), but the patient remains conscious until just before death; and (2) the hyperpnœa is not very obvious at first, but the patient becomes deeply unconscious a long time before death. More usually the patient shows a mixture of these two types. The blood pressure is low in both types, and the tension of the eyeball is very low. Constipation is always marked, and the contents of the intestines after death may be enormous.

(*b*) *Local infections*, such as boils and carbuncles, often occur, and the

latter is often a fatal complication. Perforating ulcers of the feet occur in long-standing cases with signs of peripheral neuritis. Pigmentation of the skin, especially on the back of the hands, occurs in bronzed diabetes.

(*c*) *Gangrene* of a limb, usually a leg, often occurs in elderly people. It is due to the associated arterial condition, and not primarily to the diabetic condition. Atheromatous changes in the arteries are present in many patients over the age of 40.

(*d*) *Pulmonary.*—Tuberculosis of the lungs is a common termination of the disease, and lobar and broncho-pneumonia are serious complications, as the patients pass rapidly into coma.

(*e*) *Renal.*—A trace of albumin is often present. Œdema may occur after two days of starvation, or after the administration of much sodium bicarbonate. Casts may be present in very large numbers in coma.

(*f*) *Nervous system.*—The knee-jerks may be lost early, but they may return if treatment is successful. Numbness and paræsthesia may be present, and the patients occasionally complain of a great deal of tingling pain in the legs and arms. Symptoms resembling those of tabes dorsalis and due to degeneration of the posterior columns may be present. The vibration sense is often diminished or even absent in the legs. The sensation of "hot and cold" may be lost, and this is associated with a lesion of the posterior nerve roots (radiculitis). The temperament of the patient often changes, partly as the result of dietetic deprivations.

(*g*) *Eyes.*—A retinitis, which can be distinguished from albuminuric retinitis, is apt to occur in elderly patients. If the blood sugar remains high the condition tends to spread and may cause marked loss of vision, but if the blood sugar is kept normal the retinitis either spreads slowly or may even retrogress. Cataract is met with in elderly patients, and in young patients with severe diabetes, which is difficult to keep under control. Operations for cataract may be safely performed if the diabetic condition is under good control. A retrobulbar neuritis may occur, especially in excessive tobacco-smoking. Lipæmia retinalis has already been described (p. 416).

(*h*) *Sexual functions.*—These may be undisturbed in the early stages of the disease, but the male may become impotent if the disease is badly treated. The female may become pregnant, but with care the pregnancy usually causes no untoward symptoms.

Diagnosis.—If the urine is tested the presence of a reducing substance is readily detected, but the nature of the reducing substance is less easily determined.

Fehling's solution is still commonly used, but the limitations of the test should be recognised. Equal quantities of solutions A and B should be freshly mixed, and equal quantities of urine and reagent boiled separately, mixed and not reboiled. If sugar is present in more than 0·5 per cent., the red precipitate comes at once, if in less than 0·5 per cent., it may not appear for one or more minutes. Fehling's solution is also reduced by glycuronic acid, uric acid, and creatinine. These substances are rarely present in sufficient amounts to reduce the copper solution, but when the urine is very concentrated they may cause a slight reduction.

Benedict's qualitative solution (copper sulphate, 17·3 g.; sodium citrate, 173 g.; anhydrous sodium carbonate, 100 g.; water to 1000 c.c.) is not reduced by these substances. It is much more reliable than Fehling's

solution and should replace it. Five or 3 c.c. of Benedict's solution and 10 or 6 drops of urine are boiled together for 2 minutes, or put in a boiling water bath for 5 minutes. If much sugar is present the precipitate develops on boiling, but small amounts may not cause a reduction before 2 minutes. The test will show the presence of sugar in a concentration of 0·08 per cent.

Benedict's solution is reduced by dextrose, lævulose, lactose, pentose and homogentisic acid (alkaptonuria), and special tests are necessary to distinguish these. Dextrose is dextro-rotatory, ferments with yeast, and yields crystals of glucosazone. Lævulose is lævo-rotatory, ferments with yeast, yields crystals of glucosazone, and gives Seliwanow's test. Lactose is dextro-rotatory, does not ferment with yeast, and yields a lactosazone with difficulty. Pentose is dextro-rotatory or optically inactive, is not fermented by yeast, and gives Bial's test. Homogentisic acid (alkaptonuria) reduces Fehling's and Benedict's solution to a deep brown colour; the urine blackens on standing, reduces an ammoniacal solution of silver nitrate to a black precipitate, and gives a momentary deep blue colour with the addition of a drop of very dilute ferric chloride. It does not ferment with yeast and is optically inactive.

If dextrose is present, disease of the other ductless glands and cerebral tumours should be excluded. The pigmentation of the skin of the body and of the backs of the hands, together with an enlarged liver (bronzed diabetes), should be looked for. Acute and chronic pancreatitis should be thought of before the diagnosis of a primary lesion of the islands of Langerhans is accepted. If small amounts of dextrose are present it is necessary to make a complete test of the sugar tolerance, with estimation of the blood sugar every quarter- or half-hour for 2 hours after a dose of sugar, in order to exclude the possibility of renal glycosuria (see p. 428).

Tests for Acetone Bodies.—*The ferric chloride test.*—Add the solution drop by drop until all the phosphates are precipitated. As soon as this occurs, a violet colour appears if aceto-acetic acid is present in the urine in any quantity. This is a test for aceto-acetic acid, which can be detected in watery solutions in a dilution of 1 in 100,000. In urine, however, the test is much less delicate, owing to the interference of the pigments in the urine. The presence of sodium salicylate in the urine may cause confusion, but the colour produced in this case is purple. The distinction can be made by boiling the urine with a little weak acetic acid, and repeating the test when the urine is cold. The aceto-acetic acid distils away, whereas the sodium salicylate is unaffected by the boiling. This possibility of confusion is avoided by always using Rothera's test.

Rothera's nitroprusside test.—Saturate the urine with ammonium sulphate crystals, add 2 c.c. of liquor ammoniæ fort., and then a few drops of a fresh solution of sodium nitroprusside. If a little aceto-acetic acid is present, the permanganate colour develops slowly; if a great deal, the colour develops instantaneously, and it is impossible to see through the mixture after 10 to 30 seconds. When the nitroprusside reaction is strongly positive, the urine should be diluted 1 in 5. If the colour still appears instantaneously and deepens rapidly there is a large amount of aceto-acetic acid present. Aceto-acetic acid can be detected in a dilution of 1 in 400,000, and acetone in a dilution of 1 in 10,000.

There is no colour test for β-oxybutyric acid, but it is always present when more than 2 g. of aceto-acetic acid are present.

Prognosis.—This depends, as in the case of other diseases, on the severity of the attack, the time which has elapsed between the onset of the disease and the commencement of treatment, the skill of the medical adviser, the care with which the patient follows the directions given, and the complications which occur. The attack is more likely to be severe and rapidly fatal in young people, but quite mild cases are often seen. In elderly people mild attacks are the rule, but severe attacks also occur. The prognosis had been much improved by the new dietetic treatment introduced in 1915. But although the prospects of life for several years were much better than they had been, the outlook remained a gloomy one for the patient with a severe form of the disease. The introduction of insulin has greatly improved the chances of life of all patients with any form of diabetes, but especially in the case of those with the severe forms. How much longer these patients will live it is impossible at present to say, but probably for many years, provided no complications occur. Out of 98 patients admitted to hospital before the end of 1923 and 1924, 55 were alive at the end of 1931, and 47 at the end of 1935. Insulin has completely altered the prognosis in the case of pregnancy. The risks usually attendant on the pregnancy and puerperium constitute the chief danger.

Treatment.—The general health of the patient should be treated. Any sources of infection, such as pyorrhœa, cholecystitis and boils, reduce the sugar tolerance considerably. The possibility of syphilis should also be inquired into, and, if necessary, treated.

Although the introduction of insulin has altered the prognosis, it has not altered the principles of treatment which have been in use for the last ten years. Great attention has always been paid to diet, but under the stimulus of insulin much more attention is being devoted to it. The principles which govern treatment are: (1) the blood sugar of the patient when fasting should be within the normal limits of 0·08 per 100 c.c. and 0·12 per 100 c.c., and should not rise above 0·19 per 100 c.c. at any time of the day. It follows from this that the urine should never contain any sugar. (2) The urine should not contain aceto-acetic acid. (3) The patient should understand that a large portion of the reserve power of the islands of Langerhans has been lost, and that additional insulin will probably be required whenever the patient has another illness.

Diet.—Although the principles of treatment have not altered, the details have changed very considerably. The chief alteration has been in the amount of carbohydrate and fat. It was believed that a diet was correctly balanced when the number of grammes of fat equalled the number of grammes of carbohydrate multiplied by two, plus half the number of grammes of protein. $F = 2\ C + \frac{1}{2}\ P$. It was soon recognised that this diet was not correctly balanced, since many patients, especially children, passed considerable amounts of acetone bodies in the urine. The amount of carbohydrate has, therefore, been increased and the fat decreased. It is too early to state what is the best balance, but the carbohydrate should not be less than the fat, and some workers believe that the carbohydrate should be twice or four times as much as the fat.

The treatment should be begun as soon as the diagnosis has been confirmed

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Rothera's nitroprusside test.—Saturate the urine with ammonium sulphate crystals, add 2 c.c. of liquor ammoniæ fort., and then a few drops of a fresh solution of sodium nitroprusside. If a little aceto-acetic acid is present, the permanganate colour develops slowly; if a great deal, the colour develops instantaneously, and it is impossible to see through the mixture after 10 to 30 seconds. When the nitroprusside reaction is strongly positive, the urine should be diluted 1 in 5. If the colour still appears instantaneously and deepens rapidly there is a large amount of aceto-acetic acid present. Aceto-acetic acid can be detected in a dilution of 1 in 400,000, and acetone in a dilution of 1 in 10,000.

There is no colour test for β-oxybutyric acid, but it is always present when more than 2 g. of aceto-acetic acid are present.

Prognosis.—This depends, as in the case of other diseases, on the severity of the attack, the time which has elapsed between the onset of the disease and the commencement of treatment, the skill of the medical adviser, the care with which the patient follows the directions given, and the complications which occur. The attack is more likely to be severe and rapidly fatal in young people, but quite mild cases are often seen. In elderly people mild attacks are the rule, but severe attacks also occur. The prognosis had been much improved by the new dietetic treatment introduced in 1915. But although the prospects of life for several years were much better than they had been, the outlook remained a gloomy one for the patient with a severe form of the disease. The introduction of insulin has greatly improved the chances of life of all patients with any form of diabetes, but especially in the case of those with the severe forms. How much longer these patients will live it is impossible at present to say, but probably for many years, provided no complications occur. Out of 98 patients admitted to hospital before the end of 1923 and 1924, 55 were alive at the end of 1931, and 47 at the end of 1935. Insulin has completely altered the prognosis in the case of pregnancy. The risks usually attendant on the pregnancy and puerperium constitute the chief danger.

Treatment.—The general health of the patient should be treated. Any sources of infection, such as pyorrhœa, cholecystitis and boils, reduce the sugar tolerance considerably. The possibility of syphilis should also be inquired into, and, if necessary, treated.

Although the introduction of insulin has altered the prognosis, it has not altered the principles of treatment which have been in use for the last ten years. Great attention has always been paid to diet, but under the stimulus of insulin much more attention is being devoted to it. The principles which govern treatment are: (1) the blood sugar of the patient when fasting should be within the normal limits of 0·08 per 100 c.c. and 0·12 per 100 c.c., and should not rise above 0·19 per 100 c.c. at any time of the day. It follows from this that the urine should never contain any sugar. (2) The urine should not contain aceto-acetic acid. (3) The patient should understand that a large portion of the reserve power of the islands of Langerhans has been lost, and that additional insulin will probably be required whenever the patient has another illness.

Diet.—Although the principles of treatment have not altered, the details have changed very considerably. The chief alteration has been in the amount of carbohydrate and fat. It was believed that a diet was correctly balanced when the number of grammes of fat equalled the number of grammes of carbohydrate multiplied by two, plus half the number of grammes of protein. $F = 2\ C + \frac{1}{2}\ P$. It was soon recognised that this diet was not correctly balanced, since many patients, especially children, passed considerable amounts of acetone bodies in the urine. The amount of carbohydrate has, therefore, been increased and the fat decreased. It is too early to state what is the best balance, but the carbohydrate should not be less than the fat, and some workers believe that the carbohydrate should be twice or four times as much as the fat.

The treatment should be begun as soon as the diagnosis has been confirmed

by the estimation of the blood sugar. In the mild type of case which occurs among elderly people, moderate restrictions of the carbohydrate may be sufficient to prevent glycosuria, but in the great majority of cases this is quite inadequate. The removal of carbohydrates from the diet without reduction of the fat and protein of the diet is a dangerous practice, and has in the past precipitated the onset of coma. Before the discovery of insulin, it was customary to starve the patient until no sugar was excreted in the urine (Allen). Such prolonged fasts are no longer used, and provided that the patient is willing to have insulin, any form of fasting is unnecessary. So many patients have a prejudice against insulin that an attempt is usually made to render the blood sugar normal by dietetic treatment. In the mild case, a fast of one day is sufficient to lower the blood sugar to normal, and always makes the patient much more amenable to the drastic change in the diet. If it is desirable to avoid a period of fasting, the patient may be given at once a diet which is just sufficient to satisfy the basal needs of the body. Whichever plan is adopted, it is of assistance to know the calories required, as the amount of food must be varied according to the size, age, and sex of the patient. An approximate figure can be obtained by multiplying the patient's weight by 11·3. Nearly always there will be an error by this method, but it will not be great. To obtain an accurate result, the following calculations are necessary. The patient's weight and height are marked on the Boothby and Sandiford Nomograph (p. 404). The figure for the surface area of the body is noted. Example: Height, 63 inches; weight, 132 lb.; surface area, 1·62 square metres. The calories required for each square metre of body surface are found in the Aub-Du Bois table below, which, in the case of a man aged 40, are found to be 1497.

AUB-DU BOIS TABLE.—Caloric Requirement per Square Metre of Body Surface.

Age (years).	Calories per day.		Age (years).	Calories per day.	
	M.	F.		M.	F.
10–12	1236	1200	20–30	948	888
12–14	1200	1116	30–40	948	876
14–16	1104	1032	40–50	924	864
16–18	1032	960	50–60	900	840
18–20	984	912	60–70	876	816

M. = males. F. = females.

Calculate requirement in children according to weight. Up to—

22 lb.	27·5 cals. per lb.
22–33 lb.	25·0 " "
33–44 lb.	23·0 " "

The number of calories is divided between the carbohydrate, protein and fat in the following way: for an adult, half a gramme of protein per one pound of body weight is allowed. In the sample case the allowance is 66 g. This figure multiplied by 4·1 (the caloric value of protein) gives 270 calories, and leaves 1227 for division between the carbohydrate and fat. In order to prevent any ketosis, the balance between these two must

be carefully struck. The carbohydrate should not be less than 70 g. This figure multiplied by 4·1 (the caloric value of carbohydrate) gives 287 calories; 1220 minus 287 leaves 933 calories for the fat, and this figure divided by 9·3 (caloric value of fat) gives 100 g. for the fat. The diet is then prescribed as: carbohydrate (C), 70 g.; protein (P), 66 g.; fat (F), 101 g.; calories (Cals.), 1497. The total amount of calories is divided into four meals, of approximately the following amounts: Breakfast: C, 20 g.; P, 20 g.; F, 30 g.; Cals., 443. Midday, C, 20 g.; P. 20 g.; F, 30 g.; Cals. 443. Tea: C, 10 g.; P. 6 g.; F, 11 g.; Cals., 168. Evening: C, 20 g.; P, 20 g.; F, 30 g.; Cals., 443. This is called the Maintenance Diet.

If a fast has been given it may be broken in many ways, but the plan set forth on p. 422, known as the "Ladder Diet" at St. Bartholomew's Hospital, is very easy for the unintelligent patient to carry out, and it can be varied very readily by means of the food tables. The value of Diet V. (C, 95 g.; P, 69 g.; F, 75 g.; Cals., 1352) is nearly the same as that of the Maintenance Diet.

Many patients with a mild form of the disease will maintain a normal blood sugar on this diet, and the urine will contain neither sugar nor aceto-acetic acid. In this case the amount of carbohydrate should be cautiously increased by 5 or 10 g., until 130 g. is reached. This amount of food is often sufficient to make thin patients gain weight, but if such should not be the case extra protein (7 g.) should be given every two weeks, until the weight does begin to increase. The fat should not be increased. Very fat patients should continue to lose weight until a reasonable weight for age, height, and sex is attained. The patients should learn how to use the food tables in order to vary the diet, but for unintelligent patients it is usually necessary to prescribe a very simple diet, *e.g.* Diet VI. or VII.

As regards food values, Table I. (shown on p. 426) contains some of the carbohydrate-containing foods, and 5 g. carbohydrate are contained in the following weights of the edible parts of vegetables, fruits and nuts. The vegetables are cooked, unless otherwise stated. Any one item, therefore, may be substituted for any other without risk of serious error.

Now that the diet contains 100-130 or more grammes of carbohydrate, it is unnecessary to prescribe the so-called diabetic bread or cake. One ounce of some of these foods contains 10–12 g. of carbohydrate, in comparison with the 15 g. of one ounce of white or brown bread. Diabetic jellies, jams and marmalades all contain a little glycerine, but the amount is so small that it may be neglected.

Insulin.—Insulin should be administered if the urine still contains sugar, or if the fasting value of the blood sugar is above 200 mg. per 100 c.c., after the patient has eaten the Maintenance Diet for three days, or has reached Diet III.

The correct dose of insulin can be discovered very easily if an estimation of the blood sugar can be made. If this is not possible, treatment with insulin can be carried out, provided the urine is collected in 3-hourly periods (approximately) and tested for sugar. So long as the blood sugar is below the threshold of the kidney, *i.e.* 180 mg. per 100 c.c., the urine will not contain any sugar (see Fig. 10). Each succeeding specimen should then be tested, so as to be able to determine when the blood sugar rises above

"LADDER DIET" AS USED AT ST. BARTHOLOMEW'S HOSPITAL

DIET.		I.	II.	III.	IV.	V.	VI.	VII.	VIII.	IX.
	Tea,	coffee,	lemon	ade an	d meat	extrac	t as de	sired.		
Eggs . .		1	1	1	1	1	1	1	1	1
Butter . .	ozs.	1	1	1	1	1	1	1	1½	1½
Vegetables Cooked / Vegetables Uncooked	The vegetables in Group I. may be eaten according to taste and appetite.									
Meat . .	ozs.	6	6	6	6	6	6	6	6	6
Bacon . .	„	—	—	—	—	—	1	1	1	1
Potatoes .	„	—	—	—	—	—	3	3	3	7
Milk . .	„	12	12	12	12	12	12	12	12	20
Apple . .	„	—	—	—	—	4	4	4	4	4
Orange . .	„	—	—	—	—	4	4	4	4	4
Banana . .	„	—	—	—	—	—	—	2	2	2
Bread . .	„	1	2	3	4	4	4	5	6	6½
Jam . .	„	—	—	—	—	—	—	—	—	½
Carbohydrate	g.	30	45	60	75	95	110	135	160	200
Protein . .	„	62	64	66	69	69	73	75	85	86
Fat . .	„	74	74	75	75	75	86	86	110	110
Calories .	„	1060	1130	1200	1270	1352	1528	1639	1890	2055

180 mg. per 100 c.c. again. By this method it is possible to ascertain that the fasting value of the blood sugar is below 180 mg. per 100 c.c., but it is not possible to determine whether it is normal or not without making an estimation. The initial dose of insulin should be 5–10 units; and if after 3 days each specimen of urine contains sugar, the dose should be increased by 2 units every day until the dose is 12 units. If the disease is severe the patient should be in bed, but if the disease is mild this is unnecessary. The diet and insulin should be supervised by a trained nurse. If this amount of insulin is not sufficient to render the urine sugar free, 5 units of insulin should be given about 7 p.m. The evening dose should then be increased by 2 units every second day, so long as the urine passed before the morning dose of insulin contains sugar. As soon as the dose of insulin is nearly adequate, the urine will be free from sugar, except immediately before and after each dose

of insulin. When the evening dose has been increased to 12 units without getting rid of the sugar, the morning and evening doses should be increased alternately by 2 units every 2 days, until the urine is sugar free. The estimation of the blood sugar is of great assistance in difficult cases. The best time of day to estimate it is before each dose of insulin and 3 hours after the morning dose. The great majority of patients need 10–20 units, but some need 100–200 units and occasionally as much as 400 or more units a day. After the fasting value of the blood sugar has been reduced to normal and the urine is sugar free all day, symptoms of hypoglycæmia may appear. The patient himself should be able to recognise these symptoms, and also should know how to treat them, either with orange juice, or two lumps of sugar, or adrenaline, 1 c.c., or pituitary (posterior lobe) extract, 1 c.c. (see p. 423). Some patients do not recognise the manifestations of hypoglycæmia, and are liable to develop serious symptoms. In these cases it is advisable to reduce the dose of insulin, and allow a little glycosuria to occur before each dose of insulin, but the urine passed between 1 and 5 p.m. should be free from sugar. The dose of insulin which caused the hypoglycæmia should the next day be reduced by 2 units. When the blood sugar is normal, the carbohydrate should be increased, every 3 or 7 days, by 10 or 15 g. portions up to 110 g. It is usually necessary to increase the insulin at the same time, in the proportion of 1 unit to 4 g. of carbohydrate. When this extra carbohydrate has been correctly balanced with insulin, the carbohydrate should be cautiously increased up to 130–150 or 250 g. It may not be necessary to increase the insulin if the patient is showing signs of hypoglycæmia. The extra carbohydrate may be divided among the usual meals, except afternoon tea, but it is often convenient to give 10–15 g. of carbohydrate before going to bed and also in the middle of the morning, if such does not interfere with the patient's occupation. If the patient loses weight in spite of the extra carbohydrate, the protein, but not the fat, should be increased by 7 or 14 g. The maximum amount of fat should not exceed 100 g. for an adult, and some authorities restrict it to 50 g. If the weight is constant, and the patient is not more than 10 per cent. under weight, the caloric value is adequate. If, on the other hand, the patient gains weight rapidly, the protein and fat should be decreased. It is sometimes necessary in cases of tuberculosis, or to meet the patient's tastes, to increase the carbohydrate to 200 or 250 g. In such cases the insulin should be increased in the proportion of 1 unit to 6 or 8 g. of carbohydrate. It may be necessary to give the insulin three-quarters to an hour before the meal, in order to prevent large carbohydrate meals raising the blood sugar too high. Since active exercise often causes hypoglycæmia, it is advisable either to decrease the insulin by 5 units or more, or to increase the carbohydrate by 10 or 15 g. at the previous meal. Sugar, two or three lumps, should always be available for such emergencies. In some cases it is very difficult to keep the blood sugar within normal limits, because it swings from hyperglycæmia to hypoglycæmia, and back to hyperglycæmia in 6 or 8 hours, instead of 10 or 11 hours. If the dose of insulin is increased in order to keep the blood sugar normal for a longer period, the patient will probably have severe attacks of hypoglycæmia at midday. In these cases the morning dose should be reduced by 10 units, and a third dose of 8 units administered immediately before the midday meal.

Intensive research work on the properties and preparation of insulin has resulted in two new preparations: Protamine insulin (trade name Retard or Delay), introduced by Hagedorn; and protamine insulin with zinc, prepared by Scott. Protamine insulin has no immediate effect on the blood sugar, but begins to work after 4 hours or so, and its effect lasts for the next 8 to 12 hours or in some cases for 24 hours. Protamine insulin with zinc does not commence to have any effect for the first 8 to 12 hours, but it continues to act for the next 14 to 16 hours or even longer. Both these insulins are now used in the treatment of patients and are very useful. The protamine insulin with zinc, either alone or in combination with ordinary insulin, will often control the blood sugar by means of only one injection in the morning. If a patient is well balanced on 20 units in the morning and 16 units at night, the change should be made to 20 units of ordinary and 12 units of protamine insulin with zinc; the reduction of 4 units is necessary to prevent the patient having overdosage, as the protamine is more efficacious. The patient is then liable to hypoglycæmia at three times in the day—before the midday meal as the result of the ordinary insulin, before the evening meal due to the protamine insulin with zinc beginning to act, and during the night when it is very active. This last reaction may come either early in the night or as late as just before breakfast. The amount of carbohydrate should be adjusted to overcome this liability to overdosage. An extra 10 or 15 g. should be given at tea-time, before going to bed, and before the morning injection of insulin. This will entail an increase of between 30 and 45 g. of carbohydrate, but this is usually well tolerated in spite of the initial reduction of the dose of insulin. The change is facilitated by the estimation of the blood sugar, but it can be achieved without this if the urine is tested regularly every 3 hours during the day, on waking, and before breakfast is eaten.

The following rules are of value:

Rules for Decreasing the Insulin in Cases of Overdosage

(1) If there are any signs of overdosage at midday, the dose of ordinary insulin should be decreased by 2 units, or if severe by 4 units.
(2) If there are any signs of overdosage between midday and the evening meal, the dose of each insulin should be reduced by 2 units, or if severe by 4 units.
(3) If there are any signs of overdosage between the evening meal and the next morning, the dose of protamine zinc insulin should be diminished by 2 units, or if severe by 4 units.

Rules for Increasing the Dosage of Insulin

(1) If the urine passed at 8 a.m. contains sugar, it means that the dose of protamine zinc insulin was insufficient and should be increased by 2 units every third day.
(2) If the urine passed at 7 p.m. contains sugar, it means that the dose of ordinary insulin was insufficient and should be increased by 2 units every third day.

The proportion of the two kinds of insulin varies, for in some cases equal amounts of soluble and protamine insulin with zinc are needed, while in others much soluble and little protamine, or little or no soluble and much protamine insulin with zinc, are necessary. Some patients can be well controlled with the mixture of insulins, and the doses of the insulins can be gradually reduced. If the case is difficult to control, the patient should be allowed to pass sugar before breakfast and before the evening meal. In these cases better results can often be obtained with a mixture of protamine (Retard or Delay) and soluble insulin twice daily, as this is equivalent to giving four doses of insulin a day. Thus, if a patient is passing much sugar at 8 a.m. and yet after 30 units of soluble insulin has symptoms of hypoglycæmia at midday and again passes much sugar at 7 p.m. he can be helped if the dose of soluble insulin is reduced to 20 units and 10 units of protamine administered at the same time. This will prevent the hypoglycæmia at midday, and also tend to prevent the blood sugar from rising so high at 7 p.m. Similarly, if the blood sugar is very low at night and high before breakfast, the evening dose is diminished by 10 units and 10 units of protamine insulin are given. By varying the dose of the two different kinds of insulin it is often possible either to control the glycosuria and hypoglycæmia completely, or to lessen considerably the inconvenience of the attacks of hypoglycæmia.

It is not possible to say which combination of soluble and protamine insulin will be most effective, as this can be discovered only by trial and error. Some patients need a mixture of both insulins night and morning; others, protamine at night and a mixture of the insulins or soluble only in the morning; and others, either a mixture of the insulins or protamine alone at night, and another combination will be necessary in the morning.

Further advances with the different kinds of insulin may be expected, and the lot of the diabetic patient will consequently be further improved.

The *after-treatment* is very important. The patient should be taught as much as is possible about the disease and diet, for if he understands the principles concerned, he is much more likely to carry out the treatment correctly. He should also be taught to test the urine with Benedict's solution. If no insulin is taken the urine passed after the evening meal should be tested, but if insulin is used the urine immediately before the injection in the morning or evening should be tested.

Medicinal treatment.—Many preparations of the pancreas or of herbs which can be taken by mouth are extensively advertised. With one exception they are all valueless as well as being expensive. Synthalin, 40 mg., with decholin, 25 mg., given for 3 days at a time with one day's rest, has a definite though slight action on the glycosuria and glycæmia in many cases. It has the great disadvantage that it often causes toxic effects, such as dyspepsia, vomiting and jaundice. It should not be recommended unless the patient refuses insulin. Purgatives are of great importance, and the necessity of an efficient daily evacuation should be insisted on. Ext. aloes, gr. 4, ext. nuc. vom., gr. $\frac{1}{4}$, in pill form, one to two at night; inf. of senna pods, ten to thirty; phenolphthalein gr. 4 to 8 or more in liquid paraffin 1 fl. oz. b.d.s., are the most efficacious; salines, together with tinct. jalapæ co. min. 30, should only be used in emergencies. General tonics which improve the health may be used. Opium used to be of assistance in the late stages of the disease, but should not be required nowadays.

TABLE I.

A. VEGETABLES

Group 1—

(These need not be weighed as they contain so little carbohydrate):

Asparagus	16
Cabbage	18
Cauliflower	15
Celery (raw)	14
Cucumber (raw)	9¾
French Beans	16
Lettuce (raw)	9¾
Mustard and Cress	20
Rhubarb	18
Radishes (raw)	6¼
Sea-Kale	29
Spinach	13
Watercress (raw)	25
Brussels Sprouts	10
Marrow	13

Group 2—

Beans, broad	2½ oz.
Beans, Haricot	1
Beetroot	
Carrots	4
Leeks	4
Onions	6
Parsnips	1½
Peas (dried)	1
Peas (green)	2
Potatoes	1
Turnips	7

B. FRUITS

Apple (raw)	2
,, (cooked)	4
Apricot (fresh, with stone)	3
Banana	1
Blackberries	3
Cherries (with stone)	1½
Damsons (with stone)	2
Gooseberries (raw ripe)	2
,, (unripe, stewed)	10
Grape Fruit	3½
Grapes	1
Greengage (with stone)	1½
Melon	3½
Oranges	2
Peaches (with stone)	2
Pears	2
Pineapple (fresh)	1½
,, (tinned)	½
Plums (with stone)	2
Raspberries	3
Red or Black Currants	3½
Strawberries	3
Tomatoes	6
Jam or Marmalade	¼

C. NUTS

Almonds	1 oz.
Chestnuts	2
Hazel Nuts	1½
Walnuts	1½

D. STARCHY FOODS

Milk	3½ oz.
Bread	
Dry Oatmeal	
Force or Cornflakes	
Rice	
Plain Biscuit	

The following contain little or no carbohydrate:

Tea	Lemon Juice	Meat Extract	Vinegar
Coffee	Soda Water	Gravy Soup	Saccharine

TABLE II.—PROTEIN AND FAT

The following articles of food contain approximately 6·5 to 7·0 g. protein, and 6·5 to 7·0 g. fat, and may be substituted for each other without causing serious error:

oz. Beef.
Mutton.
Pork
Lamb.
1½ ,, Tripe
,, Veal.
Egg.
oz. Sardines.
,, Salt Herring.
,, Salmon.
,, Chicken with the addition of ¼ oz. Butter.

1 oz. Rabbit, with the addition of ¼ oz. Butter.
1 ,, White Fish, with the addition of ¼ oz. Butter.
1 ,, Ham.
1 ,, Cheese.
1½ ,, Bacon, but ¾ oz. Butter should be deducted from the Butter ration.
2½ ,, Bread.
6 ,, Milk.

Fat, 5 oz. cream = 1 oz. Butter.

g. Protein = 4·1 Calories.
Carbohydrate = 4·1 ,,
,, Fat = 9·3 ,,
,, Alcohol = 7 ,,

6·25 g. Protein = 1 g. Nitrogen.
1 kg. = 2·2 lb.
30 g. or cubic centimetres (c.c.) = 1 oz.

A patient at rest requires 25 calories per kilo body-weight per 24 hours, approximately 1 calorie per kilo per hour.

Complications—Coma.—This requires prompt and energetic treatment with large doses of insulin. The patient is sometimes very cold and collapsed, and he should be made warm as soon as possible, by means of a hot air bath, or, if this is not available, by hot water bottles, as in the treatment of surgical shock. The blood sugar is usually high, 300–800 mg. per 100 c.c., and it is safe to give 50–100 units of insulin, subcutaneously, as soon as the diagnosis is made without waiting for a blood-sugar determination. If the condition is very grave, the insulin should be given intravenously. If it is not possible to estimate the blood sugar, a dose of 50 g. (2 ounces) of dextrose should be given by mouth or by an œsophageal tube, and 50 to 75 units of insulin. If there are no signs of returning consciousness in 3 hours, another 50 or 70 units of insulin, together with 50 g. of dextrose in solution, should be given. The urine should be collected every 3 hours. If it is necessary to pass a catheter, a self-retaining one should be used and the urine tested every hour. The urine for the first 3 hours after insulin is certain to contain sugar, and if the urine for the 4th to 6th hours contains sugar, it is safe to give 30 to 50 units of insulin. If, however, the urine for the 4th to 6th hours does not contain sugar, it is dangerous to give any more insulin, unless sugar, in the proportion of 4 g. to 1 unit of insulin is given by the mouth or intravenously at the same time. If there is any doubt as to whether the patient is recovering, this latter procedure should always be followed. If the condition, however, is improving, no insulin should be given until sugar reappears in the urine. Water in as large amounts as is possible, either by mouth or by nasal catheter, should be given; at least 10 ounces each hour for some 6 hours. If the condition is grave, especially if the patient is vomiting, the fluid should always be administered by an intravenous drip. A solution of 10 per cent. dextrose in $\frac{1}{4}$ normal saline should be given. 2000–3000 c.c. should be administered in 24 hours if nothing is taken by mouth. An estimation of the hæmoglobin should be made at intervals, in order to determine whether sufficient fluid is being given or not. Two ounces of castor oil should be given with the first drink, as these patients are nearly always very constipated. In coma the alkali reserve is always much reduced, and sodium bicarbonate is of assistance, although the enormous doses which were administered before the discovery of insulin should not be given. A dose of 12 g. (3 drms.) 600 c.c. of 2 per cent. sodium bicarbonate should be given intravenously, and no advantage is to be gained by giving a bigger dose.

Every patient in coma should be examined most carefully each day, in order to determine whether any other disease is present. In 7 out of 9 cases admitted to St. Bartholomew's Hospital in the first year of insulin treatment, an acute infection, *e.g.* acute otitis media, parotitis, or gangrene of the lung, was present. The appropriate treatment should be instituted as soon as possible.

Acute infections, such as influenza, usually cause a considerable diminution of the sugar tolerance. If the infection is of mild degree, it may be sufficient to increase the dosage of insulin by 2 or 4 units for some days. If, however, the infection is of severe degree, it is important that the condition should be adequately treated, so as to prevent (1) any danger to life, and (2) any permanent diminution of the sugar tolerance. The same procedure should be adopted as in the treatment of coma (Fig. 11), but the dose of insulin should be much smaller, unless the patient is very ill. Provided the urine is collected

in 3 hourly periods and tested for sugar, a sufficient dose of insulin may be given with safety every 6 or 9 hours, and thus the ill-effects of the infection reduced as much as possible.

Surgical operations were always contra-indicated before insulin was known, but they may now be carried out, provided certain precautions are observed. The patient's blood sugar should be reduced to normal, provided that there is time to achieve this. Gas and oxygen, local or spinal anæsthetics cause no ill-effects. Neither ether nor chloroform should ever be given alone, but the former may be given with gas and oxygen, if deep anæsthesia is required, but as little as possible should be used. Fifty g. (2 oz.) of sugar, together with 16 units of insulin (1 unit to 4 g.), should be administered about 2 hours before the operation, in addition to the usual dose of insulin, in order to have plenty of sugar and insulin in the body at the time of operation. After the operation the appropriate diet for the surgical disease, together with adequate amounts of insulin, should be given for the first few

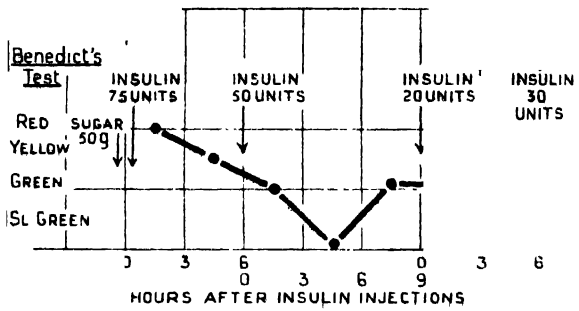


Fig. 11.—Figure showing how an adequate dose of insulin can be arrived at by testing the urine in a patient in diabetic coma.

days, but as soon as possible the usual diabetic diet should be given and the blood sugar controlled again. If pregnancy occurs it should not be terminated unless there are other complications.

Renal Glycosuria

This is an uncommon condition which is apt to occur in several members of a family. Although the blood sugar lies within normal limits, dextrose may be present in the urine, either throughout the day or only after a carbohydrate meal. The sugar is usually small in amount, *i.e.* less than 10 g. per diem, but several cases are reported in which 20 to 30 g. were excreted in the day. The amount of sugar in the diet has little influence on the total sugar excretion. The diagnosis should only be made after a series of observations. A complete test of the sugar tolerance with doses of 25 to 50 g. of sugar should be made when the patient is eating plenty of carbohydrate food and the urine contains no acetone bodies. Estimations of the blood sugar should be made at intervals of half an hour for 2 to 3 hours after the dose of sugar, and the amount of sugar excreted in the urine should be estimated. If sugar is present in the urine, although the blood sugar does

not rise above 180 mg. per 100 c.c. at the end of 30 minutes and has returned to the normal level after 2 hours, the patient probably belongs to the renal glycosuria class.

The prognosis is good, and no treatment is required once the diagnosis is made. It is wiser to treat all doubtful cases with moderate restriction of the carbohydrate ration (100 g.) and to repeat the sugar tolerance test in 1 to 3 months' time. Very little harm can be done by this procedure, while much damage can be done if a case of true diabetes is treated with no dietetic restrictions (Salomon, Graham).

Lævulosuria

Lævulosuria is a sign of some importance of the liver and should direct attention to that organ. Slight reduction of carbohydrates and of fruits is usually sufficient to check it.

Lactosuria

This occurs (1) during lactation, (2) when suckling suddenly ceases, and (3) in breast-fed infants with enteritis.

Pentosuria

This is a rare occurrence. Many of the patients are Jews. Of 7 cases, 3 were Jews, 2 Greeks, and 2 English (Cammidge).

GOUT

A disease in which there is a disturbance of the purin metabolism and an increase of uric acid in the blood. The clinical sign is an attack of acute arthritis with a deposition of sodium biurate in and about the joints.

Ætiology.—*Predisposing causes.* — Gout is much commoner among certain races, *e.g.* the English and German. It is very uncommon among native races. It does not follow, however, that this is a racial peculiarity. It is much commoner in temperate than in tropical climates, but it is unlikely that the climate plays any part in the causation of the disease. The evidence in favour of gout being an hereditary disease is very strong, as a history of a gouty ancestry can be obtained in 50 to 80 per cent. of the cases. A history of gout in the family was obtained in 75 per cent. of well-to-do patients and in 50 per cent. of hospital patients (A. B. Garrod). This evidence suggests that the disease is chiefly hereditary but may be acquired. It is not the disease which is inherited, but only the predisposition to it, and the disease may lie latent until it is evoked by other causes (Llewellyn). It is a disease of middle life—between the ages of 35 and 50—but it may occur much younger, even in schoolboys who have a strong hereditary taint. The malady is very much more common in men than in women. Women form only 5 to 20 per cent. of the patients in most statistical tables.

Exciting causes.—Food plays a part in the causation of the disease, but it is rather the quantity than the quality which matters. Meat and the purin bodies in tea, etc., probably have little effect, but sweetbreads, liver,

kidneys, fish roes, tripe may be actively harmful. Spirits have little effect, and gout is almost unknown in Scotland. Beer is much more potent and is probably partly responsible for the prevalence of gout in England and Germany. The strong wines like port and sherry, and the red wines such as Burgundy and claret, are also probably responsible for much gout among the well-to-do classes, and champagne has a bad reputation. The light white wines like Graves and hock and cider are less evil. Gout was formerly very common among lead workers in England, and it seems to be a concomitant cause. Trauma plays a great part in the causation of the acute attack. The big toe may be affected so frequently because of the pressure of the boot. An injured joint may be the seat of the first attack of gout. Syringing the ear of a gouty patient for cerumen was followed by an acute attack in the external auditory meatus (A. E. Garrod). Local sources of infection are very common among gouty patients, *e.g.* septic gums and tonsils. These used to be called gouty manifestations, but Llewellyn thinks that they may be responsible for causing the attack of gout.

Physiology and Pathology.—The fact that sodium biurate was deposited in and around the joints suggested that uric acid played an essential part in the causation of gout. After A. B. Garrod had demonstrated by means of his thread test that the blood of gouty patients contained uric acid in abnormal quantities the hypothesis seemed to be proved. The problem is, however, not so simple as was thought at first.

The uric acid which is excreted in the urine of healthy people on an ordinary mixed diet comes from two sources, exogenous and endogenous. When all the exogenous sources of uric acid, *e.g.* meat, fish, sweetbread, tea and coffee, etc., are removed from the diet the output sinks to a level of 0·5 to 0·7 g. per day. The amount is fairly constant for each individual. If all proteins are removed from the diet, the endogenous uric acid output falls to a lower level than before (Folin). The removal of carbohydrates and a reduction of the caloric value of the diet also cause a decrease in the endogenous uric acid output to the lower level (Graham and Poulton). The endogenous uric acid output is believed to come from the breakdown of the cell nuclei of the body, *i.e.* wear-and-tear, but it can also be synthesised from histidin and arginin (Hopkins and Ackroyd). When the exogenous purins are eaten, or when uric acid is injected, there is an increase in the uric acid output, but the whole of the uric acid is not excreted in one day. If cinchophen is given at the same time, the excretion-rate of the uric acid is increased.

The blood always contains uric acid, and the limits of normal variation in health are 1 to 3 mg. per 100 c.c. The total uric acid in the blood of a man weighing 10 st. 3 lb. or 65 kilos would be 50 to 150 mg., assuming that the blood constitutes $\frac{1}{13}$th of the body-weight, *i.e.* 5000 c.c.

In cases of gout there is usually a considerable increase in the amount of uric acid in the blood. Before an attack the blood may contain 4 to 6 mg. of uric acid per cent., though occasionally between the attacks there may be only a slight increase. The uric acid may also be increased in some people who have never had gout; as, in leukæmia, where there is a great destruction of leucocytes, and in severe cases of nephritis. The increase in the uric acid in the blood is, therefore, not pathognomonic of gout, although it is extremely suggestive of it.

In gout the output of uric acid varies widely. It may be quite small in amount, less than 0·20 g. per day, or it may be equal to that excreted by healthy people. Before the attack of gout it is usually very small in amount, but the paroxysm always causes a great increase in the output for a few days only. When purin bodies are eaten by a gouty patient, or if uric acid is injected, there is great delay in the excretion of uric acid. If cinchophen is given at the same time, the uric acid is excreted much more quickly. The diminution in the uric acid output may be due to an increased destruction in the body or to its retention by the kidneys. There is no evidence of increased destruction in the body, as the blood of a patient before an attack may contain 4 to 6 mg. of uric acid per 100 c.c. This suggests that

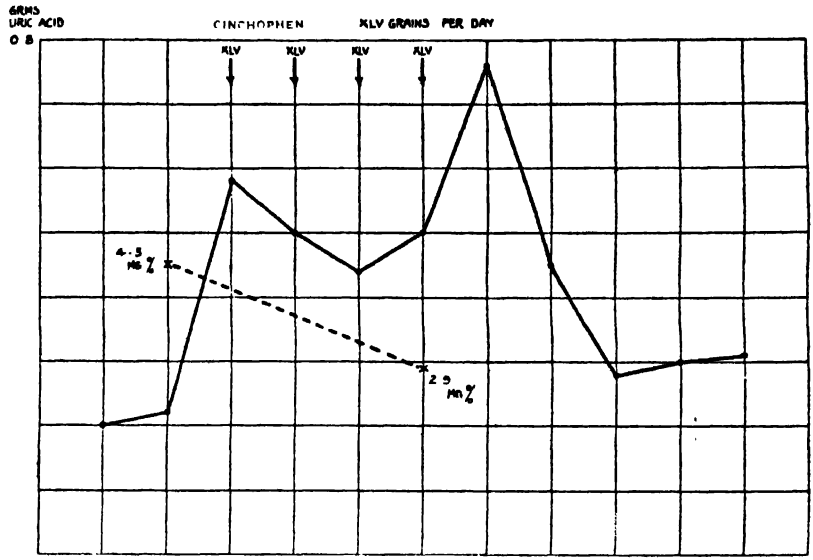


FIG. 12.—Figure showing the increase in the output of uric acid in the urine and the decrease in the uric acid in the blood after cinchophen.

the uric acid is retained by the kidneys. When cinchophen is given to a patient whose blood contains 4 to 5 mg. per 100 c.c. uric acid there is a great increase in the uric acid output and a decrease in the uric acid in the blood (Folin and Lyman). The " extra " uric acid excreted in 6 days (Fig. 12) was 1·9 g., while the blood uric acid decreased from 4·5 mg. to 2·9 mg. per cent. The " extra " uric acid must come from the uric acid in the body fluids, as the blood does not contain enough uric acid (Graham) (Fig. 12).

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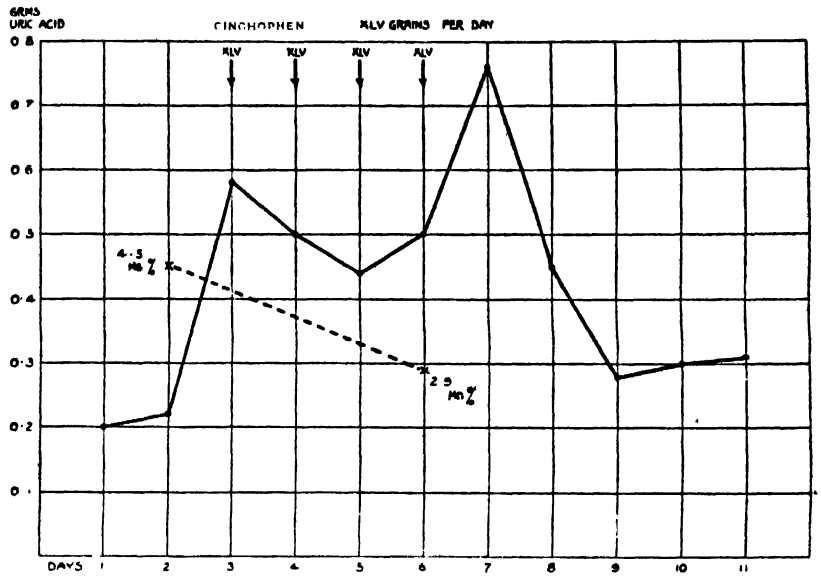


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The essential change is the deposition of uric acid as sodium biurate in the joints. The sodium biurate appears to be plastered over the surface of the cartilage, but on microscopical examination it is seen that there is a

layer of cartilage over the deposit, which is always interstitial. The deposits may be quite small or enormous. In many cases the structure of the bones is destroyed and replaced by sodium biurate. The ligaments, tendon sheaths and bursæ are also infiltrated. The big toe joints may contain sodium biurate, although the patient has never had an acute attack of gout. The skin covering a tophaceous deposit may ulcerate and break down, and small masses of sodium biurate may be discharged (chalky gout).

Tophi.—Sodium biurate is also deposited in the cartilage of the ear, especially in the outer margin of the pinna. The tophi appear as white nodules, and uric acid crystals can be recovered from them, which also give the murexide test and a blue colour with Folin's phospho-tungstic reagent.

The kidneys.—An uratic deposit may occur in the pyramids. Norman Moore found it in 12 out of 80 cases. Well-marked changes of chronic interstitial nephritis are often found.

Symptoms.—The earliest sign of gout is sometimes the deposition of sodium biurate in the cartilage of the ear (tophus). This stage usually passes unnoticed, but is sometimes accompanied by an intolerable itching or tenderness.

Acute gout.—The first attack of "classical" gout usually occurs at night. There may have been a few preliminary symptoms, such as dyspepsia, slight pain in the hands, and irritability of temper, but the patient goes to bed feeling well. "The patient suddenly wakes with pain, more or less intense, in the ball of one great toe, frequently accompanied with a slight shivering; the pain in the toe gradually increases and is attended with a sensation of burning, throbbing, together with great tension and stiffness; heat of skin and other symptoms of febrile disturbance usually follow the shivering, accompanied with a considerable degree of restlessness" (A. B. Garrod). The temperature is raised to 101° or 102° F., but after a few hours the patient begins to sweat and finally falls asleep. "In the morning the toe is swollen, the skin shiny, tense and dark red, and the whole joint is extremely painful" (A. B. Garrod). Usually the acute pain lessens in the daytime, but returns with great violence in the night hours. The temperature remains high and the temper of the patient is irascible in the extreme. The attack may last many days or pass away in two days. When the attack is ceasing "the inflamed joint becomes less intense and swollen, and pitting is readily produced on pressure" (A. B. Garrod). The attack may spread from the great toe to the other joints of the tarsus or to other joints of the body. The first joint of the big toe is most commonly affected. The ankles, knees and small joints of the hand and wrists are next in the order of frequency.

During the attack there may be a considerable degree of leucocytosis, 20,000 to 25,000, and all but 2000 to 3000 are polymorpho-nuclear cells as the lymphocytes and other cells are unaltered by gout. The uric acid output, which was low before, is greatly increased for a few days. Sodium biurate is deposited in the cartilage of the joint and head of the bone, but the swelling and stiffness may eventually disappear completely. The acute attack may be complicated by a severe gastro-intestinal disturbance which may be fatal. There may be other symptoms, such as dyspnœa, delirium and coma, but these are probably due to a coincident uræmia. Phlebitis of the veins of the limb may be a complication of an acute attack.

After the attack, whether as the result of illness or as a consequence of

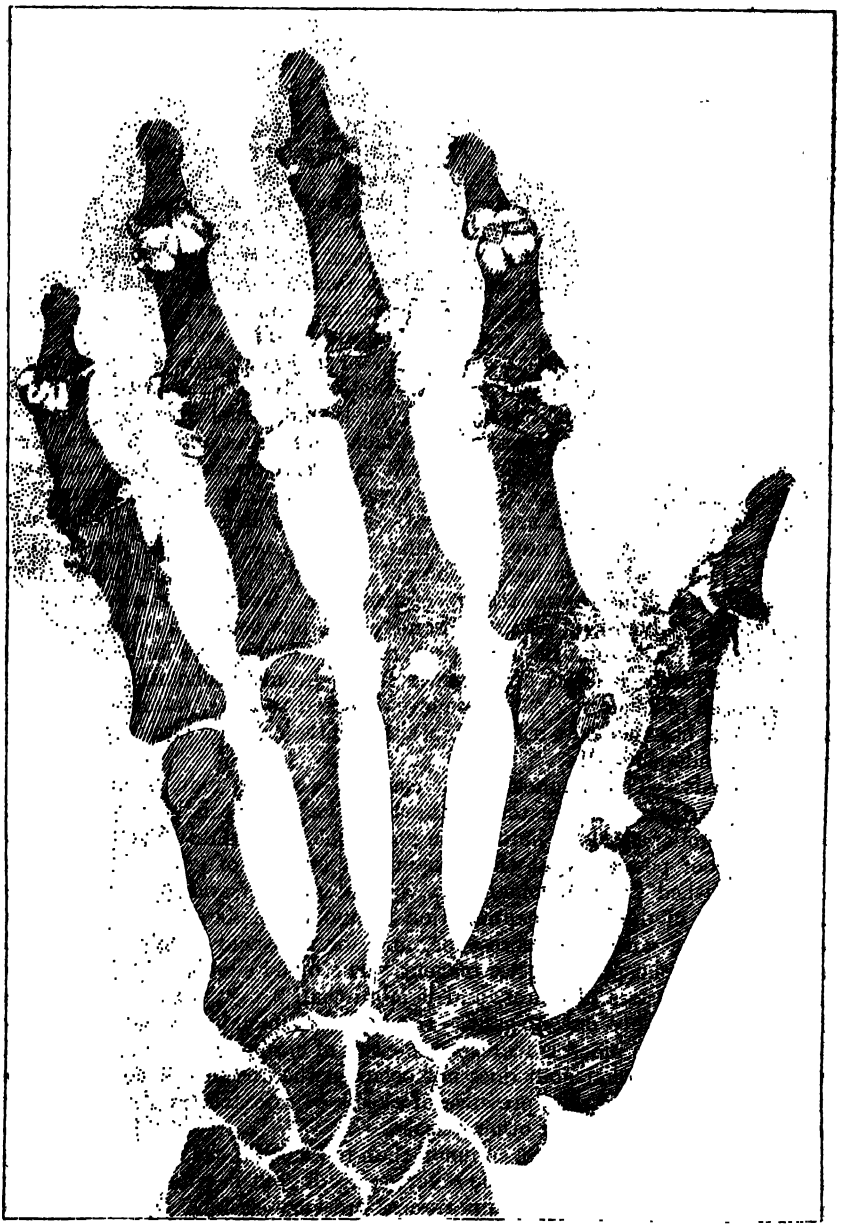


FIG. 13—Line drawing from a radiograph, showing the changes which take place in the bones due to the deposition of sodium biurate.

the simple living which the patient has endured, the general health of the patient is much improved. The attack usually follows in the spring and autumn. The second attack may follow at once, or may be delayed for many years.

Chronic gout.—After several attacks the joint does not recover completely. The deposits of urates occur in the ligament and capsule, as well as in the articular cartilages and bones. The joint, therefore, becomes swollen and irregular in its shape. The urate is especially deposited in the bursæ about the joints. In the advanced stages the skin over the uratic deposits breaks down and masses of chalky material are extruded, and the wounds heal with difficulty. The general health of the patient suffers after several attacks and does not recover completely. Dyspepsia is complained of, and the patient may show signs of high blood-pressure and arterial disease. The urine is increased in amount, and may contain albumin and casts.

Irregular gout.—Almost any symptom or physical sign which occurred in a person who was of a gouty disposition was formerly ascribed to gout. Cutaneous eruptions, such as eczema, gastro-intestinal disorders, cardio-vasular symptoms and pericarditis, headache, migraine and neuralgia, were all thought to be gouty. A gouty patient may develop any of these diseases, but the belief that there is a general type due to gout is now regarded as unfounded. The urine is usually acid, and on cooling often deposits uric acid crystals. This does not mean that there is an excess of uric acid in the urine, but that the urine is too acid to keep the uric acid in solution. On heating the urine the urates are re-dissolved. Gouty persons may suffer from calculi. Glycosuria occurs in some cases, but usually responds readily to treatment. Albuminuria and casts are present when the kidneys are also affected. Elderly persons often suffer from chronic bronchitis. Gout has been accused of rendering patients more disposed to iritis, retinitis and glaucoma. It is possible that iritis and retinitis have a gouty basis though they may arise independently.

Diagnosis.—The diagnosis in a case of classical gout, with recurring attacks of arthritis in the toe or tarsus, is easy, especially if the patient comes of a gouty stock or indulges in good food and drink. The presence of tophi is proof positive that the patient is a subject of gout. Tophi must be distinguished from Woolner's tip, fibroid nodules and sebaceous cysts, and in cases of doubt an examination should be made for the crystals of sodium biurate with the microscope, and for uric acid with the murexide test or Folin's phospho-tungstic reagent. The blood should be examined for uric acid in all cases of doubt, and if more than 3 mg. per cent. are found the case is probably one of gout. It must be remembered, however, that the uric acid in the blood is increased in cases of chronic interstitial nephritis. While it is certain that gout does not occur in the absence of an increase of uric acid in the blood, the presence of excess of uric acid in the blood does not exclude the presence of other diseases.

Classical gout is much less common than it was, and the modern tendency is to overlook the disease. In the severe cases of gout in which the joints are severely damaged, the X-ray appearances are very striking (Fig. 13). The negative shows dark areas where the sodium biurate is deposited in large amounts and replaces bone or cartilage, since sodium biurate is not opaque, like the calcium ion. In the less severe cases there may be—(1) lipping at

the articular margins; (2) a localised atrophy of the bone; (3) a narrowing of the joint space. These changes occur in other kinds of arthritis and are in no way characteristic of gouty arthritis (Llewellyn).

Prognosis.—If a patient has once had an attack of gout he will always be liable to another attack, unless he alters his way of living. The frequency and severity of the attacks can be modified by treatment. The prospect of long life depend upon the state of the heart, arteries and kidneys.

Treatment.—*Dietetic.*—In perhaps no other disease have a greater number of dietetic fads been recommended. The total quantity of the food should be kept within reasonable limits, and civic dinners should be avoided. The meals should be simple but attractive. There is little difference between the different kinds of meat, except that for those who have dyspepsia chicken is more easily tolerated than beef and mutton. There is no need to deprive the patient of sugar, which is a common fad, or of starchy food, but they should be eaten in moderation. The same is true of fat. Some gouty persons are much too stout, and a reduction of weight is beneficial.

All protein foods contain purin, but their content varies widely (see table below). The foods which contain more than 0·1 g. per 100 g. should be avoided, as the uric acid which is formed from the breakdown of the purin is excreted more slowly by the gouty patient than by the healthy one.

THE PURIN CONTENT OF VARIOUS FOODS (R. A. M'CANCE)

Material (All cooked)	Purin Nitrogen per 100 g. of Edible Food
Brains	0·033
Mutton (general average)	0·063
Fish (,, ,,)	0·065
Pork (,, ,,)	0·069
Beef (,, ,,)	0·081
Birds (,, ,,)	0·094
Hearts	0·116
Cod roe (hard)	0·120
Livers and kidneys	0·140
Herring (no roes)	0·150
Smelts	0·168
Sprats	0·180
Sardines	0·234
Whitebait	0·323
Throatbreads, Sweetbreads, etc.	0·426
Herring roe (soft)	0·480

Attacks of gout have followed very quickly after eating sweetbreads and after the administration of purins for experimental purposes. The fruits and vegetables which contain an excess of oxalates, *i.e.* strawberries, rhubarb, spinach and asparagus, should be forbidden if oxaluria is present.

Heavy beers, strong wines like port and sherry, all red wines, and also

champagne, should be forbidden for gouty patients. The white wines, like Graves and hock, may be allowed in moderation if especially desired. If drunk in moderate amount and well diluted, whisky is probably the least harmful beverage. Mineral waters may be of considerable benefit to gouty persons. Their mode of action is uncertain, but is probably due not so much to the ingredients of the waters as to the amount of water drunk, the simple and restricted diet, and the regular and supervised life which the patient leads at a spa. Hot baths and douches are of assistance in aiding the recovery of stiff joints. The waters of Buxton and Bath in England, Vichy, Aix-les-Bains and Contrexéville in France, Wildbad and Homburg in Germany, Carlsbad and Marienbad in Moravia, and Saratoga, Bedford and White Sulphur in America, are the best known.

Local.—During the acute attack the joint should be covered with cotton-wool, placed on a pillow, and the bedclothes raised by means of a cradle. Hot fomentations or cold lotio plumbi c. opio may be applied.

Internal.—The treatment should be started with a purgative, and calomel is recommended. Colchicum is specific for the acute attacks. The pain is usually relieved quite quickly, and the redness of the skin and swelling of the joint subside. Fifteen to 30 minims of the tincture in an alkaline mixture should be administered every 4 hours. The drug may cause vomiting or purgation, and its action must be carefully watched. Its mode of action is quite unknown, and it is of no value in averting an attack. Cinchophen (Trade names : atophan, agotan, phenoquin, quinophan) is useless in relieving the pain of an acute attack, but it is most useful in averting attacks. It is given in tablet form, gr. 15 three times a day for 1, 2 or 3 days consecutively in each week and should never be given continuously. It increases the output of uric acid in the urine and decreases the amount of uric acid in the blood, and thus prevents the continuous accumulation of uric acid in the body. The drug may, however, produce unpleasant symptoms, such as urticaria, dyspepsia and jaundice. The complication of jaundice may be a very serious matter, for acute yellow atrophy of the liver may develop and death ensue. These toxic effects have usually, but not always, occurred : (1) when the drug has been given continuously, *i.e.* without an intermission of 4 to 5 days between the courses ; and (2) when its administration has been continued after minor symptoms of toxic action have appeared. The results of the treatment of undoubted cases of gout with cinchophen are so good that its toxic action is most unfortunate. It would seem that its use should be restricted to the treatment of gout, and only given in short courses each week and discontinued at the first indication of intolerance. Further, as soon as the acute joint condition has passed, the dosage should be reduced to 15 gr. twice a day, one day each week for 2 to 3 months. In a long-standing case, it should then be given once a month, or once in 3 months for an indefinite period. Aspirin and sodium salicylate have a similar action to cinchophen and may be used instead of it. Aspirin gr. 10 with glycine gr. 20, is given three times a day for one or two days each week in the chronic case, or more frequently if an attack is threatening.

The general health of the patient must be attended to and all causes of sepsis should be removed. Radiant heat and massage are very useful for restoring the movements of a crippled joint.

OBESITY

Obesity is a condition in which there is an excessive amount of body fat.

Ætiology.—Certain races are more prone to become fat than others, *e.g.* the Dutch, South Germans, South Italians, Maltese, Hebrews, the natives of India and Ceylon, and some African races. A clear history of heredity was obtained by Futcher in 60 per cent. of his cases. Obesity may develop at almost any age, but it is more likely to occur at certain ages: in babies, in children at puberty, in men after the age of 40, and in women during pregnancy or after the menopause. It is commoner among females than males.

Pathology.—The deposit of fat indicates that the caloric value of the diet is in excess of the individual's needs. This may be due to the large amount of food which is eaten, or to a small energy consumption in the body. Some fat people have a very large appetite and eat much more than is necessary to satisfy their energy requirements. The amount of exercise which is taken has a great influence on the amount of fat which is deposited. Thus, a patient who is lying in bed will gain in weight on a diet which contains less caloric value than that which he eats when he is up and about. Although many cases of obesity are easily explained on the above grounds, there are many instances which cannot be explained so simply.

The investigations of the basal metabolism help us to understand many of these cases. The amount of oxygen which is burnt depends on the state of the patient. More combustion of oxygen takes place when the patient is taking exercise than when he is at rest, and when he has a meal than after a short fast. The metabolism of the resting, fasting individual is termed the basal metabolism. This is expressed in cubic centimetres of oxygen per minute per square metre of body surface. The basal metabolism (p. 403) is lower for adults than for children, and gradually decreases with each decade. It is lower for females than males. The basal metabolism can be altered by prolonged undernutrition and by the influence of the ductless glands. One of the results of underfeeding is a lowering of the basal metabolism, but the oxygen consumption of such a patient during exercise is unaltered. The action of the thyroid gland on the basal metabolism has been carefully studied, as there are two clinical conditions in which the thyroid plays an important part, namely, (1) in hypothyroidism, and (2) hyperthyroidism. In the first, the patients, among other symptoms, tend to increase in weight, and the basal metabolism in these cases is much lower than usual. In the second, one of the prominent complications is the rapid loss of weight which occurs, and the basal metabolism is much increased in these cases, and can be increased by giving thyroid extract and decreased by removal of large portions of the gland. When the basal metabolism is low, it is clear that the patient will tend to get fat, although he is eating less food than a patient whose basal metabolism is high. These experiments help us to understand many cases of obesity.

The action of the other ductless glands is not so well understood. When the posterior lobe of the pituitary gland is damaged by a tumour, considerable changes take place in the metabolism. The patients grow fat, and the fat is deposited in the characteristic feminine situations, *i.e.* the breasts and hips in male and female patients (Fröhlich's syndrome). When the anterior

lobe is removed in dogs there is an increase in the weight of the animal (Cushing).

The sex glands have a considerable influence on the metabolism. When the glands develop at puberty there may be an increase or decrease in the fatty deposits. The female lays down fat around the breasts and hips, and assumes the characteristic feminine form. Removal of the testicles, as in eunuchs, usually causes an increase in the body-weight. During a pregnancy women often grow stout long before they have to restrict their normal activities, while after the pregnancy is terminated, the patient may lose weight, and recover her figure. At the menopause many women tend to become stout.

In obesity the fat is deposited in the subcutaneous tissues, the great omentum, mesentery, and around all the organs, such as the heart and kidneys.

Symptoms.—The presence of large deposits of fat limits the activities of the patients and destroys their good looks. Many of the patients feel well, but some complain of difficulty in moving about, because of their great bulk. Others complain of shortness of breath on the least exertion. Some of the patients are anæmic. Eczema may occur on those parts of the skin which touch each other.

Treatment.—*Dietetic.*—If the patient has only gained a little weight, moderate restriction of the carbohydrate and fat of the diet, together with an increase of exercise, may be sufficient. This is the basis of the well-known Banting cure. When the obesity is considerable, more drastic treatment is necessary if the patient really wishes to lose weight. The treatment may be started in two ways. (1) With a fast day, when the patient should stay in bed. Tea and coffee, with milk and sugar, and gravy soups may be taken in any quantity. The fast day will often cause an initial drop of 1 or 2 lb. in weight and also a reduction in the size of the patient's appetite. The fast day should be repeated once a week, and after a few times the patient need not stay in bed. (2) With a fruit day. A sufficient amount of fruit and vegetables is taken to provide 80 g. of carbohydrate (see Food-Tables, p. 426). The fruit day causes less discomfort than a fast day, partly because of the bulk of the food eaten and partly because the carbohydrate maintains the blood sugar at the normal level, and so prevents the formation of acetone bodies. The patient will be more willing to repeat a fruit day than a fast day once or twice a week.

The three components of the diet, *i.e.* fat, carbohydrate, and protein, should be reduced in different proportions. The fat should be reduced as much as possible, because it has a very high caloric value and the patient has already an excess of fat in his body. Butter, cream, the fat of meat, and especially that of ham and bacon, should be avoided. Chicken is better than mutton or beef, as it contains less fat, while white fish contains no fat. The carbohydrates should be considerably reduced, but this must be done cautiously; for many patients are made miserable, complaining of lassitude and extreme hunger. This is probably due to the blood sugar being too low, since these symptoms occur as a result of an overdose of insulin (p. 413). The protein should be reduced least of all, for its combustion causes an increase in the metabolism of the body—the specific dynamic action of proteins. The total caloric value of the diet may have to be reduced to 1500 calories

(carbohydrate (C), 150 g.; protein (P), 70 g.; fat (F), 64 g.); 1000 calories (C, 100 g.; P, 70 g.; F, 32 g.); 500 calories (C, 60 g.; P, 40 g.; F, 10 g.) (see Table of Food Values) before the patient begins to lose weight. The weight should not be decreased too rapidly. When the fat in the diet is small in amount the patient will suffer from a lack of vitamins A and D. This should be given in the form of radiostoleum, or adexolin, min. 3 once daily. A decrease of 1 to 2 lb. a week and 7 to 8 lb. a month is sufficient. The treatment should be persevered with until the patient's weight is about the average for the height and age. The patient should be encouraged to take more exercise, but this should stop short of inducing undue shortness of breath. Physical drill and massage are of considerable assistance in increasing the energy needs of the body. Care should be taken not to eat more than usual after exercise, for this will neutralise any good effects of the exercise.

Thyroid has been used in the past rather indiscriminately, as it increases the basal metabolism. If the patient has a low metabolic rate (B.M.R.), it should be prescribed; but if the B.M.R. is already normal, it may cause harm. The usual dose is 1 to 2 gr. twice daily. A careful watch should be kept for the onset of tachycardia, tremor, sweating, and glycosuria. When the B.M.R. is raised, more insulin has to be provided, and an elderly patient with a low sugar tolerance may develop glycosuria and have the symptoms of diabetes mellitus as the result of the administration of thyroid.

LIPODYSTROPHIA PROGRESSIVA

This is a rare condition, in which the subcutaneous tissues of the upper part of the body lose their fat, while those of the lower half remain unchanged.

Ætiology.—Females are affected more often than males. The cause of the condition is quite unknown.

Symptoms.—The patient feels perfectly well, but complains that the appearance of the face has altered, having become much thinner. The arms and trunk may also be similarly affected. The condition starts in the face and gradually descends to the arms and trunk. The legs are usually unaffected. On examination, the skin can be picked up easily and it is obvious that there is no fat in the subcutaneous tissues. The malar bones are very prominent. The whole appearance of the patient suggests a severe wasting disease. The breast and mons veneris in females are usually unaffected.

Course.—The condition progresses slowly.

Diagnosis.—This is made by comparing the subcutaneous tissues of the upper half of the body with those of the lower. The presence of a severe wasting disease must of course be carefully excluded.

Treatment.—Nothing is known which has any effect on the condition. The patient should be assured that no serious disease is present.

THE LIPOMATOSES

Localised deposits of fat may occur in many situations. Various types with special symptoms have been prescribed, but it is probable that they are only

variations of a common morbid process.[1] The main types of the disease are:

1. *Adiposis dolorosa* (*Dercum's disease*).—See p. 440.

2. *Nodular circumscribed lipomatosis.*—The lipomata may be few in number or very numerous, symmetrical or asymmetrical, large or small. Most of them are painless, but some are very tender and painful. Asthenia and mental changes, such as occur in adiposis dolorosa, may be present.

3. *Diffuse symmetrical lipomatosis of the neck*—This condition occurs chiefly in males, and the tumour usually appears after the age of 20. The thyroid and pituitary glands showed pathological changes in two cases. The fatty tumour is diffuse and symmetrical. The common sites are beneath the chin, at the nape and base of the neck, and the pre- or post-auricular region, and occasionally on the trunk. The tumour bears no relation to the general obesity of the patient. It is usually complained of because of the disfigurement which is caused. Pain, asthenia and mental disturbances may be present.

4. *Neuropathic œdema, pseudo-œdema, pseudo-lipoma.*—Swelling of the limbs may occur in patients with hysterical affections. This resembles at first sight an œdematous swelling, but it does not pit on pressure. It is due to a deposition of fat in the subcutaneous tissues.

Treatment:—This is very unsatisfactory. Thyroid gr. 1 t.d.s. has given the best results, but pituitary (posterior lobe) extract should be also given a trial. Aspirin may relieve the pain.

GEORGE GRAHAM.

[1] Lyon, *Arch. Int. Med.*, VI., 1910, p. 28.

SECTION VII

DEFICIENCY DISEASES

VITAMINS

A COMPLETE and balanced diet must contain a sufficiency of each of the vitamins as well as the correct amount and proportion of protein, fat, carbohydrate and mineral salts. In the absence of vitamins from the diet the so-called deficiency diseases, scurvy, rickets, beriberi and pellagra and other syndromes arise. Vitamins are present in only minute amounts in various foods and were simply described by the letters, A, B, C, D, etc. Nearly all have been isolated, their chemical constitution established, and synthesised by chemists, and they have been more suitably named according to their properties and functions. The list of vitamins is as follows:

Fat soluble.

A = axerophthol
from carotene.
D =
from 7-dehydrocholesterol.
D_2 = calciferol
from ergosterol.
D_3 = same as D.
D_4, D_5 } from other sterols.
E = α- and β-tocopherol.
K =
methyl phytyl naphthaquinone.

Water soluble.

B_1 = aneurine or thiamine (F).
B_3, B_4, B_5 } not yet identified.

B_2 complex:

B_2 (G) = riboflavin.
B_6 = adermin (H).
B_7 = nicotinic acid or amide.
C = ascorbic acid or cevitamic acid.
P is doubtful.

VITAMIN A OR AXEROPHTHOL

The presence of an unknown substance in fats became obvious from the normal growth of rats on some fats, but not on others. Animal fats, except lard, and the fat of green leaves promoted growth, while vegetable fats extracted from seeds did not. The growth-promoting values of the fats were very different, the very high value of cod-liver oil being most striking. Green leaves were superior to butter. The vitamin A value of milk was low, and was derived from the green food of the animal. Green leaves, carrots, and other parts of plants contain the substance carotene, formed in the plant at the same time as chlorophyll. Carotene has also

growth-promoting properties, and yet it is not vitamin A. The connection between carotene and vitamin A was shown by Moore, who proved that carotene was converted in the liver into vitamin A. Three varieties of carotene are distinguished, α, β, γ, of very similar formulæ. β-carotene yields two molecules of vitamin A; the others only one. Other carotenoid pigments in plants are also precursors of vitamin A. The chemical formulæ of these pigments and of vitamin A show clearly how the latter is derived from the carotenoids. Vitamin A (as well as carotene) is stored in the liver; body fat stores very little of it. Storage of vitamin A is helped by fat in the diet. Normal human liver contains 200 international units per gram of wet tissue: at birth, however, the liver contains very little vitamin A. Vitamin A_2, a slightly different compound, is found in the livers of fresh-water fish.

On account of the numerous precursors in plants and different forms in which vitamin A (an alcohol) may exist in animals, chemical methods of estimation of vitamin A values of foods are difficult. The estimation has to be made by feeding experiments. As standard, pure β-carotene is used; 0·6 microgram (millionth of a gram, μg.) is one international unit. One gram of axerophthol from fish livers equals 3,000,000 int. units. The approximate values of some foods are: halibut-liver oil, 16,000,000; cod-liver oil, average 200,000; calf's liver, 46,000; ox liver, 16,000; spinach, 13,000; cream cheese, 4600; butter, 2600; egg yolk, 3000; cheddar cheese, 5500; milk, 2300 international units per 100 grams or 3½ oz.

The daily requirements of adults are reckoned as from 3000 to 4000; of infants 2000 to 2500; and of older children and nursing mothers 4000 to 6000 int. units.

In the absence of vitamin A from the diet, young animals cease to grow, and as soon as stores in the body are exhausted become very susceptible to bacterial infections entering through the mucous membranes. The function of the vitamin is to keep healthy the moist surfaces of the epithelia and prevent hyperplasia, metaplasia, and keratinisation. If the supply of vitamin A is insufficient the fur of animals and feathers of birds become dry and ruffled, and the first visible symptoms are a peculiar and characteristic eye disease similar to xerophthalmia which had been observed in children. The eye disease is a special instance of keratinisation. The only treatment is vitamin A in cod-liver oil or other fish-liver oil. Local treatment is of no avail. Cases of xerophthalmia were described by Budd in 1842, recorded by the explorer Livingstone in Africa in 1857, and Bloch, 1917–1924, observed many cases in Copenhagen.

After the eye symptoms, diets low in vitamin A lead to respiratory infections and broncho-pneumonia. Abscesses at the base of the tongue, suppurating glands, pus in the middle ear, septic nasal sinuses, and infections of the digestive and genito-urinary tracts are noticed in animals. They have also been clinically observed in man. Urinary calculi are common in experimental rats. In India, where stone is prevalent, McCarrison found that foods with vitamin A counteracted their formation. Toad skin is another symptom of vitamin A deficiency.

The epithelium at the junction of the teeth and gums in dogs was shown by May Mellanby to become overgrown and infected with micro-organisms (pyorrhœa). Vitamin A is necessary for the formation of dentine and enamel.

Lack of vitamin A causes degenerative changes in the spinal cord and the medullary sheaths of the sciatic nerves, and to disturbance of the œstral cycles and failure of ovulation. In puppies E. Mellanby has described bony overgrowth and deformity at the base of the skull, causing destruction of the divisions of the auditory nerve with production of deafness.

Hemeralopia or night blindness is specifically due to lack of vitamin A; visual purple is derived from axerophthol. This peculiarity forms a handy method, by means of the dark adaptation test, of examining individuals for their state of vitamin A nutrition. Harris and his colleagues have made a special study of this test, and point out that the technique must be carefully controlled. By night blindness tests 30 per cent. of children in an elementary school were deficient in vitamin A, and 39 out of 40 became normal after treatment. All children in a home where vitamin A was abundantly supplied were normal.

Vitamin D

The early work of E. Mellanby showed that the fats preventing rickets were the same fats as those containing vitamin A, which suggested that vitamin A was the antirachitic substance. There were, however, several differences. McCollum found that cod-liver oil, after aeration at a high temperature, was still antirachitic but not anti-xerophthalmic. The antirachitic substance was stable to heat, and distinct from vitamin A. McCollum called the antirachitic substance vitamin D. The existence of two vitamins in fats was confirmed from experiments with spinach; spinach was strongly growth-promoting and anti-xerophthalmic, but failed to prevent rickets. Spinach and green leaves contain vitamin A, but not vitamin D. Butter contains vitamin A, and very little vitamin D. Cod-liver oil contains vitamins A and D in large amounts. The irregular distribution explains the varied behaviour of fats.

Mellanby later investigated the rickets-producing effect of cereals in the diet. It was counteracted by vitamin D. The addition of calcium salts was also compensatory. The rachitic substance in cereals is phytin. Phytin has no toxic action, but forms an insoluble calcium salt and so removes it from solution; it has also an inhibiting action on the assimilation of calcium and phosphorus. The phosphorus of phytin is not available. Soluble phosphates are necessary in a low phosphorus diet. May Mellanby carried out parallel experiments on the teeth. Perfect teeth were produced with an ample supply of vitamin D in the diet. Decayed teeth were associated with too little vitamin D; and similarly, with cereals in the diet if the calcium, phosphorus, or vitamin D were too low.

The physiological action of vitamin D is to regulate the absorption of calcium and phosphate from the food in the intestine so as to maintain these elements at their proper and optimal level in the blood. In the diagnosis of rickets the estimation of calcium and of phosphate in the blood is of value. A better indication of incipient rickets, however, is the estimation of blood phosphatase, a high blood phosphatase being an early symptom of rickets.

The curative action of sunlight upon rickets was well known, and could not be explained by the existence of a vitamin. The demonstration by Huldschinski, in 1920, of the curative action of ultra-violet light from a mercury vapour lamp made possible the experimental study of the action

of light. Hume and Smith, at the Lister Institute, made the first observations leading to the explanation. Rats were kept in cages with sawdust as bedding. Some cages were exposed to ultra-violet light and others not so. Rats kept in the exposed cages did not get rickets, while the others did. The rats were seen to eat the sawdust. Light had produced in the sawdust an active substance having the effect of vitamin D. Next, foods known to be rachitic were exposed to ultra-violet light; they became antirachitic. The substance so activated was located in the fat, and traced to cholesterol and finally to an impurity in the cholesterol, later identified as ergosterol. Pure ergosterol from yeast on exposure to ultra-violet light is converted into active vitamin D. The new vitamin was isolated and called calciferol, and lettered D_2, as it was not proved to be the same as that in cod-liver oil. Two factors were thus needed in the prevention of rickets—the one ergosterol and the other ultra-violet light. Foods may contain the sterol or the activated sterol. The latter prevents rickets. The former is activated directly in the food, or indirectly after consumption in the fat under the skin. As a preventive measure against rickets the irradiation of foods is not altogether practicable. The food may become unpalatable and vitamin A is destroyed. Irradiated yeast is sometimes given to cows to improve the vitamin D value of their milk. Since calciferol has become a cheap commercial substance the best way of improving the vitamin D content of foods is by its direct addition in suitable quantity, as is carried out with dried milk and with margarine. Calciferol is available for medical use in various forms. Overdosage with calciferol must be avoided. The effect of high doses produces a big rise of calcium and phosphate in the blood, leading to abnormal deposits of calcium phosphate in the vascular system, spleen, kidneys, liver and lungs. The best method of securing vitamin D is in ordinary foodstuffs with the sterol which is activated later by sunlight.

The vitamin D content of foods is expressed in international units. The international unit of vitamin D is 1 mg. of olive oil containing 0·025 microgram of calciferol. One unit daily heals rickets in young rats in 8 days. Coward and Morgan have given the following figures per 100 grams: halibut-liver oil, average 257,000; cod-liver oil, 12,700; butter, average, 100 to 200; cream, 50; milk, 10 to 100; egg yolk, 150 to 400; canned salmon, 600 to 800 international units.

The daily requirement of vitamin D varies with the available sunlight, the amount of sterol in the food, and the proportions of calcium and phosphorus. The League of Nations Nutrition Committee recommends at least 150, and for full growth and vigour 400–500. L. J. Harris advises for infants 1500 units daily as preventive quantity, and 3500 as curative. A suitable supplement is 500 to 1000 units a day for a child or mother. A teaspoonful of cod-liver oil gives 300 units.

Vitamin D_2, or calciferol, is not identical with vitamin D in fish-liver oils. A sterol, 7-dehydrocholesterol, can be made from cholesterol by oxidation and activated by ultra-violet light into vitamin D_3, which is as active as vitamin D_2. The same substance has been isolated from fish liver oils, so it seems that vitamin D_3 and D are identical. Both D_2 and D_3 are equally active in preventing or curing rickets in rats and man; in chicks, however, vitamin D_3 is more active. The production of an active vitamin D from a sterol by ultra-violet light depends upon the structure of the sterol. Many

sterols have been examined, and several give active vitamins, D_4, D_5, etc. Many are present in various foods, and will serve as precursors of vitamin D. In skin the precursor is 7-dehydrocholesterol derived from fish in the food.

Vitamin E

The failure of rats to reproduce on a diet containing cod-liver oil (vitamins A and D) and yeast (vitamins B_1 and B_2), announced by Evans and Bishop in 1922 and corroborated many times, is due to the absence of another fat-soluble vitamin E. Rats do not need vitamin C. Vitamin E is found in the oil of lettuce and green leaves, and in the germ of whole cereals. Vitamin E has been isolated from wheat germ oil, identified and synthesised. Two varieties exist, known as α- and β-tocopherol. Vitamin E resists oxidation, but is destroyed by contact with rancid fats or with iron salts.

The failure of reproduction is "resorption gestation," *i.e.* death of the fœtus in the uterus and its resorption into the maternal organism. Females recover after giving wheat germ oil, but in males the germ cells degenerate and sterility is permanent. The ordinary human diet contains enough vitamin E, but an insufficiency may arise from diets having little green vegetable and too much white flour. Cases of habitual abortion in cattle, and a few cases of persistent miscarriage in women have been treated successfully with wheat germ oil. Other effects of vitamin-E deficiency are degeneration in the kidneys, discoloration of the uterus, muscular dystrophy, and alimentary exudative diathesis. Synthetic α-tocopherol prevents these symptoms.

Vitamin K

A deficiency disease characterised by subcutaneous and intramuscular hæmorrhages with delayed clotting of blood in chickens was described by Dam and Schonheyder, in 1934, and ascribed to lack of a fat-soluble thermostable vitamin K. Their results have been fully confirmed. Vitamin K is most abundant in hog's-liver fat, and green leaves. Two natural substances vitamins K_1 and K_2 have been isolated and identified as 2, 3-derivatives of 1, 4-naphthaquinone. The simple 2-methyl-1, 4-naphthaquinone has similar properties. Clinically, injections of emulsions of vitamin K have produced a reduction in the clotting time of the blood of patients with obstructive jaundice, and hæmorrhagic states in infancy have responded to treatment with the vitamin.

Vitamin B_1

Eijkmann's observations (1897) that fowls on a diet of white rice suffered from a peculiar form of paralysis called *polyneuritis gallinarum*, very similar to the symptoms of beriberi in man, and the cure of both birds and man on being given whole rice or rice bran, were the foundation of investigations on deficiency diseases. Whole cereals, pulses, and nuts were also found to be preventive, whereas white cereals led to the disease. The idea that a disease was due to the absence of some unknown substance from the food is due to Grijns (1901). The idea was strengthened by Fraser and Stanton's

extraction of the preventive substance by means of alcohol, and Funk's isolation of an impure substance, vitamine, which cured polyneuritis in pigeons.

The occurrence of beriberi amongst our troops in the Dardanelles and Mesopotamia during the War of 1914–1918 stimulated further investigations. Numerous foods were tested for their anti-beriberi value by Cooper, and by Chick and Hume at the Lister Institute using the pigeon as test animal. Their data on the cure and prevention of polyneuritis in pigeons were so similar to those on the growth of rats on foods tested for water-soluble B that these two unknowns seemed identical, but there were some differences to cause doubt. Another difference was in the stability to heat. The anti-beriberi vitamin is destroyed by high temperatures, especially in presence of alkalis, but the water soluble growth vitamin is stable. The Vitamin Committee of the Medical Research Council adopted the view of two different vitamins. They called the anti-beriberi vitamin B_1, and the growth-promoting vitamin B_2. The irregularities in distribution were due to differences in amount: yeast contains both equally; wheat germ has more B_1 than B_2; egg white has B_2, but not B_1; and meat has more B_2 than B_1. The comparative vitamin B_1 values of most common foods were examined by Plimmer, Rosedale, Raymond, and Lowndes, but in the absence of a definite standard at that time the data were quoted in terms of dried yeast as 100. Their figures correspond in most cases with the figures by newer methods in terms of the international standard. Vitamin B_1 is most abundant in dried yeast, yeast extracts, germ of cereals, pulses and nuts, with very little in leaves and fruits. Liver, heart, kidneys, egg yolk and cod's hard roe contain appreciable quantities, but lean flesh and fish flesh very little.

The estimation of vitamin B_1 in foods is by the bradycardia method, developed by Harris and Birch. The rate of the heart-beat of rats on a diet deficient in vitamin B_1 falls from about 550 to 300, and is rapidly restored on giving food containing vitamin B_1. The vitamin B_1 value of the food is estimated by determining the amount of the food which restores the heart-beat in comparison with a standard preparation made from rice bran or a standard quantity of pure vitamin B_1. Many foods have been analysed in this way by Baker and Wright. A newer purely chemical method, in which the vitamin B_1 is extracted and determined after oxidation to thiochrome is used by Pyke (1940).

Vitamin B_1 was isolated from rice bran and yeast, and its chemistry fully established. The pure synthetical vitamin, called aneurine or thiamine, is available for medical use and other purposes. Aneurine hydrochloride was adopted in 1938 as standard of measurement. Three micrograms corresponds with one international unit. The amounts of aneurine in some common foods in micrograms μg. per 100 grams are: dried yeast, average 9000; yeast extract, marmite, average 6000; wheat germ, bemax, average 3900; whole wheat, average 900; whole wheat bread, 360; brown breads, 150 to 420; white bread, 30 to 60; oatmeal, 300 to 510; lentils, 630; haricots, 360 to 480; fresh peas, 90 to 120; canned peas, 360; walnut, hazelnut, 450 to 600; vegetables, 30 to 210; fruits, 30 to 120; potato, 90 to 120; lean meats, 90 to 150; pork, ham, lean, 660 to 960; fish, 90 to 120; milk, 70; cheese, 0 to 90; liver, kidney, 450 to 570; egg yolk, 420.

Aneurine is closely connected with the metabolism of carbohydrate. In

the form of its pyrophosphoric ester it becomes co-carboxylase, which is concerned with the removal of pyruvic acid. In the absence, or with too little aneurine pyruvic acid accumulates in the blood, tissues and brain. The excess of pyruvic acid in the brain causes the head retraction, the symptom of polyneuritis, in birds, and is the cause of bradycardia. In man the heart beat increases in rate. The estimation of pyruvic acid in the blood is a possible means of detecting and confirming beriberi.

Aneurine is excreted in the urine. It can be adsorbed on kaolin and determined by the bradycardia method. A better method consists in adsorbing it, extracting with butyl alcohol and oxidising to thiochrome. Thiochrome shows a marked fluorescence in ultra-violet light according to quantity. Harris suggested the estimation of aneurine in urine to ascertain the level of nutrition of vitamin B_1. The resting level of the subject is determined and a test dose of 1050 μg. is given. In normals about 25 per cent. is immediately excreted as estimated 3 hours later. If less is excreted, the body is not saturated and the subject is on too low a level. The normal excretion varies according to diet from 50 to 170 μg. in 24 hours; 90 μg. is subnormal. On the reputed daily requirement of 900 μg. the output is 137 to 233 μg. On diets deficient in aneurine the output is 50 to 80 μg., in cases of beriberi almost 0. Women show lower values during and after pregnancy.

The requirement of vitamin B_1 by man depends on body weight and energy metabolism. The amounts of vitamin B_1 in diets leading to beriberi were calculated by Baker and Wright to be 450 to 750 μg.: a 10-stone man consuming 3000 calories requires 900 μg. daily to protect from beriberi; and a 14-stone man, 1125 μg. Other authors estimate a daily requirement of 900 to 2700 μg. The typical diet of white bread, butter, meat, sugar, and vegetables contains 600 to 1050 μg., and in the case of the poorer classes usually the smaller amounts. A large proportion of the population is consequently on a borderline diet. The effect of borderline diets, *i.e.* hypovitaminosis, can be judged from the numerous experiments on birds and rats. With very little, the animals soon die with typical symptoms; with larger but still insufficient amounts, life is longer; with still more, the animals live longer and die without showing the typical symptoms. Post-mortem examination shows enlarged heart, and intestines full of undigested food. McCarrison found these symptoms in the early stages of beriberi. The chronic enlarged heart and dropsical tissues were considered to be due to too little vitamin B_1. M. J. Rowlands particularly studied the effects of too little vitamin B_1 on rats. He observed distension of the stomach and visceroptosis, and a slower evacuation of the bowels. Resistance to infection was weakened, and bacteria entered the body through the degenerated mucous membranes of the intestinal walls and infected other parts of the body. Drummond, Baker, and Wright (1938), in continuation of Rowlands' work, found that rats had a shorter duration of life, smaller litters, and a greater incidence of gastro-intestinal lesions, especially ulcerations. Constipation, ulcers, and cardiac troubles may thus in many cases be attributed to diets low in vitamin B_1.

The nature and functions of vitamins B_3, B_4, and B_5 which are associated with vitamin B_1 are uncertain.

Vitamin B_2 Complex

Vitamin B_2 is composed of several factors, B_2, B_6, B_7 and at least one more, the filtrate factor or pantothenic acid. The main medical interest of the vitamin B_2 complex is in B_7 or nicotinic acid, which cures the chief symptoms of pellagra. Adermin, B_6, and riboflavin, B_2 are also required.

Generally, but not invariably, associated with a maize diet, pellagra occurs in parts of S.E. Europe, Egypt, and in southern districts of U.S.A. It was first described by Pedro Casals in 1707 under the name of *mal de la rosa*, and attributed by him to a poor diet. Goldberger in U.S.A. eliminated the disease in parts of U.S.A. with an increase of animal foodstuffs. Hence pellagra was attributed to lack of animal protein, or more specifically to absence of one or more amino acids not present in the proteins of maize. Experimental work did not support this idea. As dried yeast, beef, liver, salmon were highly curative but not casein, Goldberger concluded that there was a special pellagra preventing or PP factor. Its distribution in foods was so similar to that of water soluble B, or vitamin B_2, that he thought the two were identical, especially as rats on a synthetic diet containing a preparation of B_1 suffered from a dermatitis seemingly analogous to the dermatitis of pellagra. The substance flavin, or lactoflavin, or more correctly riboflavin, was next isolated from egg white, milk and liver. It cured the rat dermatitis. Pure synthetical riboflavin, however, did not have the same result, and so it was assumed that an impurity, B_6, in the isolated riboflavin was the curative vitamin. Preparations of vitamin B_6, free from riboflavin, cured the dermatitis, but the animals failed to grow. Growth was restored with riboflavin. For rats the two vitamins are thus essential. Rats on a pellagra producing diet of maize and other cereals do not experience the dermatitis. The cereals contain vitamin B_6. Vitamin B_6 is not the PP factor, and rat dermatitis is not analogous to pellagrous lesions in man. Rats are not suitable animals for the study of pellagra. Vitamin B_6 was subsequently isolated and synthesised, and called adermin.

It was known that dogs on a pellagra-producing diet suffered from sore mouth and tongue—" black tongue "—and were cured by diets with yeast, beef, liver, etc. One of the best curative materials of both black tongue and pellagra is liver extract. Elvehjem (1937) isolated from liver extract a substance resembling nicotinic acid. On testing pure nicotinic acid on dogs with black tongue, they were cured. Four cases of pellagra were treated by Fonte *et al.*, and were cured, and later eleven cases were cured by Spies *et al.* with intravenous injections of 30 to 100 mg. daily. Doses of 50 to 1000 mg. have been given to man without harm, but large doses give a sensation of heat with flushing of the face, chest and back and tingling of the skin. Martin, Chick *et al.* found that pigs on a pellagra-producing diet suffered from lesions similar to pellagrous lesions in man, and again nicotinic acid was curative. Rats differ from man, dog, pig and monkey in not requiring nicotinic acid, but all need riboflavin and adermin. In man not all the symptoms of pellagra are cured by nicotinic acid. The absence of riboflavin leads to scaliness and inflammation of the lips, and cracks at the corners of the mouth—" angular stomatitis." Chick, Macrae and Worden have discovered that rats on a prolonged deficiency of adermin suffer from epileptic fits, also previously observed in pigs. For the prevention of

pellagra nicotinic acid, riboflavin and adermin are essential, though the significance of adermin is not clear.

Harris and Raymond devised a method of estimating nicotinic acid applicable to urine and have used it to determine the level of nutrition of this vitamin. The average excretion is 4 to 5 mg. a day. It is higher on diets with more nicotinic acid, such as yeast extract, and the output varies with the intake. In animals with a deficiency of nicotinic acid the output sinks almost to 0.

Vitamin C

In the Middle Ages it was recognised that fresh fruits and vegetables cured and also prevented scurvy, that dried fruits and vegetables had no effect, and that among fruits the orange and lemon were the best anti-scorbutics. A daily ration of not less than 1 oz. of lemon juice was used to prevent scurvy in the Navy; this quantity is man's minimal daily re-requirement.

Holst and Frölich's discovery that the guinea-pig on a diet without fresh fruit or vegetable suffered from scurvy made it possible to compare the antiscorbutic values of fruits and vegetables. These tests, first made by Chick and Hume in 1914–1918 for Army use, were extended to ascertain the effect of cooking and the addition of soda and of citrate to milk. Fruits and vegetables vary considerably in antiscorbutic value. Orange, lemon, tomato, and cabbage have a high value; grapes, beetroot, and turnip a low one. These findings became of practical use in feeding infants to prevent infantile scurvy. Orange or swede juice is given instead of grape juice.

Cooking is destructive of vitamin C; rapid cooking being less harmful than long slow cooking. The heating of vegetables a second time destroys the vitamin. Cooking with soda is destructive, as also is bicarbonate and the use of citrate with milk. Vitamin C is very sensitive to heat in the presence of air, and still more so with alkali. There is, however, little or no destruction of vitamin C in the canning of fruits and vegetables by modern methods in the absence of air. Jams and marmalade produced by long boiling do not contain vitamin C. Condensed and dried milk made by processes in which air is excluded retain their vitamin C value. Milk is low in vitamin C. Orange juice can be similarly concentrated and combined with dried milk. A most important source of vitamin C is sprouted peas, beans and grains of wheat or oats. Sprouted seeds are very valuable when fresh fruits and vegetables are scarce, and on long expeditions far from a base, though in these cases synthetical ascorbic acid is now taken.

Vitamin C was isolated from lemon juice by Waugh and King, and found to be identical with a hexuronic acid obtained from suprarenal gland by Szent-Gyorgyi. The best natural source is fresh paprika. Its chemistry is established, and the synthetical product is known as ascorbic acid or cevitamic acid.

Ascorbic acid is a reducing agent, and decolorises 2, 6-dichlorophenol-indophenol. This reaction, discovered by Tillmanns, was employed to distinguish lemon and fresh fruit juices from artificial and boiled juices. This reducing property has become (under properly controlled conditions) the standard method of estimating ascorbic acid in fruits and vegetables. The amounts of ascorbic acid in mg. per 100 grams in some common fruits

and vegetables are: orange and lemon juice, 60; apple, 3; banana, 15: grapes, 3; cabbage, 100; spinach, 40; potato, new, 20; old, 8; lettuce, 5; human milk, 6; cows' milk, 2.

Vitamin C or ascorbic acid is excreted in the urine, and is estimated in acid solution by the reduction of 2, 6-dichlorophenolindophenol. The daily excretion varies from 15 to 30 (mean 20) mg. on a diet with plenty of fruit and vegetable, and from 5 to 11 mg. on diets with little antiscorbutic food. Many of the body tissues contain considerable quantities of ascorbic acid, especially the suprarenal, intestinal mucosa, liver and eye lens. In scurvy in guinea pigs these organs have little or even none. Harris and Ray devised the saturation test for assessing the level of nutrition of the individual. The test consists in feeding a large dose, 700 mg. or more, of ascorbic acid as such or as orange juice and ascertaining if the output rises above that previous to the dose. If there is no rise, the body is unsaturated, but if 50 per cent. of the dose is excreted in 24 hours the body is saturated. A considerable number of people so tested were unsaturated. A simpler but less reliable test which serves as a guide is Gothlin's capillary resistance test. A pressure band is applied above the elbow. Bending the elbow produces increased pressure, and minute hæmorrhages appear if the capillaries are weak. Many children tested in Sweden had a low antiscorbutic intake, and improved on being given more. Ascorbic acid can also be estimated in blood: 0·7 mg. in 100 ml. is normal; 0·4 to 0·69 is subnormal.

Man's minimal requirement of ascorbic acid to prevent scurvy is 1 oz. of lemon juice, or 20 mg. ascorbic acid. Höjer found that the teeth of guinea pigs rapidly degenerated with too little vitamin C, and that at least twice the minimal quantity was needed for prevention. Man would thus require 40 mg. Saturation tests have shown that 60 to 70 mg. are daily required. Babies are said to require 10 mg. daily. It is easier to give the figures as 1 mg. per kilo for man and woman; and 2 mg. per kilo for babies, pregnant and nursing mothers, and preferably also for older children.

A marked drop in the urinary excretion of ascorbic acid is observed at times of influenza or feverish cold. Patients with acute rheumatism, or tuberculosis, or osteomyelitis, or rheumatoid arthritis excrete less than non-infected control subjects. Such patients are in a state of lower saturation. In infections there is increased use or destruction of ascorbic acid in the body. There is no connection between ascorbic acid and antitoxin formation, but a connection has been traced with complement. The special action of ascorbic acid is, according to Wolbach, the production and maintenance of intercellular material, cementing the individual cells into a tissue. This explains the weakness of the blood vessels allowing hæmorrhages, and the lack of tone in skeletal muscles. The general disintegration of the tissues begins before the appearance of pain and the acute symptoms of scurvy.

Vitamin P

It has been supposed that the fragility and permeability of the capillary walls to plasma proteins is due to a separate vitamin P, but this has not been verified and is the result of too little ascorbic acid.

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SCURVY (SCORBUTUS)

Scurvy belongs to the group of "deficiency" diseases, being due to the absence from the diet of a sufficiency of a specific "accessory food factor" or vitamin. It consists in a general disorder of nutrition, characterised by debility, mental apathy, anæmia, sponginess of the gums, ulceration of the mouth, and a tendency to hæmorrhage.

Ætiology.—The theories, long entertained, that scurvy is the result of poisoning by a ptomaine or of a deficiency of potassium salts or alkaline compounds in the blood, have now been abandoned, and it has been abundantly proved by the experimental work of Holst and Fröhlich and their successors that the disease results from a deficient intake of the anti-scorbutic vitamin C (ascorbic acid) (see Vitamins, p. 449). Bad hygienic conditions appear to favour a development of the disease; but as a rule it seems to require an exposure of from 4 to 8 months to scorbutic conditions before it appears.

Pathology.—The pathological changes are: (1) An increased permeability of the capillaries to the red cells. This is responsible for hæmorrhages into the skin, subcutaneous tissues, under the periosteum, into the joints, and sometimes into the pleura and pericardium. (2) An interference with the normal growth of the erythrocytes. This produces an anæmia, which is usually orthochromic and normocytic, but may be microcytic and, on rare occasion, macrocytic. (3) A change in the bone, the result of unorganised provisional bone, which occupies a wide area at the growing ends of the bones. This bone is very friable.

Symptoms.—Scurvy is a disease of insidious onset. The earliest symptoms are weakness and lassitude, dizziness on standing up, and bruising or bleeding from the gums on slight provocation. Pains in the lower limbs are often complained of, and there may be a characteristic hardness of the calf muscles. Follicular keratosis is an early sign (Wiltshire), and in appearance is similar to the hyperkeratosis of follicles met with in other malnutritional states. Meanwhile the patient looks ill. The face becomes sallow and drawn, and the eyes lustreless and encircled by dark rings.

Such symptoms may precede by a few days, or even weeks, the more characteristic signs. Among these the most striking, though not necessarily always present, are the changes in the mouth. The gums begin to swell, especially around stumps or carious teeth, and as the process goes on the swelling may become so great as to amount to a veritable hypertrophy, so that the teeth become buried in a mass of soft fungous tissue of a bluish or purplish tint. Ulceration quickly follows along the margins, the process being accompanied by the discharge of a sanious fluid which imparts great fetor to the breath. Finally, the teeth become loosened in their sockets and may fall out, while necrosis of the alveolar edges ensues.

Equally characteristic and constant are hæmorrhages into the skin and subcutaneous tissue, which assume the form either of petechiæ or of ecchymoses. The former occur as small red or purple spots resembling flea bites, which appear first around the hair follicles of the lower extremities, and impart, by the elevations which they produce, a slight feeling of roughness to

the skin. They remain for about a week, and then gradually fade into greenish spots, which soon disappear; their disappearance being followed by a slight degree of desquamation. The production of the petechiæ is determined by the slight irritation caused by the friction of the clothes, and hence they are always to be found first on the outer surface of the leg, and the outer and anterior aspects of the thigh. Here and there the petechiæ may coalesce into larger areas or maculæ. In severe cases the slightest pressure on the skin is sufficient to cause ulceration, the ulcers having thick edges and bleeding surfaces with offensive discharge. Such ulcers may spread rapidly and invade surrounding tissues, giving rise in some cases to dangerous, and even fatal hæmorrhage. Ecchymoses, the other characteristic surface lesion of scurvy, are produced by hæmorrhage into the subcutaneous or intermuscular tissue. They may occur spontaneously or as the result of injury, and vary greatly both in size and extent, being commonest in the lower extremities, where they may form quite large swellings. The part affected by them is brawny, tender, and pits on pressure, the indentation persisting longer than it does in ordinary œdema. The skin over them is red, shiny and hot. Such effusions are common, also, in the popliteal space and in the bend of the elbow, as well as in the loose tissue around the malleoli, and beneath the muscles of the jaw. In these situations they form indurated swellings which fill up the natural hollows of the part, and greatly interfere with the movements of the adjacent joint. Where such effusions occur over the shins they are apt to be mistaken for syphilitic nodes. There is no marked tendency to bleeding from the internal organs; but hæmorrhages may take place from the mucous surfaces. Of such hæmorrhages, epistaxis and bleeding from the mucous membrane of the mouth are commonest. Bleeding may also occur from the mucous membrane of the intestine when there is a coexisting diarrhœa. Hæmoptysis, hæmatemesis and hæmaturia are rare. Hæmorrhagic effusion into the pleura and pericardium has also been described. Not uncommonly hæmorrhage occurs under the conjunctiva, and may be so extensive as appreciably to raise the ocular layer, leaving the cornea at the bottom of a pit surrounded by swollen and red conjunctival membrane.

As the disease progresses anæmia becomes a marked feature, though its degree has no constant relation to the extent of the ecchymoses. The blood picture is that of a secondary anæmia, the red cells being sometimes reduced to 2 millions per c.mm, or less. Poikilocytosis and anisocytosis are common, nucleated forms rare. The hæmoglobin is reduced roughly in proportion to the red cells, but the colour index may be less than 1·0 and on rare occasions over 1·0. Observers differ as to the white cell count. Some have described a leucopenia; others a moderate lymphocytosis. All are agreed that polynuclear leucocytosis is not present unless inflammatory complications coexist. Apparently the coagulability of the blood is not diminished, and the serum is not hæmolytic; but although the presence of a diminished alkalinity has been alleged our knowledge of the chemical changes in the blood is still limited.

Alimentary symptoms may be absent. Appetite is not necessarily impaired; but dyspepsia may be present, as the result of the dietetic conditions which produce the disease. Constipation is the rule; but the conditions in which scurvy develops often favour the production of a

dyspeptic type of diarrhœa with sanguineous discharge. The urine may be albuminous.

Complications—Gangrene of the lung is one of the most frequent and dangerous of the complications. Bronchitis and bronchiolitis also occur. Night blindness is met with not unfrequently, and is due to an associated deficiency of vitamin A.

Diagnosis.—If all the characteristic symptoms are present, and if the disease arises simultaneously in a number of subjects in circumstances known to favour its development, the diagnosis is easy. Difficulty only occurs when one has to deal with sporadic cases, such as those of land-scurvy, met with in ill-fed individuals.

The disease which perhaps most closely resembles it is purpura hæmorrhagica (morbus maculosus of Werlhof); but in this the affection of the gums is absent, and the hæmorrhages have not, as they have in scurvy, an inflammatory character. Mercurial cachexia, which in many points closely simulates scurvy, is now but rarely seen, and an inquiry into the history will usually lead to a correct conclusion. Acute lymphatic leukæmia, which is so often marked by ulceration in the mouth, can be distinguished by an examination of the blood.

Prognosis.—This, except in the severest cases, is favourable, provided that proper treatment is adopted. The outlook depends less upon the severity of the local lesions than upon the condition of the internal organs, and the presence or absence of complications. Extensive bronchitis or severe diarrhœa is of grave omen, and gangrene of the lung nearly always proves fatal. Even in uncomplicated cases, sudden death may be brought about by severe hæmorrhage or heart failure. In the most favourable circumstances convalescence is apt to be protracted, and when recovery is otherwise complete there may still be results left behind in the shape of cicatrices in the skin or partly anchylosed joints.

Treatment.—Prophylaxis consists of a diet containing from 25–50 mg. of ascorbic acid (500–1000 international units), for this will prevent scurvy. (For details see p. 449.)

If the disease develops, a sufficiency of ascorbic acid should be administered at once. This can be given either as pure ascorbic acid, or in the form of the juice of a lemon, orange, or of grapefruit, or blackcurrants, all of which are rich in ascorbic acid. The patient will recover most quickly if 1000 mg. of pure ascorbic acid is prescribed daily for 3 to 5 days. After this, at least 100 mg. of ascorbic acid should be given in the form of orange juice until complete recovery has occurred. It is usually unnecessary to administer iron, since the anæmia recovers rapidly, but it is advisable to prescribe an adequate amount of the other vitamins, because the patient may also be suffering from a lack of these. Local treatment for the gums is advisable, the teeth should be scaled, and the gums sponged with hydrogen peroxide.

The Sub-Scurvy State

Recent work has shown that many people are in what is termed the sub-scurvy state as the result of diets containing very little ascorbic acid. The symptoms are latent until an individual is wounded or operated on. Then the wounds heal very slowly and the operation wounds are apt to break

open. Again, ulcers are liable to bleed. In such cases the diet should always be considered, and if found to be unsatisfactory, 2000–3000 mg. of ascorbic acid should be given. In cases of pyloric stenosis 300 mg. should be administered intravenously for 3 days prior to operation, and the usual dose immediately after it.

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INFANTILE SCURVY

Infantile scurvy—known on the Continent as Barlow's disease—is identical in its pathology with the adult form of the disease, its special clinical features being due to the anatomical and physiological peculiarities of early life.

Ætiology.—The disease usually appears between the eighth and twelfth months — both sexes being equally affected. As in adult scurvy, the essential cause is the absence from the dietary of a sufficiency of anti-scorbutic vitamin. Any heating of milk reduces the amount of vitamin C present. Certain commercial processes in condensing or drying milk may completely destroy the vitamin. Pasteurisation is the least harmful process. In any case the addition of vitamin C to the diet is so easy that it is better to make milk a safe food by some heating process rather than to rely on it as a source of anti-scorbutic vitamin. A few cases have been recorded in which the child had been fed on the breast only ; it is probable that in these the mother's diet had been deficient in fresh constituents.

Pathology.—The chief changes are in the neighbourhood of the bones. A section made across a limb at the site of a swelling shows that the periosteum is hyper-vascular, thickened and separated from the subjacent bone by a layer of partially organised blood clot. There is no sign of inflammation, and no hard bone is formed in the periosteum, except in very long-standing cases ; in which circumstances the muscles surrounding the bone may be infiltrated with blood or serum, and look sodden. The bone exhibits rarefaction, and may be fractured. There may be hæmorrhagic effusions into the joints or serous cavities. The organs exhibit no characteristic change.

Symptoms.—The onset is gradual, the first symptoms noticed being often a refusal of food, along with fretfulness and restlessness. There is a tendency for the child to resent being handled. Meanwhile the general nutrition is usually unimpaired, and the child's colour is often fresh and healthy looking. After a variable period the more prominent symptoms appear. The most striking of these is extreme tenderness of the legs, which causes the child to scream loudly when touched or even when approached. In a well-marked case some swelling will be found, usually of the lower end of the femur or upper end of the tibia. Involvement of the arm bones is much rarer. The skin over the swelling is often tense and glossy, and may be slightly œdematous ; but there is no local heat. Soft crepitus may be elicited on handling the limb, indicating a fracture or a separation of the epiphysis. In some cases hæmorrhage takes place into the orbit, giving rise to proptosis and ecchymosis of the eyelid. Rarer sites of hæmorrhage are around the ribs, clavicles or bones of the skull.

Changes in the gums are not nearly so pronounced as in adult scurvy, and are not usually present, unless some teeth have been cut; in that case the gum around them is usually swollen and of a purplish colour. Petechiæ and subcutaneous ecchymoses are very rare in infantile scurvy, and hæmorrhage from mucous membranes is not common. Hæmaturia, however, is not infrequent, and red blood cells, in microscopical examination, are nearly always present. Fever is not a conspicuous feature, but may be present if extensive hæmorrhages have taken place; it rarely exceeds 102° F. The blood changes are the same as have been described in the adult form of the disease.

Diagnosis.—This is easy in a well-marked case, provided the leading features of the disease are known to the observer. The screaming of the child on examination, the swelling and tenderness of the legs, and the condition of the gums leave no doubt as to the nature of the affection with which one has to deal. All cases, however, are not so pronounced in type. Not infrequently one encounters mild or incipient forms which it is easy to overlook. In these, tenderness when the child is handled, or when it is put in the bath, may be the only symptom. In other cases again, slight sponginess around the incisor teeth may also be present, or one may have to deal with an apparently causeless hæmaturia. In any case in which there is doubt two points will help. One is the nature of the feeding. If this has been of such a kind as is known to favour the development of the disease the diagnosis will be greatly strengthened. The other point is the application of the therapeutic test. If the symptoms present are really due to incipient scurvy then they will certainly disappear rapidly so soon as appropriate treatment is begun; if they fail to do this, then some other condition must be thought of.

Infantile scurvy may be mistaken for rheumatism, although the mistake should not occur if it be remembered that acute rheumatism is hardly ever seen below the age of 2. The distinction between scurvy and suppurative periostitis or epiphysitis is much more difficult, especially if the gum changes are absent. A very high temperature and much constitutional disturbance are against scurvy. The nature of the diet will also be of weight in the diagnosis. A skiagram will be of great assistance in coming to a conclusion. In scurvy the shadow due to subperiosteal hæmorrhage, and a sharp dark epiphyseal line, are characteristic.

The absence of swelling in the affected limb and of the other symptoms of scurvy should distinguish those cases of infantile paralysis in which there is much tenderness of the paralysed leg, and the blood examination should enable one to differentiate a case of acute leukæmia or chloroma.

Prognosis.—This is quite favourable, provided the disease is recognised in time and proper treatment adopted. Nothing in therapeutics is more striking than the rapidity with which such patients improve on a change of diet, although some degree of thickening of the bones may persist for a long time. Death, when it occurs in the more severe cases, is usually the result of intercurrent disease, such as broncho-pneumonia and chronic diarrhœa, although sudden hæmorrhage, cardiac failure or exhaustion may occasionally lead to a fatal issue.

Treatment.—The first step is to bring the disease under control by administering vitamin C in concentrated form as ascorbic acid. This can be given in tablets by mouth, crushed just before use, in a dose of 50 to 100

mg. daily for 2 or 3 days for an infant of 9-10 months. During this period dietetic changes can be made, such as the introduction of orange juice or tomato juice, the institution of mixed feeding (baked potato is particularly valuable), and a change from any over-heated milk or milk product to plain milk just brought to the boil for safety. In very severe cases ascorbic acid can be given intravenously. Iron is useful if there is anæmia present.

Scorbutic infants should be handled carefully, and the clothing so made that it can be easily taken off and on. If it is necessary to move the child about it should be carried on a pillow. The affected limb should be steadied by light splints or wrapped in wet towels, which, if allowed to dry in position, afford considerable support. In mild cases a covering of cotton-wool secured by a light bandage is sufficient protection.

RICKETS

Definition.— Rickets is a disease of nutrition occurring in early childhood. It mainly affects the growth of the bones, but may be accompanied by tetany in some cases. Associated nutritional disorders produce anæmia and a tendency to catarrh of the mucous membranes in many instances.

Ætiology.—Various theories have been held in the past as to the cause of rickets, but it is now clear that it is essentially due to absence of vitamin D in sufficient amounts to promote adequate calcification of growing bones. The fault is usually dietetic and not only because of deficiency of vitamin D containing foods but also because excess of carbohydrate promotes more rapid growth than calcification can cope with. The ultra-violet rays of sunshine can manufacture vitamin D in the skin. Hence all those conditions which prevent the free access of unfiltered sunshine to the skin of the growing infant may be regarded as predisposing to rickets.

Pathology.—The chief changes are in the bones. Section through the end of a long bone shows that ossification, instead of proceeding in an orderly way, is greatly disorganised. In the zone of proliferation of the cartilage the cells show excessive multiplication, and are arranged irregularly instead of in columns. A broad bluish area results, which is the cause of the thickening of the epiphysis. In addition to this, calcification between the cells is defective, the affected area shows excessive vascularity, and the new bone formed is soft and deficient in lime. The whole process has been summed up in the statement that " there is an excessive preparation for ossification and a defective accomplishment of it." In addition, the vascular layer of the periosteum is thickened and the marrow congested.

Chemical analysis shows that the bones contain only from 30 per cent. to 50 per cent. of calcium, instead of the normal 60 per cent. or more. They may show signs of old or recent fracture. Other organs show no characteristic change.

Symptoms.—The disease can rarely be recognised before the sixth month. Amongst the earliest indications to attract attention are restlessness and irritability, sweating about the head, especially when asleep, and a tendency on the part of the child to kick off the bedclothes at night. There is no wasting, indeed the infant may be abnormally fat, though usually flabby and pale. The appetite is capricious.

As the disease progresses, it will be found that dentition is delayed, and that changes in the bones become manifest. They first show themselves in the epiphyses of the ribs, which enlarge and form a row of knobs down the sides of the chest (the rickety rosary). Enlargement of the epiphyses of the bones of the limbs then takes place, being most conspicuous at the lower end of the radius.

The softening of the bones leads to various deformities. The chest sinks in at the line of junction of the ribs and cartilages, so that a broad groove forms, running downwards and outwards towards the axilla (Harrison's sulcus). The bones of the limbs bend, the femur curving forwards and outwards, and the tibia bending sharply forwards and often also outwards at its lower third; there may also be a curving of the upper part, leading to "bow-leg." The humerus and bones of the forearm may become bent in an outward direction, as the child sits supporting itself on the hands, and the clavicle may show a sharp kink at the junction of the inner and middle third. The pelvis becomes flattened. Greenstick fractures of the limb bones are not uncommon.

The skull shows striking changes. It is usually somewhat enlarged, elongated and flattened on the vertex (box head), the anterior fontanelle remaining widely open long after the normal period of closure at the eighteenth month. There may be pronounced thickening of the frontal and parietal eminences, leading to the so-called "hot-cross bun" or bossed head, especially in cases complicated by anæmia with enlarged spleen. Areas of defective ossification in the parietal and occipital bones in the neighbourhood of the occipital suture (cranio-tabes), which yield on pressure a characteristic parchment-like sensation, are not uncommon, especially in young infants, even before six months of age.

The muscles are often so weak and flabby that paralysis is simulated, and the ligaments may be so lax that the limbs can be bent into almost any position ("acrobatic rickets"). In consequence also of the laxity of ligaments, kyphosis often develops in the lower lumbar region (rickety spine).

The blood usually shows a varying degree of anæmia of the hypochromic type, and in a few cases the changes are so profound as to resemble those met with in chlorosis.

The digestive system is usually deranged. Chronic diarrhœa with pale, offensive stools is not uncommon. The abdomen is distended so that the child has a pot-bellied appearance. In the production of the distension, muscular weakness, intestinal fermentation, and the pushing down of the diaphragm by the sinking in of the chest all play a part. The edge of the liver can often be felt at a lower level than normal, partly from displacement and in part from enlargement through fatty change. The spleen is also palpable in a considerable number of cases, although this is due more to its being pushed down than to actual enlargement.

In the respiratory system bronchial catarrh is very often present, and not uncommonly results in broncho-pneumonia. In the nervous system the disease shows itself by general nervousness and irritability, and in some cases by the development of laryngismus stridulus, tetany, or even convulsions, of all of which rickets is a strong predisposing cause.

Diagnosis.—In a fully developed case the diagnosis is easy. Early cases, and those in which the rickety element is overshadowed by some

complication, such as broncho-pneumonia or diarrhœa, are more apt to be overlooked. The suggestive points will be delayed dentition, an open fontanelle, and the presence of the rickety rosary. A skiagram will show some cupping of the diaphysis; the epiphyseal line will be irregular and ill-defined, and the epiphysis itself poorly ossified. There will also be a tendency to osteoporosis throughout the whole bone. The appearance of the epiphyses of the carpus and tarsus may be retarded.

The rickety head is apt to simulate hydrocephalus, but in the latter condition the skull is more globular, and bulges above the ears, the fontanelle is tense, and the eyeballs, in marked cases at least, pushed downwards. The kyphosis of rickets may be mistaken for spinal caries; but in the former the bend straightens out as a rule when the child is held up by the armpits. In severe cases this may not happen, and a radiograph may be required to settle the diagnosis. If the muscular weakness is pronounced infantile paralysis may be imitated; but the history, the retention of the reflexes, and the presence of other signs of rickets should prevent mistakes.

Prognosis.—Rickets is not fatal *per se*, and usually passes off spontaneously after the second year, although the deformities of the bone may persist for a long time. Even these, however, have a wonderful way of righting themselves without any special treatment. On the other hand, rickets is a very serious complication of other diseases, especially of broncho-pneumonia and diarrhœa, and adds greatly to their fatality if present, so that the dictum of Sir William Jenner that "in its indirect results rickets is one of the most fatal diseases that peculiarly affect childhood" is still perhaps true.

Treatment.—Rickets can be prevented if the child is properly fed and cared for. Breast-feeding for the first 9 months is the best safeguard, provided that the mother's diet is satisfactory; but it must always be remembered that the disease is apt to develop in children who are kept *too long* on the breast. After weaning, the premature and excessive use of starchy foods must be avoided. Care should be taken that the diet contains an adequate amount of animal fat. Plenty of fresh air, sunlight and exercise are also important factors in prophylaxis. It is probable that all infants in temperate and cold climates require a daily supplement of cod-liver oil ($\frac{1}{2}$ to $1\frac{1}{2}$ teaspoonfuls) between six months and two years of age.

If the disease has already developed, the diet should be altered in accordance with the requirements indicated above, the most important point usually being to increase the allowance of cow's milk, which should not fall below $1\frac{1}{2}$ pints per diem during the second year of life. Yolk of egg is also a valuable food. Cod-liver oil and halibut-oil (or one of the artificial substitutes containing vitamin D) are most useful, having a specific influence on the disease; but iron may also be given with advantage if there is anæmia. It is wise to start with a pure vitamin D concentrate in adequate dosage for about a month to bring the disease under control. Sun-baths or exposure to the rays of the mercury-vapour lamp have a definitely curative effect.

To prevent bending of the legs, long splints may be applied, projecting beyond the feet, so as to make standing impossible. Orthopædic treatment may be required for the more permanent deformities. Alimentary and respiratory complications should be treated by the measures appropriate to them.

Late or Adolescent Rickets

This term is applied to a disease apparently identical with ordinary rickets in its bony changes, but which sets in much later, usually between the ninth and fourteenth years. The patient may have been the subject of ordinary rickets in earlier childhood—hence the use of the term "recrudescent rickets"—or the disease may have appeared at the later age for the first time. Nothing is known of its causation, but in some cases it is associated with fibrosis of the kidneys (renal rickets) or with cœliac disease.

The manifestations of the disease are practically confined to the skeleton, the long bones being particularly affected. The epiphyses become much enlarged, and pronounced deformities ensue as the result of bending. The skull escapes almost entirely, and there is no tendency to any disease of the internal organs, except in the renal cases, or to complications.

The disease is not dangerous to life; but the deformities may be lasting. The general treatment is the same as that of ordinary rickets; but most cases will require the help of the orthopædic surgeon.

"Fœtal" and "congenital" rickets are ambiguous terms which have been loosely used to cover several distinct pathological conditions, amongst which are achondroplasia, mollities ossium, and osteogenesis imperfecta. They are best avoided. So-called "scurvy-rickets" and "acute rickets" are identical with infantile scurvy, although rickets often coexists with the latter, seeing that both are due to faulty feeding.

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BERIBERI

Synonyms.—Polyneuritis Endemica; Hydrops Asthmaticus; Kakke; Barbiers.

Definition.—A dietetic disease or group of diseases especially related to deficiency in vitamin B_1, occurring frequently in tropical regions where polished rice constitutes the main article of dietary. It is characterised by neuritis of the peripheral nerves and vagus. Several different clinical types are described.

Ætiology.—The rice-eating populations of India, Japan, Malaya, the Dutch East Indies and Philippine Islands are mainly affected, but the disease is also endemic in Newfoundland and Labrador, where the population eat chiefly white wheaten flour. Though the disease is specially rife amongst people eating polished rice, rice *per se* is not essential, any dietary deficient in the antineuritic vitamin B_1 being a potential source of danger. Parboiled and undermilled or husked rice are not deficient in vitamin B_1. During milling the husk, pericarp and germ, which are rich in protein, fat, phosphorus and vitamin B_1 (see p. 445) are removed, leaving the white polished rice poor in these constituents. Milled rice, white flour, breakfast cereals, macaroni, spaghetti and cane sugar contain practically no vitamin B_1. This vitamin, known also as "aneurine" or "thiamine," was synthesised in 1937 in crystalline form (1 mg. = 300 international units), and is now available

for therapeutical purposes. It is mainly found in yeast, marmite, whole seeds, the germ of cereals, pulses and nuts. Aneurine is a precursor of cocarboxylase, which removes, by oxidation, an important intermediary product of carbohydrate metabolism—pyruvic acid—from the tissues and blood. The chemical tests for the estimation of pyruvic acid and aneurine are dealt with on p. 447. Excess of pyruvate can be demonstrated in the blood in beriberi, the value rising from a normal of 0·4–0·6 mg. to 1–7 mg. per 100 c.c. The quantity normally present in the cerebrospinal fluid is also increased. When no complicating factor is present, 5 mg. of vitamin B_1 will restore the blood to a normal value in 10 to 15 hours.

Pathology.—Cases of so-called " dry beriberi " rarely come to autopsy. In " wet beriberi " there is an acute congestion of the mucosa of the duodenum and lower end of the stomach, sometimes associated with pin-point hæmorrhages. The peripheral nerves show a Wallerian degeneration, with possibly an axonal degeneration of the neuron involved. The sheath of Schwann may exhibit multiplication of its nuclei and invasion by leucocytes. The vagus and sympathetic system may present stigmata of degeneration, and sometimes the anterior-horn cells of the spinal cord and the nuclear connections of the vagus in the floor of the fourth ventricle are said to be implicated. The cardiac muscle may show œdema and degenerative changes, while the naked eye appearances are those of fatty degeneration associated with dilatation and hypertrophy, especially involving the right side. Nutmeg-liver, œdema of the soft tissues and effusions into the serous cavities are common. Adrenal hypertrophy, similar to that described by McCarrison in avian polyneuritis, has been recorded in man. In experimental animals the process underlying the nervous manifestations is a dysfunction and non-inflammatory; it has in consequence been suggested that the term " neuropathy " is more accurate than " polyneuritis." In long-term deficiency, however, damage to tissues may ensue which cannot be repaired merely by correcting the vitamin deficiency.

Symptoms.—There is generally a latent period of some two to three months before deficiency symptoms become manifest. Typically the onset is gradual, being characterised in the initial stages by epigastric discomfort, nausea and perhaps vomiting and diarrhœa. Later, polyneuritis, with palpitation, shortness of breath and weakness develop, the subsequent clinical picture varying according to involvement of the peripheral nerves, the vagus, or the sympathetics. The disease runs an afebrile course, except possibly in its early stages. Several different types are described:

(1) Larval or Ambulatory Cases.—There is numbness of the legs with patchy anæsthesia and diminution of knee-jerks, all of which quickly disappear if the condition is recognised and a more varied diet containing vitamin B_1 be given.

(2) Ordinary Beriberi.—(*a*) *Wet form.*—Prodromata include paræsthesias and heaviness of the limbs. The knee-jerks are at first exaggerated and then lost. Tenderness of the calf muscles, blunting of sensation, and patches of hyperæsthesia and anæsthesia appear. The patient becomes weak, and cannot rise from the squatting position. Varying grades of œdema, at first involving the subcutaneous tissues over the tibiæ, appear and, later, effusions into the serous cavities with water-logging may develop. Shortness of breath, dyspnœa and tachycardia indicate involvement of the cardiac

nerves. There are manifestations of dilatation of the heart, especially the right side (see pp. 857 and 956). Several factors may contribute to the œdema: (1) intracellular œdema associated with failure of cell nutrition; (2) cardiac failure or an increased tension of the capillaries; (3) decreased plasma proteins; and (4) secondary renal insufficiency. When the nervous manifestations are slight and the patient can still do muscular work, œdema is more likely to develop. Sudden death may occur without clinical evidence of cardiac involvement. (*b*) *Dry form.*—This is similar to the above except that œdema is absent and the disease runs a more chronic course. The onset is insidious, gastro-intestinal disturbances may be absent, the dominant features being wasting and weakness of the muscles, associated perhaps with cardiac irritability. Wrist drop and the high-steppage gait may be present, but though the patient walks unsteadily there is no true ataxia or Rombergism. Clinically, the disease closely resembles alcoholic neuritis and that encountered in pellagra, both of which are now regarded as being due to a deficiency in B_1. Wet beriberi may develop at any time, but this is less likely if the neuropathy is sufficiently severe to keep the patient resting.

(3) Acute Fulminating Beriberi.—Cardiac symptoms may predominate from the onset, or suddenly supervene in either the wet or dry forms. Cardiac decompensation of the congestive variety (see p. 856) rapidly ensues. Alteration of the voice or aphonia resulting from pressure of the dilated right auricle on the recurrent laryngeal nerve has been reported. The diaphragm also may be paralysed. Owing to renal insufficiency there may be a scanty urine containing albumin and casts, and a high blood urea which falls as the output of urine increases with treatment. Death may supervene in a few hours to a few days.

(4) Infantile Beriberi.—This disease occurs especially in the Philippine Islands and Japan, where it is responsible for many deaths in breast-fed infants whose mothers are affected with latent or clinical beriberi. More than 50 per cent. of cases show symptoms between the third and fourth weeks of life. The disease occurs in both acute and chronic forms. In the latter gastro-intestinal features like anorexia, vomiting, diarrhœa or constipation occur, associated with wasting, pallor, œdema, mainly involving the face and extremities, dyspnœa, and other evidences of cardiac insufficiency. Aphonia is often striking, and loss of knee jerks is present in 75 per cent. of cases. In the acute form death may occur with great rapidity, the infant developing convulsive attacks, suffering severe pain and presenting cyanosis, dyspnœa and muscular rigidity.

(5) Other Clinical Types.—These include *ship's beriberi*, which is now rare amongst sailors, and *pellagroid beriberi*, in which there is a mixed deficiency, the skin and mucosa membrane lesions being cured with nicotinic acid and the neuritic manifestations with vitamin B_1. *Secondary beriberi* may be associated with (1) gastro-intestinal diseases leading to defective absorption of vitamin B_1, (2) chronic alcoholism, or (3) pregnancy, diabetes, febrile states, or diseases increasing metabolism which lead to a relative deficiency by increasing the demand for B_1.

Epidemic Dropsy, which is met with in India and other parts of the tropics, occurs in epidemics amongst rice eaters and is often classified as a type of beriberi. Gastro-intestinal features, especially diarrhœa, are common.

Some degree of fever is, however, generally present, progressive anæmia is frequent, a vascular mottling of the skin over the tibia and inner side of the thigh is not uncommon, as well as a tendency to hæmorrhages involving the mucous membranes. Clinical evidence of neuritis is not obvious; the knee jerks are generally normal, and cutaneous anæsthesia and deep hyperæsthesia of the muscles absent. Some hold it is due to toxic substances developed in degenerating or diseased rice; others that it is caused by poisons in mustard oil. Its relationship to nutritional œdema in which there is a lowering of plasma proteins, does not appear to have been adequately investigated. Though simulating wet beriberi in some respects, there are obvious clinical differences, and the disease is probably not a pure B_1 deficiency.

Diagnosis.—Wet beriberi has to be diagnosed from cardiac failure, nephritis and severe ancylostomiasis, while the dry form has to be differentiated from alcoholic and arsenical neuritis, tabes dorsalis and progressive muscular atrophy. The dietetic history is important, and multiple cases of neuritis, especially if associated with œdema, should always suggest beriberi. Vitamin B_1 is greatly decreased or practically absent from the urine in cases of beriberi, and this test (p. 447) may determine the diagnosis in doubtful cases. Volhard's diuresis test may also be helpful, since there is water retention in beriberi.

Prognosis.—This depends on the institution of appropriate treatment at a reasonably early stage of the disease. Aneurine promptly cures the early neurological manifestations of "dry" beriberi, and relieves many of the advanced cases. It improves the cardio-vascular disturbances in "wet" beriberi, and is often a life-saving measure in acute fulminating beriberi with cardiac failure, provided it be given intravenously in adequate dosage. If the patient survives the first two weeks and an adequate maintenance dosage of B_1 be continued, recovery is probable. Cases which return to their previous polished rice diet are liable to relapses and sooner or later die of the disease.

Treatment.—PROPHYLACTIC.—Prophylactic measures consist in providing a balanced dietary adequate in B_1, *i.e.* 1–2 mg. daily. In institutions where polished rice or white bread is the main article of dietary, under-milled or parboiled rice and whole-wheat flour should be substituted. The addition of cooking soda to vegetables should be avoided, since boiling in the presence of alkali destroys B_1, though heat alone does not.

CURATIVE.—Dietary is an all important factor in recovery, and the introduction of crystalline vitamin B_1 (aneurine) has revolutionised treatment. In moderate cases 5 mg. of aneurine hydrochloride (thiamine hydrochloride, U.S.P.) should be administered daily in tablet form, but in acute fulminating beriberi intravenous injections are essential. Initially, injections of from 5 to 50 mg. may be necessary in severe cardiac cases, followed by daily injection of 5 mg. until symptoms are well controlled; subsequently, the aneurine can be given orally. Careful nursing and absolute rest in bed are necessary, and where there is cardiac failure small feeds containing marmite are given 2 hourly; later, a dry, low carbohydrate diet rich in vitamin B_1 and containing such articles as yeast, marmite, oatmeal, lentils, haricot beans, meat, eggs, liver, ham and heart muscle is advisable. Milk, butter and cream should also be included but rice is contraindicated. If there is

right-sided cardiac failure venesection is of great value. In infantile beriberi, artificial should be substituted for natural feeding or a healthy wet-nurse employed. Extract of rice polishings have proved effective therapeutically, in 2-hourly feeds, and toddy made from coconut milk fermented by yeast has been used with great benefit in certain Pacific Islands. Vitamin B_1 (aneurine hydrochloride) in adequate dosage should now be prescribed if available.

When there is polyneuritis, a cradle should be put over the feet and splinting may become necessary to prevent muscular contractures. After the acute symptoms have disappeared, massage and electricity to the limbs will help to restore the circulation and muscle tonus.

Mild cases of dry beriberi may be treated on a rice-free diet, low in carbohydrate and high in vitamin B_1; aneurine tablets in a dosage of 5 mg. daily should be given. Muscular work must be avoided as this is liable to precipitate wet beriberi.

When the plasma proteins are found to be low, intravenous serum or reconstituted plasma should assist in dispersing the œdema, as it does in the disease known as nutritional œdema.

PELLAGRA

Synonyms.—Mal de la Rosa; Mal del Sole; Maidismus; Malattia della Miseria; Asturian Leprosy; Alpine Scurvy.

Definition.—Pellagra is a chronic relapsing disease occurring especially in maize eaters, due to a deficiency in certain proteins and factors contained in the vitamin B_2 complex. Clinically, it is characterised by buccal and gastro-intestinal disturbances, psychical and nervous features, and a symmetrical eruption especially affecting areas of skin exposed to the sun's rays or to friction.

Ætiology.—Pellagra (pelle, the skin; agra, rough) prevails endemically in the Southern States of the U.S.A., lower Egypt, Turkey, Roumania, the Balkans, Spain and Italy, and has been reported from India, China, Japan, parts of Africa, Mexico, West Indian Islands, etc. People of any race, age or sex are susceptible, and the malady is more common amongst the poorer classes. The incidence of the disease is greater in the spring. It occurs particularly amongst maize eaters, and in poorer communities living on cereals containing a low protein content or protein of low biological value. Following the work of Elvehjem on canine black tongue, nicotinic acid (B_7) and its amide have been found to clear up the early dermal changes and mucous membrane lesions in pellagra and to relieve many symptoms referable to the central nervous system. Certain coenzymes contain nicotinic acid amide (Warburg and von Euler), and severely ill pellagrins usually have a low coenzyme content in the blood (Vilter and Spies). It has been suggested that an interference with general cellular metabolism may result from a deficiency of available respiratory enzymes. When infection or hyperthyroidism increase the oxidative activity of the body and when the enzymes which facilitate such activity are wanting owing to a deficiency of their precursors, a deficiency syndrome follows. Other factors in the B_2 complex, *i.e.* riboflavin (B_2) and adermin (B_6), as well as proteins, are also

Canine rays have some effect [illegible]

essential in preventing pellagra and probably have a closely inter-related function (see p. 448). Sporadic cases of true pellagra occur in alcoholics or are secondary to disease of the alimentary tract. They arise from mal-absorption of pellagra-preventing factors or from deficiencies in the dietary prescribed. Irrespective of whether the development of pellagra follows poverty, erroneous dietary habits, dietary idiosyncrasies, organic disease, chronic alcoholic addiction, or some combination of these factors, the lesions, symptoms and methods of treatment are essentially the same (Spies).

Pathology.—Emaciation is marked and the internal organs, including the heart and spleen, are small and atrophic. Skin lesions consist of an initial erythema involving the superficial layers, terminating later in a true exfoliative or exudative dermatitis. Stomatitis and glossitis with ulceration of the tongue, denudation of its epithelium and ultimate atrophy may ensue. The jejunum is congested and atrophic, and small round ulcers involving the jejuno-ileum, colon and rectum are described. The mesenteric glands may be enlarged. Demonstrable pathological changes in the nervous system are generally slight but there may be a subacute combined degeneration of the cord involving the posterior and lateral tracts, and especially Clarke's column (Wilson). Degeneration of the anterior-horn cells in the lumbar region, and subacute inflammation of the ganglion cells in the posterior roots are described, while Briauchi recorded meningeal thickening and adhesions, atrophy of the cerebrum, and hydrops of the ventricles and subarachnoid space. More than 50 per cent. of pellagrins show achlorhydria which is histamine-fast, but Castle's intrinsic factor appears to be secreted normally by the pyloric glands and megalocytic anæmia is rare. The total white count is generally normal in uncomplicated cases, there is often a lymphocytosis, and some degree of secondary anæmia is common. The cerebro-spinal fluid exhibits no abnormality.

Symptoms.—The exact incubation period is unknown, and it should be realised that prodromal symptoms may recur over long periods before the classical oral or dermal features develop. In this stage a definite history is most important in making a correct diagnosis. Generally there is a history of having lived for a long period on a diet high in fat and carbohydrate, and poor in proteins and vitamins, such articles as red meat, eggs, milk, fish, fresh vegetables and fruit being lacking.

Prodromal Symptoms.—These include anorexia, loss of weight and strength, dyspepsia, flatulence, vomiting, sensations of burning or discomfort in the epigastrium, constipation or diarrhœa, insomnia, headache, palpitation, vertigo, numbness, forgetfulness, nervousness, mental irritability and mental confusion. Later, characteristic involvement of skin, alimentary tract and nervous system may supervene, but all three systems are not necessarily affected in any one pellagrin, while the sequence and the severity of the symptoms show considerable variation in individual cases.

Alimentary features.—The glossitis and stomatitis which usually appear early in the disease are diagnostic. In the early stages the tip and sides of the tongue are red and swollen; later the whole organ becomes fiery red (beet tongue) and inflamed, with lateral indentations from the teeth. Deep ulcers may develop on the sides and tip, while the dorsum becomes covered with a thick grey membrane, containing Vincent's organisms. A similar condition may involve the buccal mucous membrane, palate, gums and the

muco-cutaneous surface of the lips. Hot, spiced and acid foods increase the ptyalism and the burning sensations felt in the tongue, pharynx, œsophagus and stomach. Other symptoms include nausea, vomiting and abdominal discomfort, flatulence and distension, especially after food. The bowels may act normally or be even constipated in the early stages, persistent diarrhœa being characteristic only of the advanced cases. In the latter the stools are non-fatty in type, diarrhœa occurs at all hours, and is often associated with colicky pain and tenderness. Sigmoidoscopy may reveal a proctitis. Associated vaginitis and urethritis are not uncommon.

Skin lesions.—Their distribution is on the back of the hands, wrists and forearms, the dorsum of the feet, the face, neck, upper part of the chest, under the breasts and in the perineal regions—in short, over those areas directly exposed to the sun's rays or friction. Commencing as an erythema resembling a severe sunburn, there is redness, swelling and tension of the skin, followed by itching, burning and possibly bleb formation, while later, a deeper dermatitis develops with desquamation and exfoliation. Pigmentation and thickening of the dermis result, but finally atrophy supervenes, the skin becoming wrinkled, inelastic and thinned. Pathognomonic features of pellagrous eruptions are their absolute symmetry and their sharply demarcated pigmented borders—the hyperkeratotic border of Merk.

Nervous system.—The early mental symptoms, which are often regarded as functional, include depression, apprehension, irritability, headache, insomnia, and bilateral burning sensations involving the extremities or other parts of the body. Later these mental symptoms are accompanied by rigidity, tremor of the tongue, coarse tremors of the limbs and head, athetoid movements and cramp; while numbness and paralysis of the extremities are common. The reflexes which at first are generally increased, later become decreased, and finally are often entirely absent. The gait may be spastic or ataxic, and cord involvement or peripheral neuritis due to associated B_1 deficiency may be factors in the production of the neurological picture. If improperly treated, insanity often results. Retardation of growth occurs in children, but fortunately neurological complications are not common in them.

The course of the disease is generally afebrile and characterised by definite attacks alternating with remissions extending over many years unless a proper diet be maintained.

Diagnosis.—In classical pellagra the glossitis, stomatitis and the characteristic skin lesions make the diagnosis easy, but these features occur only in the well-established disease and it is the subclinical cases or those presenting vague prodromal manifestations which are so important to recognise early. A reliable history of dietary deficiency is all important in this regard. The urinary test for nicotinic acid excretion devised by Harris and Raymond (p. 449) may clinch the diagnosis in doubtful cases. Pellagra sine pellagra may be confused with sprue or ergotism, while erythema multiforme and dermatitis venenata may cause difficulty (Stitt).

Prognosis.—In endemic pellagra if patients receive modern treatment and a maintenance diet adequate in vitamin B_2 complex and good biological protein, the mortality should be low. In the past, about 40 per cent. have been estimated to develop mental trouble, and many of these died in asylums. Fever is an unfavourable sign, and in the absence of intercurrent disease

occurs either as a terminal event or in the fulminating form known as typhoid pellagra, which is characterised by intense prostration, tremor, muscular rigidity, convulsions and death. In secondary pellagra, the prognosis depends on rectification of a faulty diet and treatment of the underlying alimentary trouble.

Treatment.—PROPHYLACTIC.—The addition to a pellagrin's diet of red meat, milk, eggs and substances rich in vitamin B_2 complex, *e.g.* brewer's yeast and marmite, will prevent the disease.

CURATIVE.—Rest in bed, a high calorie, nutritious diet low in carbohydrate but rich in protein, and foodstuffs containing vitamin B_2 complex are desirable. The diet should include fresh milk, lean scraped red meat, liver, canned salmon, tomato juice, fresh fruit and vegetables. Articles which have been found to possess curative value when given in large dosage include Brewer's yeast (75–100 g. daily), marmite (30–60 g. daily), wheat germ (250–300 g. daily), ventriculin (200 g. daily) and liver extract (75–100 g. daily). The discovery of the curative effects of adequate doses of nicotinic acid on many of the manifestations of pellagra has revolutionised the treatment of the disease. The drug is administered by the mouth, in tablet form and in divided doses, the daily dosage ranging from 200–1000 mg., 500 mg. being generally effective. After 10 days the dosage may be decreased. Flushing, burning and itching, nausea, vomiting and colic may follow, especially if the drug is given in large dosage on an empty stomach. Nicotinic acid also stimulates gastric activity and acid secretion, and is liable to elicit a mild histamine-like type of reaction. The mucous membrane lesions, including pellagrous glossitis, stomatitis, vaginitis, urethritis and proctitis, are healed and bowel function restored to normal, the early erythematous lesions are blanched, while the early and late mental relapse symptoms are greatly benefited. The chronic skin lesions, however, are not cured by nicotinic acid therapy. Associated symptoms of peripheral neuritis are not relieved by nicotinic acid, but both pain and numbness disappear after daily injections of 50–100 mg. of crystalline vitamin B_1 (Spies).

TROPICAL MACROCYTIC ANÆMIA

Synonyms.—Nutritional Macrocytic Anæmia; Tropical Megalocytic Anæmia.

Definition.—A severe nutritional anæmia, megalocytic in type, especially affecting pregnant women in the tropics and subtropics, and responding specifically to marmite or liver extract therapy. Non-hæmolytic and hæmolytic types are encountered.

Ætiology.—The disease affects both sexes but is especially common in women during the child-bearing period owing to the superadded nutritional demands of pregnancy and lactation; it develops during the latter half of pregnancy. It has been reported from India, China, Africa and Macedonia. The malady is found in rice-eaters in the southern half of India, where it affects all communities and grades of society (Wills). In Macedonia, it is prevalent in the refugee population, whose diet is poor in animal proteins and fat. Castle holds that lack of extrinsic factor in the diet is responsible, but Wills and Evans believe it is due to deficiency in a new hæmopoietic

factor contained in crude liver and autolysed yeast. The factor concerned has not been identified with any constituent of the vitamin B_2 complex. Most frequently the condition is associated with chronic malarial splenomegaly, which introduces a superadded hæmolytic factor through excessive phagocytosis of red cells by a hypertrophied and pathological reticulo-endothelial system resulting from repeated malarial infections over many years (Fairley).

Pathology.—In uncomplicated non-hæmolytic cases the organs are pale and may show fatty infiltration secondary to the anæmia. In fatal cases, there may be cardiac dilatation associated with fatty changes in the myocardium, a congested enlarged liver, œdema and other evidence of cardiac decompensation. Megaloblastic hyperplasia of the red marrow is found, and Ehrlich polychromatic megaloblasts are demonstrable in smears or sections. In cases of hæmolytic type associated with splenomegaly, there is, in addition, a generalised hypertrophy and hyperactivity of the reticulo-endothelial cells, which may contain malaria pigment and phagocytosed red cells, fine hæmosiderin deposits in the parenchyme cells of the liver and spleen, and a decrease of lymphoid tissue in the latter organ in which the Malpighian bodies may have disappeared. Hæmorrhages may be found in the skin and serous or mucous membranes. The bone marrow shows general hyperplasia of the myeloid cells, with increase in the activity and numbers of hæmocytoblasts and erythroblasts. Basophilic and polychromatic megaloblasts are common, but ripening sufficient to produce a really pink cytoplasm in a cell with a finely stippled primitive nucleus is a rarity. Pathological changes in the precursors of the white cell series are common, and megakaryocytes are liable to be atypical or scanty.

The condition is one of panmyelopathy in which some more primitive cell type than the megaloblast must be implicated. The reticulo-endothelium lining the marrow sinusoids is the ultimate source of erythrocytes, leucocytes and platelets, and it appears not improbable that the deficiency factor no less than malaria itself is exerting its deleterious influences on primitive reticulo-endothelium.

Symptoms.—In the uncomplicated *non-hæmolytic type* the symptoms are essentially those associated with a grave anæmia. The patient often first seeks advice for cardiac palpitations, giddiness, shortness of breath, weakness on walking and physical fatigue. Sore tongue, anorexia, vomiting, flatulence, abdominal distension and diarrhœa may be complained of, and fever or cough may or may not be present. Physical examination generally reveals a well-nourished patient with pale mucous membranes, a low blood pressure and rapid pulse, and often hæmic cardiac murmurs. Later frank congestive cardiac decompensation (see pp. 853–857) may ensue. The blood picture resembles that of pernicious anæmia with megalocytes and often nucleated red cells present in the blood smears. Red cell counts of between 500,000–1,000,000 erythrocytes per c.mm. are not uncommon. The colour index generally exceeds unity. The mean corpuscular volume is increased, and the Price-Jones curve shows a shift to the right, and an increased variability and mean corpuscular diameter. Leucopenia is common, the reticulocytes are not increased, the serum bilirubin values are normal and the fractional test meals show that, unlike pernicious anæmia, the oxyntic cells retain their power of secreting HCl after the administration of histamine.

In the *hæmolytic type* of tropical macrocytic anæmia, certain features are superadded. The spleen is invariably enlarged and hard but not tender. Petechial eruptions involving the skin, epistaxis and bleeding gums or bleeding from other mucous membranes occur in about 25 per cent. of cases, and are invariably associated with thrombocytopenia. An icteroid tinting of the skin or conjunctivæ is not uncommon, while hyperbilirubinæmia and dark brown stools are characteristic findings. The blood picture resembles in many respects the megalocytic anæmia already described, but reticulocytosis is the rule, and megalo-spherocytosis may be found which is not the case in the non-hæmolytic type. Leucopænia and thrombocytopænia are frequent findings. Apart from cardiac decompensation, the more common complications include uterine sepsis in the puerperium, *B. coli* infections of the genito-urinary tract, and respiratory infections; the last is predisposed to by the increased pressure on the diaphragm exerted from below by the pregnant uterus and greatly enlarged spleen, which so many of these patients present. Typical paroxysms of malarial fever at this late stage are rare, and parasites are not demonstrable between attacks.

Diagnosis.—An adequate hæmatological investigation is essential in diagnosis. The non-hæmolytic type has to be distinguished from other megalocytic anæmias. It differs from pernicious anæmia in that HCl is secreted in response to histamine injections, and nervous manifestations are absent, while the atrophic, distended abdominal parietes, marked loss of weight and the bulky pale fatty stools so characteristic of tropical sprue are not observed in tropical macrocytic anæmia. The hæmolytic type clinically resembles acholuric family jaundice, but there is no family history, the corpuscular fragility is not increased to hypotonic saline solutions, and the anæmia is of an entirely different type in the two diseases.

Prognosis.—Balfour estimated the death-rate as 40 per cent. before the introduction of liver therapy. With modern treatment and in the absence of complications patients whose condition is diagnosed at a reasonably early stage should recover completely. The non-hæmolytic type responds more readily than the hæmolytic type, in which very large doses of liver parenterally may be necessary.

Treatment.—Prophylactic.—Prevention depends on the adoption of a well-balanced diet containing adequate amounts of protein of good biological value and vitamin B_2 complex.

Curative.—Uncomplicated cases of non-hæmolytic type generally respond to marmite (Wills) in a dosage of 30 grammes daily, to liver extract by the mouth equivalent to 1 lb. of fresh liver daily, or to daily injections of 2 c.c. of injection of liver (campolon type). Maximal reticulocytosis develops about the seventh to ninth day, and provided treatment is maintained satisfactory blood regeneration follows.

In the hæmolytic variety, or where complications exist, much larger daily doses of marmite (60 grammes) or preferably of parenteral liver extract (6–8 c.c.) are necessary, and in severely ill patients, it is often advisable in addition to parenteral liver therapy to give an immediate blood transfusion (20 fl. oz.) in order to tide the patient over the critical few days before specific therapy initiates the hæmopoietic response. Successful termination of labour and the cessation of lactation decrease the nutritional demands on the body and may result in spontaneous cure, but it is important

to remember that skilled medical and nursing attention during the puerperium, and the daily examination of the patient for the onset of complications such as cardiac failure and pulmonary infections may result in saving the patient. Throughout treatment a nutritious diet containing meat, eggs, milk, and foods rich in vitamin B_2 complex is desirable.

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SECTION VIII

DISEASES OF THE ENDOCRINE GLANDS

DISEASES OF THE PITUITARY GLAND

THE pituitary, a small gland, 0·5 gm. in weight, is situated in the sella turcica in close relation to the optic nerve, and connected to the base of the brain by the infundibular stalk. It is 13 mm. broad, 9 mm. from back to front, and 6 mm. high. Apart from its own special functions, it has a stimulating effect on most of the other ductless glands, which latter tend to atrophy after removal of the pituitary gland (hypophysectomy). The influence, however, is reciprocal and hyper- or hyposecretion of the other endocrine glands influences the activity of the pituitary. The hypothalamus, on either side of the third ventricle, contains many nerve nuclei which are connected with the pituitary gland. They provide the mechanism for an intimate relationship between hypothalamic stimuli and pituitary function.

The anterior lobe of the pituitary gland arises from an upgrowth of the buccal ectoderm (Rathke's pouch); and the posterior part is a downgrowth from the floor of the fourth ventricle, continuity with the latter being maintained by the infundibular stalk. In the fœtus, a cleft appears in the posterior part of the anterior lobe, separating off a few layers of cells which, lying between the anterior and posterior lobes, are termed "pars intermedia." The cleft tends to disappear in adult life. A tongue-like projection of the anterior lobe towards the tuber cinereum is called the *pars tuberalis*. The anterior lobe is composed chiefly of three kinds of cells, classified according to their staining properties: cells which absorb but little stain are termed chromophobe (60 per cent.); those taking eosin, eosinophil cells (29 per cent.); and those taking a basic dye, basophil (11 per cent.). It is probable that the chromophobe cell can give rise to both eosinophil and basophil cells. The relative proportions of the different types of cells varies with physiological conditions, such as pregnancy or the climacteric, and with experimental conditions, such as castration or adrenalectomy.

The posterior lobe secretes two hormones, pitressin and oxytocin. The former has a vaso-pressor action, is anti-diuretic, and produces an increased urinary excretion of chloride. The latter, oxytocin, produces contraction of the pregnant uterus. Recently, it has been shown that pitressin causes contraction of the non-pregnant uterus. The pars intermedia secretes the melanophore expanding hormone, which produces dilatation of the pigment spots of the frog; and probably also the specific katabolic factor of Collip, which has not yet been separated from the melanophore-expanding hormone. This Collip katabolic factor raises the metabolism, even in the absence of

the thyroid gland; and it also appears to have a ketogenic, diabetogenic and glycotrophic action, and can antagonise the hyperglycæmic effect of adrenaline.

The anterior pituitary gland appears to secrete 10 or more hormones, but it is uncertain whether they are all distinct chemical substances. It has been postulated that one hormone may have different actions under varying physiological circumstances. Description is facilitated by assuming the existence of separate hormones:

1. Growth-producing hormone.
2. Lactogenic hormone. This initiates and maintains mammary secretion.
3. Thyrotrophic hormone (thyrotrophin). This produces (*a*) hyperplasia of the thyroid gland and hypersecretion of thyroxine; and (*b*) exophthalmos, even after thyroidectomy.
4. Gonadotrophic hormone (gonadotrophin). This factor has been chemically separated into two components, Prolan A and Prolan B, which under certain conditions produce different gonadotrophic reactions. Thus, Prolan A stimulates development of the Graafian follicles and of the spermatic tubules; whereas Prolan B produces luteinisation of mature follicles, or of the theca of immature follicles, and hyperplasia of the interstitial cells of the testis or ovary. Some doubt the absolute qualitative differentiation, and, with large doses over long periods, the actions of both factors can be obtained with an extract thought to represent only one factor.
5. Diabetogenic hormone. This hormone produces hyperglycæmia, glycosuria and ketonuria. The effect appears after 2 or 3 daily injections, and owing to the appearance of anti-bodies cannot be sustained ordinarily for more than a few weeks. If, however, the daily dose of hormone is progressively increased, permanent diabetes results even when injections cease, and the islets of the pancreas are then seen to have undergone degeneration. The diabetogenic hormone can act in the absence of the adrenal glands; but their presence augments the diabetogenic effect, since they undergo cortical hyperplasia (associated adrenotrophic hormone) and this itself tends to produce hyperglycæmia. A diabetogenic effect is best seen on the hypophysectomised depancreatised dog (Houssay dog). Secretion of the diabetogenic hormone may be produced by electrical stimulation of the ventro-medial nuclei of the hypothalamus.
6. Glycotrophic hormone. A glycotrophic factor of anterior pituitary extracts can antagonise, or prevent, the hypoglycæmic action of insulin without, however, having the power to produce hyperglycæmia. It is part of, but can be separated from, the diabetogenic complex, and it is probably more correct to refer to it as a factor rather than a hormone. It is also closely associated, but not identical, with prolactin. The glycotrophic factor acts by preventing glycogen formation by insulin. It does not depend upon the presence of the adrenals or thyroid glands for its efficacy.
7. Ketogenic hormone. This produces ketonæmia, ketonuria and an increase of liver fat. It can be separated from diabetogenic anterior lobe extracts.

8. Pancreatotrophic hormone. This produces hyperplasia of the islets of Langerhans, and increased secretion of insulin. Its separate entity is not certain, and the initial action of the diabetogenic hormone in certain species appears to be pancreatotrophic.
9. Adrenotrophic hormone (adrenotrophin). This produces hyperplasia of the adrenal cortex. As with other tropic hormones, the effect is best demonstrated after the hypoplasia, or atrophy, of the adrenal cortex that follows hypophysectomy. It is associated with but can be separated from the thyrotrophic factor.
10. Parathyrotrophic hormone (parathyrotrophin). This has been described but its existence is not firmly established.

It is not always possible to classify diseases of the pituitary gland into hyperfunction and hypofunction of its various components. If one attempts to do so it would appear that gigantism, acromegaly and Cushing's basophilism syndrome are due to hyperfunction of the anterior lobe; infantalism and dwarfism (certain types) and Simmonds's cachexia to hypofunction of the anterior lobe; diabetes insipidus to hypofunction of the pars posterior and intermedia; and diabetes tenuifluus to hyperfunction of the pars posterior and intermedia. Fröhlich's syndrome is probably due to hypofunction of the anterior lobe (but adiposity is also associated with hyperfunction of the anterior lobe, as in Cushing's syndrome). An attempt to correlate the various disorders with the types of cells can only be incompletely successful, since there are 10 known functions and only 3 types of cells. Fortunately there are well-known clinical syndromes which will form a basis for the subsequent considerations.

ACROMEGALY

Definition.—Acromegaly is a condition due to a hypersecretion of the growth hormone of the anterior pituitary gland. It is characterised by enlargement of the hands and feet, and of the bones and cutaneous tissues of the face, and by splanchnomegaly. It is frequently superimposed on gigantism.

Ætiology.—The disease occurs at any age but usually before 40, and in both sexes. There is a mild familial type. The immediate cause is an excessive secretion of the growth hormone.

Pathology.—There may be an adenoma of the pituitary gland consisting of eosinophil cells, or merely a relative hyperplasia of these cells. There may be enlargement of the adrenal cortex, the thyroid and the parathyroids. The testes and ovaries are usually atrophic. The islets of the pancreas may be hyperplastic or atrophic. Diffuse lymphoid hyperplasia is frequent. All the viscera are enlarged.

Symptoms.—The patient may first seek advice because of increasing size of the hands and feet, or of a blunting and distortion of facial features, or visual disturbance due to a pituitary tumour. The latter is associated with optic atrophy, bitemporal hemianopia, progressive loss of vision and severe headaches. Ocular palsies may result from pressure on the third, fourth or sixth nerve.

The enlargement of the extremities is partly due to bony enlargement and thickening, but there is also overgrowth of the soft tissue. The vault

of the skull may be somewhat thickened, but considerable bony overgrowth is more common in the base of the skull and in the facial bones. The overgrowth of the lower jaw leads to prognathism and spreading of the teeth. The vertebræ undergo changes, and kyphosis and scoliosis are common. The soft tissues of the face, nose, and lips undergo hypertrophy, which together with the bony changes, may transform the facial appearance. The skin and subcutaneous tissue are thickened, and the sebaceous and sudoriferous glands hypertrophied, producing a greasy perspiring skin. The hair too is thick and greasy, and may be abundant over the trunk. Enlargement of the tongue leads to difficulty in articulation, and enlargement of the larynx produces a deep voice. Speech is also sluggish and memory poor. The general behaviour may be characterised by apathy and lack of initiative. Generalised muscular hypertrophy may initially be associated with great strength, but later weakness and atony result. The heart is enlarged, but hypertension or hypotension may occur.

Complications and Sequelæ.—1. Thyroid—exophthalmic goitre rarely complicates acromegaly. More commonly there is an increased basal metabolic rate without other features. The thyroid gland is diffusely enlarged in some 50 per cent. of cases, but this is not necessarily associated with thyroid symptoms or even with a raised metabolism. Sometimes myxœdema follows hyperthyroidism or may be produced initially. 2. Adrenals. Virilism in the female and increased hirsutism in the male may be prominent features, suggesting adrenal hyperplasia resulting from an adrenotrophic stimulus. 3. Diabetes Mellitus. This disorder is present in a small proportion of patients; but some degree of intermittent or chronic hyperglycæmia with glycosuria, in the absence of diabetic symptoms, may be detected in some 50 per cent. The pituitary diabetogenic hormone is probably responsible. 4. Diabetes Insipidus or Diabetes Mellitus. There may be in different patients, or in one patient in different phases of the disorder, evidence of deficiency or excess of the anti-diuretic hormone. 5. Mental Changes. Depression, irritability, negativism, melancholia, mania and delusional insanity are possible complications.

Prognosis.—The course is gradually progressive, with intermittent phases of apparent arrest of the pituitary hyperfunction. These phases may be prolonged over many years. As myxœdema may follow exophthalmic goitre, so hyperactivity of the pituitary may be succeeded by hypoactivity, with secondary hypofunction of the thyroid and adrenal glands.

Diagnosis.—The increase in size of hands and feet, and thickening and blurring of the facial features, with prognathism, makes diagnosis easy, especially if gigantism is already present. Osteitis deformans is a bony disorder which distorts the vault of the skull and does not affect the facial bones. In acromegaly, radiographic examination may reveal an enlargement of the sella turcica, which if associated with optic atrophy or bitemporal hemianopia, indicates a pituitary tumour.

Treatment.—If there is progressive involvement of the optic nerves, with danger of complete blindness, the treatment is surgical removal of the pituitary tumour. Otherwise deep radiation of the pituitary region should be tried first, and relief results in some 50 per cent. If sight is not threatened, and there appears to be an arrest of pituitary hyperfunction, treatment is symptomatic, including hormone substitution where indicated, *e.g.* thyroid

for myxœdema, testosterone for impotence, and œstrone for amenorrhœa. Exophthalmic goitre may be treated by radiation of the thyroid, or thyroidectomy. True diabetes mellitus will need dietetic regulation and insulin, but symptomless glycosuria can be ignored.

GIGANTISM

This is a condition of rapid and excessive growth of bone resulting, among other manifestations, in a height above normal. Like acromegaly, it is due to excessive secretion of the growth hormone by the eosinophil cells of the anterior pituitary (hyperplasia or tumour), but this hypersecretion operates in childhood, or adolescence, before the epiphyses of the long bones have united. If the hypersecretion persists, acromegaly will be superimposed on the gigantism. In uncomplicated gigantism, there is no sharp dividing line between normal tall people and pathological giants, and the characteristic of tallness is probably a familial and racial feature dependent upon constitutional hyperactivity of the anterior pituitary. Eunuchoid individuals, as well as pre-pubertal castrates, are often excessively tall. This may be due to two factors: (1) growth hormone acting over a longer period, since the union of the epiphyses is delayed; and (2) hyperactivity of the anterior pituitary secondary to failure of gonadal function, assuming the latter to be primary.

The treatment of pathological gigantism is the same as for acromegaly, namely, radiation of the pituitary gland, or surgical removal of a pituitary neoplasm. Inhibition of pituitary activity by large doses of testosterone, or œstrone, may be of some benefit.

CUSHING'S BASOPHILISM SYNDROME

Synonyms.—"Multiglandular syndrome of the fat-bearded diabetic woman"; Achard-Thiers syndrome.

Definition.—A condition of virilism in females (or of feminisation in males) associated with adiposity, hypertension, diabetes mellitus, plethora, and softening of the bones.

Ætiology.—The disease is commonest in the second and third decades, but may occur at any age. It is much more common in females than males. The immediate cause is a hypersecretion of the anterior pituitary (especially of the basophil cells), and an associated hyperplasia of the adrenal cortex.

Pathology.—Cushing found the essential feature to be an adenoma of the basophil cells of the anterior pituitary. It is now established that the complete chemical picture may result from a neoplasm or hyperplasia of the adrenal cortex, or more rarely from a neoplasm of the thymus gland, or even from a chromophobe adenoma of the anterior pituitary. Although a basophil adenoma is not always present, hyalinisation of the basophil cells of the anterior pituitary is a common feature. Crooke believes that it is responsible for all features of the syndrome except virilism or feminisation. The latter two features are very probably resultants of the hyperactivity of the adrenal cortex, which in some cases is primary and in others secondary.

Symptoms.—Virilism is shown by cessation of menstruation, loss of hair of the head, and growth of hair on the face and body, as in the male; feminisation is indicated by testicular atrophy and impotence, and by mammary development. For a fuller description the reader is referred to the subsection on Diseases of the Suprarenal Glands. In all cases the adiposity is diffuse, but it is especially noticeable on the face, trunk, and upper arms and thighs. It is occasionally a painful adiposity. Where the skin has been stretched by fatty deposits, *e.g.* in lower abdomen, thighs, breasts, and axillæ, there are linea distensæ, which are not white but of a deep red colour. The face is plethoric and of a dusky tinge, suggesting a polycythæmia basis, which is not necessarily substantiated by a red cell count. The anterior aspects of the legs show bluish mottling with contrasting patches resulting in a marble appearance, from which is derived the dermatological name, cutis marmorata.

The bones are rarefied (seen in X-ray photographs) and softened, so that the vertebrae are compressed, and the patient develops kyphosis and round shoulders, with a diminution in height. Lordosis helps to accentuate an adipose pendulous abdomen, and may give rise to troublesome backache. The blood pressure is raised, and there may be a secondary ischæmic nephritis. In a few patients, fatal malignant nephrosclerosis has been recorded. Diabetes mellitus may be present in varying degrees of severity, and those patients who manifest no diabetic symptoms invariably show a delayed fall in blood sugar in the carbohydrate tolerance test. Pigmentation of the orbits and nipples may be present. Migrainous headaches are not infrequent, but changes in the optic nerves or visual fields are rare, since basophil adenomas are usually microscopic in size. The thyroid gland may be enlarged, but there is rarely evidence of hyperthyroidism.

Complications.—The patients are liable to intercurrent infections, especially staphylococcic.

Diagnosis.—Adipose corpulent women with plethoric faces, rounded shoulders, and hirsutism, suggest the diagnosis. Radiograms may show osteoporosis, but the sella turcica is usually not enlarged. Glycosuria and hypertension are additional features. Hirsutism is of male distribution, but quite frequently not excessive. The possibility of an adrenal tumour is suggested by considerable hairiness, gross enlargement of the clitoris, and a gross excess of androgenic hormone in the urine (*e.g.* more than 300 capon units daily). In doubtful cases, iodoxyl (pyelectan, uropac, uroselectan) radiographic examination, or perirenal insufflation, or even laparotomy is called for (see adrenal section). Thymus tumours can be excluded by radiographic examination of the chest, and ovarian tumours (a rare cause) by bi-manual examination. The urinary calcium excretion may be increased, but the serum calcium is not raised, as in the case of hyperparathyroidism.

Mild and incomplete forms of Cushing's syndrome are not at all uncommon, and are often familial. They do not necessarily call for any special treatment. It is questionable whether they are more correctly regarded as variants of normality than as pathological.

Prognosis.—In the absence of treatment, the course is usually progressively downhill, but only gradually so. As with acromegaly, there may be spontaneous arrest of the process for many years. If an adrenal tumour is removed surgically, in the absence of malignant recurrence the patient may

return to complete normality. In the case of basophil adenoma, deep radiation applied to the pituitary gland may be followed by remarkably good results, with disappearance or considerable amelioration of most symptoms, including the diabetes mellitus.

Treatment.—An adrenal tumour should be removed surgically. A thymus neoplasm is malignant and deep radiation of the thymus area is unlikely to prove of more than temporary benefit in such cases. In the absence of proof of any primary lesion outside the pituitary gland, a basophil adenoma is assumed, and deep radiation applied to the pituitary gland. Unilateral adrenalectomy for a supposed bilateral hyperplasia of the adrenal cortex is illogical, and cannot produce appreciable amelioration.

DWARFISM

Synonym.—Infantilism; Levi-Loraine Syndrome; Brissaud's Infantilism.

Definition.—By dwarfism is meant a failure to grow, resulting in subnormal height, and due to a deficient secretion of growth hormone by the anterior pituitary gland. It may or may not be accompanied by other endocrine stigmata. Infantilism is a variety of dwarfism, implying a degree of growth and also of sexual development not qualitatively abnormal but not commensurate with the age of the individual. The term was first used by Loraine in 1871 in connection with a case of infantilism associated with tuberculosis. It was later applied by Levi (1908) to hypopituitarism beginning in childhood. Brissaud extended the term to include infantilism associated with hypothyroidism (Brissaud's infantilism).

Ætiology and Pathology.—In both dwarfism and infantilism there may be a pituitary tumour, usually chromophobe adenoma, or a parapituitary tumour. In most cases, however, there is no gross lesion. One can postulate a hypoplasia of the eosinophil cells, since these secrete growth hormone. In colonies of congenitally dwarfed mice there is a relative diminution in the proportion of eosinophil cells. Dwarfism may be part of the Fröhlich syndrome, or of cretinism. In pathological sexual precocity, and in some otherwise normal people, dwarfism appears to be due to premature closure of the epiphyses. Inadequately treated diabetic children fail to grow at the normal rate.

Non-endocrine causes are rickets, renal rickets, fragilitas ossium, coeliac disease, pancreatic disease, von Gierke's glycogen disorder, vitamin deficiency, and achondroplasia. There is no evidence of an endocrine basis for achondroplasia.

Symptoms.—In the majority of cases, the only features are a failure to grow at the normal rate and (or) a cessation of growth at an early age. Normally the epiphysis of the lower end of the femur closes at 18 or 19, but that of the head may close as early as 15 or as late as 18. The majority of normal boys continue to grow after puberty, but some 30 per cent. of girls cease to grow after menstruation has commenced. In the latter cases, there may be premature union of the epiphyses. Failure to grow adequately is not usually associated with that of sexual development, but the latter is an essential feature of Levi-Loraine infantilism. Failure to attain an average height is

often familial, and one family may have both very tall and very short members, their numbers determined by Mendelian laws. The mechanism, however, as with congenitally dwarfed mice, is through the anterior pituitary gland.

Diagnosis.—With simple failure of growth, or in infantilism, the relative proportion of arms, legs and trunk is normal. In achondroplasia, the arms and legs are short compared with the body (human dachshund), and the nose is broad and flat. It is important to radiograph the epiphyseal junctions, since growth hormone cannot act after epiphyseal union.

Prognosis.—Growth hormone is not effective in all cases of subnormal growth. It is obviously useless if the epiphyses have prematurely united. It may be equally so in endocrine dwarfism if not applied until adult life, even when the epiphyses remain ununited. This is in keeping with the observation that growth hormone fails to be effective in the hypophysectomised animal if its use is too long delayed. Growth hormone is sometimes ineffective in cases where one might expect good results and there is probably an important genetic factor to be considered. Nevertheless therapy with growth hormone is worth trying and good results are obtained.

Treatment.—The essential treatment of deficient growth is anterior pituitary growth hormone, 100 to 200 rat units weekly, in two or three divided doses, administered intramuscularly in the buttock. There may be painful local reactions which, however, tend to diminish with repeated injections. As an anti-growth principle develops in the blood, injections should not be continued for more than 6 weeks, but may be repeated after an interval of 2 months. Thyroid extract, $\frac{1}{2}$ gr. to 1 gr. daily, is valuable, especially if there is some evidence of thyroid deficiency, but even in other cases. There is no reason to believe that anterior pituitary tablets by mouth are efficacious. In infantilism, the question of hastening sexual maturity by gonadotrophic hormone arises, but some feel that this effect might produce union of the epiphyses and prevent growth. On the other hand, most boys continue to grow after the sexual maturity of puberty.

SIMMONDS'S DISEASE

Synonyms.—Pituitary Cachexia; Hypopituitarism.

Definition.—A disorder due to destruction or atrophy of the anterior pituitary gland, and manifested by cachexia, anorexia, subnormal metabolism, and hypogonadism.

Ætiology.—The disease is more common in women since the commonest cause is atrophy of the anterior pituitary resulting from a local vascular lesion during the puerperium. Multiparæ are especially prone. It may, however, occur at any age and in either sex associated with a pituitary or parapituitary tumour.

Pathology.—Simmonds's original case showed atrophy and fibrosis of the anterior pituitary gland as a result of an embolus in the main artery in a fatal case of puerperal fever. The vascular lesion is, however, more commonly thrombosis. Suprasellar cystic tumours and chromophobe adenomata are other important causes, and rarely malignant metastases, tuberculosis, syphilis, and xanthomatosis. An unusual but important ætiological occurrence is simply diminution in the relative number of eosinophil cells. As in the

case of hypophysectomy, the gonads, thyroid and adrenal cortex are hypoplastic or atrophic. The viscera are diminished in size in contrast to the splanchnomegaly of acromegaly.

Symptoms.—Weakness, wasting, and anorexia are cardinal features, but of equal importance is the invariable failure of sex function. Thus, in the female, amenorrhœa is associated with a hypoplastic or infantile uterus, and, in the male, the gonads and penis fail to develop or, if already adult in size, they undergo atrophy. In both sexes the secondary sexual characteristics, *e.g.* pubic, facial and axillary hair, are lost, and the eyebrows and hair of the scalp also become thin and lustreless, or disappear. The skin is pale and dry, and may become wrinkled, giving a senile facies, known as progeria. The lower jaw may become atrophic (opposite of prognathism), and the teeth decay and fall out. The low metabolism, *e.g.* —40 per cent., is manifested by a subnormal temperature and hypersensitivity to cold. Bradycardia and hypotension are usual features. The blood sugar is also subnormal and the carbohydrate tolerance usually increased. Spontaneous hypoglycæmic attacks occur, and may be fatal. Anæmia and a relative lymphocytosis, with perhaps some degree of eosinophilia, are not uncommon.

If the disorder commences in childhood; the lack of growth hormone results in failure to grow, although the epiphyses remain ununited in adult life. The latter is probably associated with failure of sexual development.

Complications.—Pulmonary tuberculosis may follow prolonged inanition. Apathy and inertia are characteristic but may progress to melancholia, with disorientation of time and place. Optic atrophy results from tumours.

Diagnosis.—The well-developed syndrome cannot escape recognition if the disorder is kept in mind. Minor and incomplete manifestations are more easily missed, but not if the possibility of the disorder following a puerperium in which there is severe hæmorrhage and (or) infection is remembered. Migrainous headaches can occur even in the absence of a pituitary or parapituitary tumour, but radiographic examination of the sella turcica and examination of the fundi for optic atrophy should not be omitted.

There are many features in common with Addison's disease, but pigmentation in Simmonds's cachexia is either absent, or very slight, and is never present in the mucous membranes. Anorexia nervosa in the late stages may show all the features of Simmonds's cachexia, and it is probable that there is an inhibition of pituitary activity via the hypothalamus. The initial and fundamental cause of anorexia nervosa is, however, psychogenic. It usually occurs in young adults, more often in females, and it is possible to elicit a history of psychic trauma, shock, disappointment, or emotional upset. In contrast to the apathy of Simmonds's cachexia, these patients are restless and perform feats of activity far beyond their apparent strength ; the loss of sexual hair is rarely extreme and may not occur ; in contrast, the trunk and perhaps the face is covered by diffuse downy hair.

Prognosis.—There is usually progressive deterioration, but patients with minor manifestations following pregnancy may recover spontaneously. Treatment is only moderately beneficial.

Treatment.—The only rational treatment is substitution therapy, and this can only be of a limited nature. Cortin, or desoxycorticosterone, will help as replacement therapy for adrenal cortical function. It produces an

increase in strength and weight. Gonadotrophic hormone and œstrone, or testosterone, may establish or to some extent replace sex function, but has no influence on the general asthenia. Thyroid is rarely beneficial and may be harmful even although the metabolism is low. Glucose counteracts hypoglycæmia. Treatment in well-developed cases is rarely entirely satisfactory, and optimistic reports of complete success raise the query of accurate diagnosis.

In the milder forms following pregnancy, the question of the advisability of another pregnancy must be considered, should the latter prove a possibility. It is established that some patients may thus make a complete recovery since the uninjured part of the anterior pituitary undergoes hyperplasia during pregnancy. If, however, the subsequent parturition is complicated by severe hæmorrhage or infection, further thrombosis may occur in the pituitary and the patient may die.

FRÖHLICH'S SYNDROME

Synonym.—Dystrophia Adiposo-Genitalis.

Definition.—A combination of adiposity and hypogonadism, usually occurring at or before puberty, and resulting from pituitary hypofunction, or dysfunction.

Ætiology.—The condition occurs in both sexes, and may be familial. Fröhlich's original case was a boy of 14 with a craniopharyngioma.

Pathology.—A small proportion of cases are due to a parapituitary tumour (cranio-pharyngioma), or more rarely to a chromophobe adenoma of the anterior pituitary. The majority, however, are not associated with a gross pathological lesion, and autopsies are rare. The lesion is sometimes in the hypothalamus rather than in the pituitary, *e.g.* encephalitis, meningitis, syphilis, and hydrocephalus.

Symptoms.—Adiposity and hypogonadism are the two essential features, but to these may be added in some cases a failure of growth hormone and dwarfism. The fat is deposited in girdle and symmetrical fashion, on the abdomen, shoulders, thighs, upper arms, mammary region, mons veneris, face and neck. The adiposity may be present from early childhood, although the syndrome is at its maximum at puberty. The legs and forearms are thin and graceful, and the fingers are usually narrow, delicate and tapering, but occasionally short. The deposition of fat is of feminine type, so that the bodily configuration of the affected male resembles that of the female. There is often a pad of fat over the lower cervical vertebræ. The skin over the outer aspect of the upper arms, thighs and buttocks shows a blueish-red mottling.

Hypogonadism in the male is shown by minute testicles, one or both of which may be undescended, and by a subnormal penis. There is little or no hair over the axillæ and pubis; and, if present in the latter site, it is of feminine distribution, being limited horizontally and not extending upwards to the umbilicus. The skin of the face is smooth, delicate and hair-free, and the complexion good. The voice is high-pitched and does not break. The walk is feminine, and the buttocks tend to sway from side to side as in the female. The feminine habit of resting the hand on the waist or knee is not uncommon. In the female the uterus is infantile, and amenorrhœa, or scanty

menstruation at long intervals, is usual. The breasts are large, but this is caused by fat, and not by glandular tissue. A tendency to sleepiness, like the fat boy in *The Pickwick Papers*, and a craving for sweet things are other features. The basal metabolic rate is normal. The mental and emotional colouring of the personality is characteristic. Periods of depression and introspection alternate with joyousness, high spirits, and euphoria. The patients are excellent company, and very popular with their school friends. They are usually musical and imaginative, with intellectual ability often above normal.

Complications.—Rarely the syndrome is complicated by the additional features of retinitis pigmentosa, mental deficiency, polydactylism and familial incidence. It is then called the Laurence-Moon-Biedl syndrome, and the patient is usually of the Hebrew race.

Diagnosis.—Unless definite hypogonadism is present, the diagnosis of Fröhlich's syndrome is not justified, but is nevertheless frequently made. This is because of lack of supplementary nomenclature. Puberty adiposity may occur with normal genital development, or even with some degree of sexual precocity, or with some features of Cushing's syndrome. In all cases it is probably endocrinological. A parapituitary tumour is indicated by optic atrophy and enlargement or distortion of the sella turcica, as seen in radiograms.

Prognosis.—The disease may be transitory, the adiposity decreasing with belated sexual development. More often it is chronic, with phases of accentuation and amelioration.

Treatment.—Gonadotrophic hormone, 500 units twice weekly for 6 weeks or more, will tend to produce sexual maturation but rarely influences the adiposity. The latter may be modified by restricted diet and thyroid. It is irrational to employ the latter in doses greater than 1 gr. of the dried gland daily, since the basal metabolism is not subnormal. The adiposity is unlikely to be fundamentally altered by any therapy at present employed. Parapituitary tumours may call for surgical removal if sight is threatened. Deep radiation of the pituitary region may be of benefit.

ADIPOSITY

Definition. Adiposity is an excessive deposition of fat in the subcutaneous tissue.

Ætiology and Pathology.—There are four main groups: (1) Exogenous—eating of excessive food. (2) Associated with endocrine syndromes: (*a*) Fröhlich's; (*b*) Cushing's; (*c*) Adrenogenital; (*d*) Dercum's disease—adiposis dolorosa; (*e*) following castration or the menopause; and (*f*) Hyperinsulinism (pancreatic tumour or hyperplasia). (3) Hypothalamic lesions, *e.g.* encephalitis, tabes, hydrocephalus. (4) Idiopathic constitutional.

The eating of an excessive amount of food may be due to habit, greed, or anxiety, but there is also a centre in the hypothalamus, a lesion of which appears to produce pathological hunger, as is seen in certain brain tumours. This may also operate in apparent idiopathic adiposity. The mere eating of an abundance of food is probably not the only factor, for anxiety states producing excessive appetite may nevertheless be associated with leanness

and an inability to put on flesh and fat. On the other hand, the majority of cases of idiopathic adiposity cannot be ascribed to food intake and it cannot be doubted that of two people on similar diet, or of two children of the same family on similar diet, one of each can be fat and the other thin. I am of opinion that it is probable that in both exogenous and idiopathic constitutional adiposity there is an underlying disturbance of the hypothalamic pituitary mechanism.

Symptoms.—Whatever the ætiology, the fat is usually deposited on the face and neck, breasts, abdomen, suprapubic area, buttocks, upper arms and thighs. Linea distensæ, which are white, except in Cushing's syndrome, when they are dusky red, appear in the overlying skin which has been stretched. Many of the idiopathic types of adiposity display in minor degree features of endocrine syndromes, *e.g.* hirsutism, scanty or infrequent menstruation, and impaired carbohydrate tolerance. Diabetes mellitus of middle age is more frequent among the adipose, and adiposity is therefore said to predispose to diabetes. It is more probable that both are due to a common pituitary lesion. It is interesting to note that when amenorrhœa is associated with adiposity, dietetic measures alone, if successful in reducing weight appreciably, may sometimes produce a return to normal menstruation. Fat is also deposited in the viscera, especially the liver and heart, and sudden heart failure does occur in extreme cases. In adiposis dolorosa, symmetrical deposition of painful fatty deposits is associated with an unstable weeping temperament.

Complications.—Diabetes mellitus, cholelithiasis, heart failure, arthritis, varicose veins, and flat feet are some complications.

Diagnosis.—In the majority of cases it is impossible in the present state of knowledge to define the underlying lesion, and therefore the vague terms idiopathic or pituitary adiposity are used, not without some justification. The recognition of the more obvious endocrinopathies presents no difficulty but minor manifestations may escape recognition.

Prognosis.—The condition tends to be chronic, with periods of amelioration and relapses.

Treatment.—This is most unsatisfactory. We have no direct attack on the essential dysfunction, neither do we know as yet whether it is essential hypofunction or hyperfunction. If the latter be true, as suggested by Cushing's syndrome and by adrenal cortical syndromes, it is useless to seek substitution therapy. Thyroid to the point of tolerance as judged by pulse rate is of limited value, as one might expect on account of the basal metabolism in adiposity being already normal or above normal. More toxic accelerators of metabolism, such as dinitrophenol, have now been abandoned. Collip's pituitary katabolic factor may prove useful, since the resulting lowering of the respiratory quotient suggests a specific attack on fat metabolism.

Low caloric diets, *e.g.* 1000 calories daily, will produce a reduction in weight, if strictly adhered to. It is rare, however, for the patient to enjoy good health and well-being on such a diet over a long period, and any minor departures from a food intake well below normal will produce increase in weight. The basis of such diets is the avoidance of fatty, sweet and starchy foods, and their substitution by green vegetables, salads and non-fatty meat. Alcohol, especially beer, should be avoided, as it tends specifically to adiposity in some patients apart from its caloric value. Salt-free diets and injections

of mercurial diuretics for a hypothetical salt water-retention type of adiposity have been advocated, but it is rare to find such an uncomplicated type of adiposity and the effects can only be temporary. Massage and exercise are helpful but not fundamental measures.

Since with the present available therapeutics it is difficult, if not impossible, to change fundamentally a constitutional fatty type, it is important to attempt to counteract any associated hypersensitivity by a psychotherapeutic approach and a philosophical evaluation.

DIABETES INSIPIDUS

Definition.—Diabetes insipidus is a disturbance of water balance, characterised by polyuria and polydipsia, but due to a destructive lesion of the posterior or intermediate lobe of the pituitary gland, or of the adjacent part of the diencephalon.

Ætiology.—The condition is sometimes familial. It may occur at any age and in either sex. It is due to a deficient secretion of the anti-diuretic hormone by the posterior lobe of the pituitary. This results from destruction of the lobe, or any interruption of its normal connection with the supra-optic nucleus of the hypothalamus. Such a lesion is followed by degeneration of the pars nervosa, but not of the pars intermedia. The anterior pituitary lobe must be present for diabetes insipidus to result, and it probably has a diuretic action by an indirect effect on metabolism. It is doubtful if the anti-diuretic hormone of the pars nervosa has been separated from the vaso-pressor hormone. In addition to decreasing the amount of urine excreted, this hormone also increases the amount of chloride excreted in the urine.

Pathology.—The lesion in the hypothalamic-pituitary mechanism may be traumatic, vascular, syphilitic or tuberculous meningitis, primary or metastatic brain tumour, acromegaly, or Hand-Schüller-Christian's disease. The condition may also follow shock, via the hypothalamic mechanism. In the majority of cases, there is no obvious cause (idiopathic).

Symptoms.—The symptoms are polyuria and polydipsia, with the passage of large quantities of urine, *e.g.* 12 litres in 24 hours, of pale colour, and low specific gravity, *e.g.* 1002. The polyuria leads to disturbed sleep and anxiety. The patient loses weight and strength, and may become very emaciated and even bedridden if untreated.

Diagnosis.—Hysterical polyuria may be difficult to differentiate apart from the hysterical background. There is a tendency in this condition, however, for the polyuria to be more marked during the daytime and the patient may sleep throughout the whole night, whereas the polyuria of diabetes insipidus is most troublesome at night. The hysterical patient remains in reasonably good health in spite of the polydipsia and polyuria. Some individuals have a familial hypersensitivity to caffeine diuretics and, if much tea or coffee is drunk, they have polyuria and frequency. Diabetes mellitus is easily distinguished by hyperglycæmia and glycosuria. In chronic nephritis the urine may be voluminous and of constantly low specific gravity, but it contains some albumin and renal casts. A Wassermann reaction to exclude tertiary syphilis is always advisable. A radiogram of the skull, and examination of the optic disks and visual fields should exclude pituitary

and parapituitary tumours. The Hand-Schüller-Christian disease is congenital and familial and characterised by exophthalmos, large liver and spleen, yellow-tinted skin, and irregular patches of xanthomatous infiltration of the skull (radiogram).

Prognosis.—The disease is protracted, and if treatment is inadequate the patient becomes emaciated and dies from intercurrent infection.

Treatment.—It is illogical to attempt to restrict the intake of fluid severely, for experimental evidence shows that the primary disorder is the polyuria, and the polydipsia is a secondary attempt to compensate for the loss of fluid. Pitressin should be injected, 10 to 20 units subcutaneously three or more times in 24 hours. Some patients react allergically at the site of injection. Other commercial brands may then be tried, but if local reactions persist, the treatment will not be effective even if continued, as the hormone tends to be destroyed at the site of injection. Nasal insufflation of the dried powder is effective, and is carried out from a curved glass tube with two open ends or with a rubber pressure bulb attached. The patient learns to know the optimum amount of powder and frequency of application. Nasal jelly and application of the fluid on cotton wool in the nostrils are other methods. As with insulin, the dose of pitressin must be increased during periods of infection, *e.g.* influenza.

DIABETES TENUIFLUUS

Definition.—A condition of supernormal secretion of the posterior pituitary antidiuretic hormone, manifested by diminution in the volume of urine excreted and an absence of thirst. Tenuifluus means "flowing slenderly," and the condition is the opposite of diabetes insipidus (tasteless urine). The latter condition might be better termed diabetes multifluus (copious urine—flowing greatly).

Ætiology and Clinical Features.—The malady is due to excessive secretion of the anti-diuretic hormone of the pars nervosa of the pituitary. It is probable that the condition occurs rarely as an uncomplicated entity, as does diabetes insipidus, although in the comparatively few occasions that it has been observed, it has appeared to be part of a pituitary syndrome. It may be found with pituitary or parapituitary tumours, with Fröhlich's syndrome, and with other varieties of pituitary adiposity. Acromegaly may be associated either with diabetes insipidus, or with diabetes tenuifluus, and one may give place to the other according to the phase of the disease. In one such case of the latter, Ellinger, Hare and Simpson observed, for the first time, that there was an excess of anti-diuretic hormone in the cerebrospinal fluid. The daily intake of fluid was small, and the output of urine even smaller, the difference apparently being explained by an obviously excessive perspiration, in contrast with the dry skin of diabetes insipidus. It is interesting to note that radiation of the pituitary gland resulted in a normal and balanced fluid intake and output, and a disappearance of excessive perspiration and of the excess of antidiuretic hormone from the cerebrospinal fluid.

The mechanism of perspiration may not always compensate for a discrepancy between intake and output of fluid, and fluid may be retained,

with a resulting increase in weight, at any rate for a time. This may explain the premenstrual gain of weight, which may occur with normal women, but which is much greater in women with pituitary obesity. The subsequent post-menstrual loss of weight is associated with a diuresis. A disorder of water balance is also one factor in certain types of pituitary obesity, as is suggested by the response to mercurial diuretics, or sometimes to the mere adoption of the prone position.

Complications.—E. I. Jones recently described a syndrome, in a man of 26, which he attributes to hyperactivity of the posterior lobe of the pituitary gland. The main features were hypertension, hyperchromic anæmic, achlorhydria, and impaired carbohydrate tolerance. Melanophore-expanding vasopressor, and antidiuretic substances were present in the urine (Noble and others).

Diagnosis.—An abnormally small daily excretion of urine in the absence of cardiac or renal disease suggests diabetes tenuifluus, especially if accompanied by excessive perspiration for which no ordinary cause is obvious.

Treatment.—Radiation of the pituitary gland appears beneficial.

ANTIHORMONES

Collip's observation that parathormone gradually lost its effect on repeated injection first drew attention to the possibility of anti-hormones or anti-hormonic substances being produced in the human body by the injection of hormones. Since then anti-hormones have been discovered for most of the pituitary " trophic " hormones, their action being especially well studied in the case of the thyrotrophic, gonadotrophic and diabetogenic hormones. Thus, if thyrotrophic hormone (thyrotrophin) is injected into guinea pigs, the thyroid gland undergoes hyperplasia, thyroxine is secreted in excess, and the basal metabolic rate increases by, say, 50 per cent., attaining a maximum in 7 to 10 days. After this, even when injections are continued, the basal metabolic rate falls to normal or even subnormal, and the thyroid again fills with colloid, as in the resting phase. This development of refractoriness to the thyrotrophic stimulus is due to the production of anti-thyrotrophic hormone which neutralises the activity of the thyrotrophic hormone. This can be proved by injecting the serum of a guinea pig in a refractory phase into a normal guinea pig, and thus rendering the second animal immediately refractory to thyrotrophic hormone. All this is equally true of man and is an obvious stumbling block to therapy, even though experimentally the resistance can be overcome by progressively increasing the dosage of " trophic " hormone.

The term anti-hormone does not necessarily indicate that the substance is a hormone and not merely a chemical anti-body or precipitin. Collip regards a hormone—anti-hormone linkage as a normal condition, but there is no evidence that these " anti " substances are produced in the endocrine glands. It has been shown in man, as in the experimental animal, that gonadotrophic hormone of the same species (pregnancy urine) does not produce anti-hormone, whereas gonadotrophic hormone from another species (*e.g.* sheep's pituitary) does. This suggests that the mechanism is a precipitin one, but this is not always so and anti-bodies can be formed from protein-free extracts.

The practical point is to remember that if the hormone is derived from a species other than man, therapy may be ineffective after some weeks, and this especially refers to parathormone, growth hormone, thyrotrophic hormone, and some gonadotrophic hormones. Antihormones tend to disappear after several weeks, when therapy may be resumed intermittently.

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DISEASES OF THE THYROID GLAND

In the absence of convincing evidence as to the existence of dysthyroidism, a division of thyroid disorders into hypersecretion and hyposecretion is at present acceptable. In the case of both, the age incidence may influence the clinical features. The essential hormone of the thyroid gland is usually considered to be thyroxine, the p-hydroxyphenyl ether of tyrosine. The colloid of the gland is thyroglobulin, a protein to which iodine is attached. On hydrolysis this yields the α-amino acids thyroxine and diiodotyrosine. Harington believes that the true active secretion contains thyroxine and diiodotyrosine linked to form a peptide. The activity of thyroglobulin is proportional to its total iodine content and not to the thyroxine contained therein. The relative insolubility of thyroxine, and the latent period after its intravenous injection, also make it difficult to accept thyroxine as the essential hormone; but even so, for the sake of convenience, this term will be used in the text.

Unfortunately a clinical classification of thyroid diseases has not a clearly defined morbid anatomical basis. This is not unrelated to the fact that hyperplasia of the gland, in the absence of sufficient iodine, may be present with the clinical manifestations of hyposecretion rather than hypersecretion. According to Marine, the thyroid gland is a very labile tissue, with a single definite morphological cycle influenced by the balance between the need for iodine and its availability. An absolute or relative deficiency of iodine leads to hypertrophy and hyperplasia of the thyroid epithelium and loss of colloid. A subsequent adequate supply of iodine produces involution to a resting epithelium and much colloid. This cycle can repeat itself, but a prolonged iodine deficiency may lead to irreversible atrophy of the gland. Experimental evidence indicates that iodine can prevent any thyrotrophic or goitrogenic agency from being effective.

A simple clinical classification is as follows:

- Hyperthyroidism
  - Graves's Disease.
  - Secondary Thyrotoxicosis.
- Hypothyroidism
  - Myxœdema.
  - Cretinism.

GRAVES'S DISEASE

Synonyms.—Hyperthyroidism; Exophthalmic Goitre; Parry's Disease; Basedow's Disease.

Definition.—Hyperactivity and hypersecretion of the thyroid gland, usually manifested by tachycardia, tremor, loss of weight, nervousness, exophthalmos, enlargement of the thyroid, and raised basal metabolic rate.

Ætiology.—The disease is more common in females than males, in the ratio of 6 to 1. This is probably associated with the greater lability of the endocrine system in the former, as indicated by the not infrequent physiological transient enlargement of the thyroid at puberty, at menstruation, and the menopause. The malady is commonest in the second and third decades, but it may occur in childhood or old age. Puberty or the menopause may be periods of initiation.

Mental stress, anxiety, shock and sexual neurosis are often precursors of the disease, but a constitutional vulnerability of the thyroid to such stimuli is probable. The latter is also indicated by a familial predisposition. Infection aggravates pre-existing hyperthyroidism, and sometimes appears to initiate the disease.

Pathology.—The cuboidal epithelial cells undergo hypertrophy and become columnar. They also divide and multiply (hyperplasia), and may project in folds into the follicles, giving a lace-like pattern. The follicles are almost emptied of colloid unless iodine has been given. Adenomata may be present. There is a generalised lymphatic hyperplasia and lymphoid infiltration of the thyroid itself. The thymus is usually enlarged. The liver may show areas of necrosis or atrophy, and is often depleted of glycogen. Experimentally, pituitary thyrotrophin will produce similar pathological changes and a raised B.M.R. in guinea-pigs and man. Nevertheless, it has not been possible to demonstrate such a hormone in the blood of patients with hyperthyroidism.

Symptoms.—The excessive secretion of thyroxine has wide systemic effects, and also disturbs the nervous stability of the patient. Many of the symptoms appear to result from overactivity of the sympathetic nervous system.

Cardio-vascular system.—Tachycardia in some degree is invariable, and is usually associated with palpitation. Extra-systoles may be present, and if the disease is of long standing or in people over 40, auricular fibrillation is not infrequent. Capillary pulsation may be seen, and vaso-motor instability is evidenced by a tendency to blush or the appearance of a characteristic patch of redness over the neck and upper sternum. The carotid and brachial vessels pulsate visibly and forcibly. The systolic pressure is slightly raised and the diastolic is normal or diminished, resulting in an increased pulse pressure. It has been suggested that hyperthyroidism may be a cause of hypertension, but the evidence is not convincing, and thyroidectomy has not been shown to produce any effect on the hypertension itself, although associated tachycardia or angina may be favourably influenced.

Nervous system.—There is a characteristic tremor of the hands, noticeable on being asked to hold out the hands, or in writing, or in lifting a cup. An anxiety neurosis is a frequent and almost invariable accompaniment of hyper-

thyroidism. The patient is also restless and unstable, and finds it difficult to remain in one position for any length of time. Conversation too is desultory and, although there is often a hyperacuity of perception and conception, this is offset by an inability for sustained effort or concentration. Increased sensitivity and sensibility trouble the patient and her associates or family, and emotional distress is common. Occasionally psychotic manifestations develop, especially paranoia and acute mania, with suicidal tendencies, but rarely does this happen in the absence of a constitutional predisposition. Sweating is often excessive, manifested by the hot, moist handshake, and it may be soaking undergarments or bedclothes. Considerable muscular wasting and weakness may be features, simulating acute bulbar palsy, or progressive muscular atrophy, or very rarely familial periodic paralysis, but they are thyrotoxic myopathies and not neurogenic in origin.

Gastro-intestinal.—The paradox of an insatiable and voracious appetite with progressive loss of weight is a source of wonder and concern to patient and relatives. The explanation is a raised metabolic rate. Excessive thirst is an effort to compensate for loss of fluid by profuse perspiration. Attacks of dyspepsia occur, sometimes with vomiting, and this may be due to hepatic disturbance, but achlorhydria and hypochlorhydria are not infrequent. Achlorhydria, or vegetative nervous irritability, may explain attacks of diarrhœa, which if severe or inadequately controlled may result in dehydration.

Ocular signs.—Exophthalmos is said to be present in 70 per cent. of cases, but if minor degrees are included the incidence is much higher. The condition is usually obvious, but early stages may be indicated by a glint in the eye, or a restless coquettish look. Although characteristically bilateral, one eye may be affected before the other, or in lesser degree, presumably because of anatomical differences. The exophthalmos is not usually associated with dilatation of the pupil. It is interesting to note that pituitary thyrotropin will cause exophthalmos, experimentally, even after paralysis of the cervical sympathetic, or after thyroidectomy. The latter fact explains why exophthalmos sometimes persists after an adequate thyroidectomy. The classical signs of exophthalmos associated with historical names have no practical significance, and are only included for examination purposes. Thus: Dalrymple's sign is the wide palpebral fissure; von Graefe's sign is lagging of the upper eyelid on looking down; Stellwag's sign is absence of blinking; and Joffroy's sign is absence of wrinkling of the forehead on looking up.

Brain has described a condition of exophthalmic ophthalmoplegia in people usually over 40, in which there is mechanical paralysis of ocular movement in one plane. One eye is nearly always more affected than the other, and diplopia is frequent. Although this severe condition may be associated with mild thyrotoxicosis, or appear after thyroidectomy, he regards it as a separate entity. Nevertheless, in both conditions, there appears to be a thyrotrophic stimulus, contractions of the orbital smooth muscle, venous compression, œdema, and ultimately swelling and degeneration of ocular muscles.

Thyroid gland.—This is almost invariably enlarged, although the degree is by no means proportional to that of the thyrotoxicosis. The enlargement usually affects both lobes, and not infrequently the isthmus. The swellings are smooth and roughly symmetrical, but one lobe may be larger than another. Small degrees of enlargement may be missed unless the proper technique

of palpation is observed. The thumb should compress the site of one lobe of the thyroid against the trachea, and the opposite lobe then becomes palpable to the thumb or fingers of the other hand. A systolic bruit over the thyroid may be heard on auscultation.

Metabolism.—The thyroid gland controls metabolism, and the increased basal metabolic rate in thyrotoxicosis is a fundamental feature. Modern mechanical apparatus which records oxygen absorption permits the estimation in 10 minutes, and is a valuable arithmetical method of measuring the severity of the disease and its subsequent progress. There is a negative nitrogen balance, and excessive creatinuria indicates a pathological breakdown of muscle tissue. The fat depots of the body tend to disappear, and the serum cholesterol is low, *e.g.* 80 compared with normal 180.

The liver is depleted of glycogen, and transient or persistent glycosuria may appear. This rarely indicates true diabetes mellitus, which is not more common among thyrotoxic patients than among the rest of the population. Nevertheless, thyroxine is antagonistic to insulin. In thyrotoxic glycosuria, the resting blood sugar level is normal, but following 50 grams of glucose there is a high and prolonged blood sugar curve. In the absence of gastro-intestinal symptoms, or partial starvation, ketosis does not occur. There may be a negative calcium balance and, although the serum calcium is not raised, as in hyperparathyroidism, the renal excretion of calcium is not infrequently excessive. There results a decalcification of the bones, which rarely may reach a severe degree. The negative calcium balance is not apparently proportional to the basal metabolic rate, and is not always cured by thyroidectomy, even when the latter is otherwise successful. There is a negative iodine balance, with a raised blood iodine and increased urinary excretion of iodine. Unless iodine is given, the thyroid gland in thyrotoxicosis contains appreciably less iodine than the normal gland, because thyroxine is rapidly secreted and not stored.

Other features.—Relative impotence may be present in the male, and amenorrhœa or scanty menstruation is common in females. Pigmentation is not uncommon in the orbital region, but may be more diffuse. Premature whitening of the hair sometimes occurs. No characteristic blood changes are met with, but a lymphocytosis may be present. Crises are an alarming feature of thyrotoxicosis, sometimes precipitated by infection, or diarrhœa, but often apparently without cause. There is an acute exacerbation of the condition, with manifestations predominantly cardiac, cerebral, or gastro-intestinal, and the patient may die. Occasionally abdominal pain may be severe enough to simulate an acute abdomen, and on laparotomy acute congestion of the pancreas has been observed.

Diagnosis.—When the classical features of tachycardia, exophthalmos, enlarged thyroid, tremor of the hands, and loss of weight are present the diagnosis usually offers no difficulty, and a raised basal metabolic rate is confirmatory evidence.

" Masked " forms of hyperthyroidism, or " formes frustes," in which the presenting feature appears to indicate some other disease, may offer difficulty, but awareness of the possibility of hyperthyroidism usually prevents a mistaken diagnosis. Thus, cardiologists are always on the look out for a possible thyroid basis in cases of auricular fibrillation, and it would seem that the latter may occur in paroxysmal form before the clinical picture of hyper-

thyroidism is well developed, while occasionally fibrillation may supervene some years after the disease is apparently arrested.

I have been impressed by the number of patients with wasting as the presenting feature, the thyroid basis being undiagnosed for some time. In some of these cases, diabetes mellitus may be suspected, especially if glycosuria and hyperglycæmia are present; but, when the carbohydrate disturbance is due to thyrotoxicosis, the fasting blood sugar is not raised, and the glycosuria is often intermittent and independent of diet. The muscular wasting and weakness of hyperthyroidism may simulate the myopathies, or myasthenia gravis. The latter is an extremely rare complication of thyrotoxicosis, and is differentiated by the selectivity for groups of muscles and the response to prostigmine. Some patients are treated for an associated neurasthenia before the thyrotoxicosis is recognised. An overactive sympathetic nervous system at the climacteric may produce many features simulating thyrotoxicosis, but only a small proportion of such patients have a true thyrotoxicosis. Neuro-circulatory asthenia may simulate hyperthyroidism, and the thyroid gland is often somewhat enlarged, but in the former the tachycardia is more dependent upon emotion and change of position, and the pulse rate at rest or when sleeping is usually not raised.

Course and Prognosis.—The natural course of the disease, in the absence of treatment, is progressively downhill, but waves of remission and exacerbation occur. Nevertheless, some patients spontaneously recover, or even become myxœdematous. The chief dangers are cardiac failure, intercurrent infection, and mental disorder.

Treatment.—It should be noted that the treatment of Graves's disease is always medical, even although more often than not an essential part of treatment is surgical removal, or radiological destruction, of the greater part of the hyperactive thyroid gland. Some patients respond to medical treatment alone, and in early or mild cases this should always be given a fair trial. Rest and quiet, together with sedatives, are obvious indications. Quinine hydrobromide is sometimes used, in dosage of 10 gr. t.d.s., the thyrotoxic patient having an increased tolerance for this drug. It is usual to advise some form of psychotherapy, such as reassurance and suggestion, and, if the anxiety-neurotic symptoms are predominant, more specialised skill in this field may produce excellent results.

The diet should be a full one, and there are no grounds for curbing the patient's appetite except in so far as fatty foods may not be well tolerated, while rapid gulping of food results in discomfort. Catabolism of carbohydrate, protein and fat is excessive, and the body has need of their replacement. Insulin (*e.g.* 10 units t.d.s. after meals) may help to increase weight, and sometimes has a beneficial effect on the symptoms. Similar anabolic effects result from testosterone propionate, 50 mg. intramuscularly three times a week, but there is a danger of virilisation in the female if this therapy is prolonged. Cortical extract (cortin) or desoxycorticosterone acetate is also of some value. Fluids should be drunk freely to satisfy thirst, and in the presence of diarrhœa and vomiting it may be necessary to give saline and 5 per cent. dextrose by continuous drip intravenously, if rectal or subcutaneous methods prove inadequate.

It is usually held that iodine should be restricted to pre-operative use, since the patient becomes refractory or even worse after 2 weeks. In my experience,

however, small doses of iodine, such as 3 minims of Lugol's iodine once daily, may be continued for months or years with benefit. It is not curative, but it appears to enable the disease to run its course at a lower level of thyrotoxicosis and has a favourable influence on all the symptoms. The gland itself, however, may become larger and more tense as the vesicles become distended with colloid. Lugol's iodine is usually taken in an ounce or two of milk after a meal. It may be replaced by diiodotyrosine, 10 mg. or more daily, but this drug has no obvious advantage. Simple tachycardia is uninfluenced by digitalis, which should only be employed when the condition is complicated by auricular fibrillation or cardiac failure (see Heart section).

Sepsis frequently produces an exacerbation of thyrotoxicosis, and removal of septic foci an amelioration. Nevertheless, tonsillectomy or even dental extraction may be followed by a severe crisis endangering the life of the patient, and when the thyrotoxicosis is of any severity it is more prudent to resort to radiation or thyroidectomy before removing the septic foci. Pregnancy tends to aggravate thyrotoxicosis, although temporary benefit is sometimes observed; and the incidence of miscarriage, premature and stillbirths, is high. Thyroid radiation or thyroidectomy within the first few months is the best treatment.

Surgical Treatment.—When medical treatment has failed to control the disease, or in those cases in which the malady is advanced when first seen, and still more so when auricular fibrillation has supervened, there should be no undue delay before resorting to surgery. The worse the cardiac condition, the more urgent the need. It should be remembered that total thyroidectomy is sometimes advocated for cardiac insufficiency even in the absence of thyrotoxicosis; and that auricular fibrillation or cardiac failure associated with thyrotoxicosis tends to be refractory to digitalis or quinidine unless thyroidectomy is performed. The use of pre-operative iodine and the improvement in anæsthesia and surgical technique have reduced the mortality to 1 per cent.

Lugol's iodine is given in doses of 10 minims t.d.s. for 10 days before operation. Bromethol (avertin), 0·1 gram per kilo weight, preceded by morphia, $\frac{1}{8}$ gr., in nervous patients, is administered per rectum. The patient is usually drowsy or asleep after 30 minutes and can then be taken to the operating theatre. Gas and oxygen, but no ether, supplement the anæsthesia, and many surgeons also use local infiltration with 0·5 per cent procaine hydrochloride (novocaine). After operation, restlessness is controlled by sedatives by the mouth or per rectum. Morphine should be used sparingly, as cyanosis is best avoided. In the presence of cyanosis, or even merely with exacerbation of general symptoms, an oxygen tent or room is of great value. The Lugol's iodine is continued as before operation, and after a week the dose is gradually reduced to 5 minims daily, which is continued for 3 months. This is thought to prevent recurrence of thyrotoxicosis, but large doses of iodine may encourage the onset of myxœdema if the thyroidectomy has been extensive. The pulse rate and temperature are usually raised for some days after operation, after which there is a gradual return to normal. A crisis may, however, follow operation, with a rising pulse rate, gastro-intestinal symptoms, restlessness, and perhaps coma. Lugol's iodine must then be administered in large doses, *e.g.* 100 minims in 12 hours. If not retained by mouth, or by duodenal tube, or per rectum, it is given intravenously, in a

litre of saline and glucose, and it may even be better to use this route without delay. Auricular fibrillation may appear for the first time after operation, but frequently disappears spontaneously after a few days. If not, quinidine sulphate is employed, 3 grains on the first day, increasing up to 3 grains five times a day. If no effect after 40 grains, digitalis is given. If fibrillation is terminated by quinidine, the rhythm will frequently remain regular on discarding the quinidine (see also Cardiac Section). It is advisable for the patient to endeavour to lead a quiet, unworried life for some months after operation. Some 60 per cent. of patients are cured, and the remainder improved in varying degree.

Radiation.—Until the last 5 years the results in this field were variable, and complicated by skin burns. With the employment of deep X-ray, however, they are much better, and it may be that those of some technicians equal surgical results. Unless the case is of great severity or complicated by auricular fibrillation, in my opinion deep radiation is justifiable therapy, and is unlikely to interfere with subsequent surgery should such prove necessary.

Treatment by radium surface application or the insertion of radon seeds is not generally considered to be as efficacious, although advocated by some.

SECONDARY THYROTOXICOSIS

Synonyms.—Toxic Adenoma ; Nodular Goitre with Hyperthyroidism.

Definition.—Hypersecretion of the thyroid gland superimposed upon a previously symptomless goitre, or associated from the first with a clinically nodular goitre.

According to many observers there is no essential difference between Graves's disease and secondary thyrotoxicosis, either on clinical or morbid anatomical grounds. It is true that every grade of transition from one to the other is clinically met with, and that the pathologist is unable to say with certainty from a study of sections of thyroid glands to which clinical group it belongs. Small multiple adenomas occur in Graves's disease, and areas of hyperplasia said to be characteristic of Graves's disease may be present in nodular goitre. Nor is there any conclusive evidence in favour of Plummer's hypothesis that in Graves's disease there is a qualitative abnormal as well as excessive secretion by the thyroid gland, and that in toxic adenoma there is simply a quantitative hyperthyroidism.

Nevertheless, clinically the following points of differentiation from Graves's disease are worthy of note. Exophthalmos is absent, or only present in minor degree ; nervous excitability is less intense, associated anxiety neurosis uncommon, and psychosis extremely rare ; the brunt of the disease appears to fall on the cardio-vascular system and auricular fibrillation is more frequent, the latter fact being associated with the greater age incidence, since the majority of cases are over 40. The response to iodine may be inadequate in some 30 per cent. of cases, but the operative mortality is less than 1 per cent., and recurrence of thyrotoxicosis is rare.

The greater part of what has been written in the section on Graves's disease is applicable to toxic adenoma, but the need for surgery is much greater and little time should be lost on other methods of therapy. The

response to radiation is also less satisfactory than in Graves's disease. It is rarely possible to deal effectively with the auricular fibrillation, or cardiac insufficiency, of toxic adenoma prior to thyroidectomy, and the sooner the operation is performed the better.

With toxic adenoma, even more than with Graves's disease, there are masked forms in which the presenting features are cardio-vascular and the other constitutional symptoms slight. This is especially true in the case of elderly people, and some cardiologists urge the diagnosis of thyrotoxic auricular fibrillation in the presence of goitre even when the basal metabolic rate is normal.

MYXŒDEMA

Synonym.— Hypothyroidism.

Definition.— A primary condition of hypothyroidism, associated with low basal metabolism, and manifested by sensitivity to cold, mental hebetude, loss of hair, and mucoid infiltration of the skin and subcutaneous tissue. It does not include hypothyroidism secondary to pituitary hypofunction, as in Simmonds's cachexia.

Ætiology.—Myxœdema usually occurs sporadically and without obvious cause, although there is occasionally a history of preceding infection. It is more frequent in women than men, in the ratio of 8 to 1, and is most common in middle age. Perhaps the condition in women is comparable to the cessation of ovarian function, which also is met with in the fourth decade. The disease, however, may have its onset in old age, or even in childhood—when it is known as juvenile myxœdema. There would also appear to be a constitutional predisposition, as several cases in the same family may be met with. Myxœdema may follow partial thyroidectomy for thyrotoxicosis, or complete thyroidectomy for non-thyroid cardiac disease, the term cachexia strumipriva sometimes being given to post-operative myxœdema. Apart from operation or excessive radiation, myxœdema may spontaneously follow chronic thyrotoxicosis. Another group of myxœdematous cases occur endemically and usually with goitre, the ætiology being a relative or absolute iodine deficiency.

Pathology.—The thyroid is atrophic, and the secreting epithelium is largely replaced by fibrous tissue. The skin and subcutaneous tissue are infiltrated with a mucoid-like material, which was wrongly thought to be mucin, and hence the name myxœdema. There is an abnormal accumulation of extra-cellular and extra-vascular protein, the osmotic pressure of which leads to a transfer of saline from plasma to interstitial tissues. The mucoid infiltration may be widespread and implicate the nasal, pharyngeal, buccal and auditory mucous membrane, salivary glands, the larynx, and the œsophagus. The kidneys are sometimes extensively involved, and there may be deposits in the vulvo-vaginal region. The heart and coronary vessels not infrequently show atheromatous changes, with some cardiac dilatation, but contrary to general belief, actual mucoid infiltration is a rarity.

Symptoms.—The onset is usually insidious, and at least half the patients have had the disease for some years before it is recognised. The general condition is comparable to hibernation, all the physical, metabolic and mental processes being sluggish and reduced much below the normal.

Integument.—The facies is pale and puffy, with baggy eyelids and a characteristic malar flush. There is thinning of the outer half of the eyebrows, and the hair of the head is dry and lustreless and falls out, sometimes with resulting patchy alopecia. The skin is dry and rough, and gives a swollen œdematous appearance, especially in certain regions, *e.g.* face, neck, supraclavicular areas, hands, legs and feet; but there is no pitting on pressure. In contrast to hyperthyroidism, obvious sweating is minimal or absent.

Cardio-vascular.—The pulse rate is characteristically slow, *e.g.* 50, but there may be tachycardia with cardiac insufficiency. The blood pressure may be raised but not necessarily so. Angina sometimes occurs. Radiography usually shows enlargement of the heart, and the electrocardiogram a flattened or inverted T wave, etc. (see Cardiac Section).

Mental changes.—Apart from the psychoses, especially melancholia, which may complicate advanced or chronic cases, there are characteristic abnormalities of behaviour. The intellectual processes appear dimmed, and memory is poor. There is a noticeable latent period before questions are answered, and speech is slow, thick, indistinct and rather toneless. The whole attitude is apathetic and lethargic, with a tendency to somnolence.

Metabolic.—The basal metabolic rate is usually of the order of −40, the temperature is subnormal, and the patient hypersensitive to cold, being especially intolerant of the winter months. There is an almost constant hypercholesterolæmia, *e.g.* value of 400 mg. per cent., compared with a normal of 180; the cause of this is uncertain. The fasting blood sugar is frequently low, and the flat carbohydrate tolerance curve shows an apparently increased tolerance. Spontaneous hypoglycæmia is rare, but there is hypersensitivity to insulin. Occasionally the opposite condition of decreased carbohydrate tolerance is met with, but in these circumstances it would appear likely that there is a coincident atrophy of the pancreas.

Blood.—There are three types of anæmia found in myxœdema: (1) Hypochromic low colour index anæmia. This variety responds to iron. It differs from other iron deficiency anæmias, however, in the absence of microcytosis. (2) Hyperchromic megalocytic high colour index anæmia. This responds to liver, and is comparable to Addisonian anæmia. (3) Simple hypochromic macrocytic high colour index anæmia. It differs from Addisonian anæmia in the absence of megalocytosis and failure to respond to liver. Neither does it respond to iron, but thyroid has a specific effect, although a gradual one. The three types may be associated with achlorhydria, which is not uncommon, but type (3) is a specific thyroid deficiency anæmia. Either of the first two types may, on treatment with iron or liver respectively, change into the last type (simple hyperchromic). It is generally assumed that thyroid is a direct hæmopoietic agent essential for maturation of red cells, but the partial atrophy of the erythron in hypothyroidism may be an adaptation to the diminished need of the tissues for oxygen.

Other features.—Constipation is common, in contrast to the diarrhœa of thyrotoxicosis. Similarly, appetite and thirst are diminished. Deposits of mucoid material may impair hearing, smell, taste and swallowing. There may be amenorrhœa or menorrhagia, and in the male relative or absolute impotence is not infrequent. Vague generalised pains may be a feature, but it is difficult to conjecture a specific relationship.

Diagnosis.—Even though well-developed myxœdema presents a characteristic clinical picture, it is perhaps the most frequently missed endocrine disorder, and this is certainly true of the early or slight cases. The best method of avoiding this is to constantly bear in mind the existence of the disorder, especially when dealing with menopausal multipara. Sluggish mental response, with thick, dry skin and loss of hair, failure of memory, and sensitivity to cold are characteristic.

Many patients will first be seen by the psychiatrist, although the disease must have been present for some time. Others will present themselves to the gynæcologist on account of menorrhagia. Again, the appearance of the patient may lead to the diagnosis of anæmia, confirmed by blood examination, but the other features should not be missed. The pale, puffy face with baggy eyes also resembles the facies of parenchymatous nephritis, and albuminuria may complicate myxœdema if the kidneys are involved in the mucoid infiltration; a further resemblance between the two conditions is the high blood cholesterol. Myxœdema may be difficult to differentiate from hypothyroid features in Simmonds's cachexia (which see), both having a low B.M.R. and sensitivity to cold. In the latter condition, however, mucoid infiltration of the skin is rare, the skin being thin and wrinkled, and the patient has lost much weight.

Localised myxœdema may paradoxically be a complication of hyperthyroidism, usually in a recurrent or post-operative phase. The B.M.R. may have changed from above to below normal, but is sometimes still raised. Thick œdematous plaques appear on the front of the shins, or the whole leg may be thickened. The overlying skin is often wrinkled and hairy, and the skin may itch or burn. Nodular lesions may also involve the face, arms, back or scrotum. The pathogenesis of localised myxœdema is uncertain, for the response to thyroid is poor.

Course and Prognosis.—In the absence of specific treatment the course is slowly but progressively downhill, and many patients end in the asylum. The response to treatment, however, is usually excellent though by no means necessarily so if a psychosis has already developed.

Treatment.—The specific treatment in myxœdema is thyroid. The drug is best given in the form of thyroideum, B.P. The maintenance dose for the average patient is about 3 grains daily. It is, however, prudent to commence with smaller doses, *e.g.* 1 gr., especially because of the extra strain that may be thrown on the heart by the increase in metabolism and the rate of circulation. A heart that was previously adequate may be unable to meet the extra demand, and cardiac failure or even angina may supervene if the initial dosage is too large. In the long run, however, thyroid in appropriate dosage has a beneficial influence on the cardio-vascular system. If an untreated myxœdematous patient is first seen with some cardiac insufficiency and a rapid pulse (in contrast with the usual bradycardia), there may be hesitation to give thyroid; but in small and gradually increasing dosage the drug has a beneficial if paradoxical effect, the cardiac rate diminishing as the heart and coronary circulation improve. With the more usual bradycardia, thyroid has the effect of increasing the pulse rate, and should this rise above 76 the dose of thyroid should be reduced. More exact criteria of dosage may be obtained by estimations of the basal metabolic rate or the blood cholesterol. It is useful to remember that thyroid, even

if administered intravenously as a single dose of thyroxine, requires 24 to 48 hours to begin to act, has its maximum effect at the end of a week, and continues to act for several weeks. There is therefore no point in giving thyroid more often than once daily, and a cumulative effect may be guarded against by missing one week in four. Thyroxine has no advantage over the dried gland, and its intravenous administration is not without danger as the initial reaction may be alarming, *e.g.* nausea, vomiting, angina, pyrexia, aching muscles, loss of hair and peeling skin.

Dinitrophenol raises the basal metabolic rate to normal but has no beneficial effect on the symptoms, and is only of scientific interest. Pituitary thyrotrophin has no influence on myxœdema, since the thyroid is incapable of responding to such a stimulus. It has, however, a beneficial and specific effect in hypothyroidism secondary to pituitary hypofunction, but this does not persist for longer than 3 weeks, owing to the development of anti-thyrotrophic substances. It is therefore of no clinical value.

Hypochromic anæmia is treated with iron; simple hyperchromic anæmia with thyroid; Addisonian anæmia with liver. Whatever the appropriate indication, thyroid will not be withheld except for scientific investigation. If exact hæmopoietic investigation is not available, most anæmias met with in myxœdema will respond to iron and thyroid, true Addisonian anæmia being very rare.

CRETINISM

Definition.—This is a condition of hypothyroidism beginning in fœtal life. In contrast, childhood myxœdema is superimposed on a normal infancy. The disorder may occur endemically or, more rarely, sporadically.

Ætiology.—The endemic form occurs in goitrous areas, the mother usually having a goitre. Iodine deficiency of the soil and water, and other theories are discussed in the Goitre section. No cause for the sporadic form is known. The sex incidence in both varieties is about equal.

Pathology.—In the endemic form, the goitre is usually the nodular adenomatous variety (see Goitre). In the case of sporadic cretinism, a goitre is rare, the thyroid being atrophic, with flattened irregular epithelial cells, small alveoli, and connective tissue overgrowth.

Symptoms.—The untreated cretin is mentally deficient, apathetic and somnolent, and tends to lead a vegetative existence. All the processes and stepping stones of childhood development are retarded, the fontanelles remain open for years, centres of ossification appear late, and the epiphyses remain ununited for long periods. Growth, however, is always deficient and cretinism is a variety of dwarfism. The facies is characteristic, being pale and pasty, and having a thick skin, wrinkled forehead, a broad nose with depressed bridge and big nostrils, and thick lips separated by a protruding enlarged fissured tongue. The hair on the head is dry and scanty, and the eyebrows and eyelashes frequently deficient. The body is characterised by a protruding, pendulous abdomen, with umbilical hernia, supraclavicular pads of fats, and some degree of scoliosis and lordosis. The hands are spatulate, with square finger tips, and the limbs lack muscular tone. Deafness is not infrequent, and speech is often impaired. Genital development is always retarded, and ultimate sexual maturity a rarity. As in the case of myxœdema,

there is a low basal metabolic rate, subnormal temperature, sensitivity to cold, a low blood sugar, sensitivity to insulin, and constipation.

Course.—If untreated, cretins remain semi-idiots and incapable of self-sufficiency. Intercurrent infection in childhood or adolescence is a common termination.

Diagnosis.—To those who have seen the characteristic appearance, the diagnosis of cretinism rarely offers difficulty. In contrast, a Mongol has mongoloid eyes, with epicentric folds, a good skin and complexion, fine but profuse hair, and a restless, bright manner.

Treatment.—Prophylactic treatment in endemic areas consists of small doses of iodine (see Goitre).

Treatment of the individual patient is specific, namely thyroid. One to three grains daily of thyroideum, B.P. may be required, as judged by the general effects and the cardiac rate. If given in infancy or early childhood, an approximation to normal may be attained, but sometimes a harmless, apathetic idiot is merely changed into a mischievous, truculent semi-idiot.

GOITRE

Definition.—A goitre is a pathological enlargement of the thyroid gland, which may be endemic or sporadic, symptomless or associated with hyperthyroidism or hypothyroidism. The contour of the gland may be smooth or nodular.

Ætiology.—Endemic goitre occurs in many regions throughout the world, including certain areas in this country, *e.g.* Derbyshire and Somerset. In Switzerland, where earlier investigations were undertaken, one factor found to be common to goitrous regions was a deficiency of iodine in the water and soil. This is not always the case in other parts of the world, and goitrogenic agents in an infected water supply have been implicated, although the deleterious effect may be obviated if the iodine content of the water is higher. Vitamin deficiency and a preponderance of calcium over iodine are other possible factors.

The ætiology of sporadic goitre is obscure. Apart from a possible relative iodine deficiency, a familial predisposition is sometimes apparent. The increased demands of the body for thyroxine at puberty may be indicated by a transient physiological thyroid enlargement, but this sometimes persists as a puberty goitre. Endemic goitre is usually obvious in childhood, and its peak incidence is at puberty. This is also true of sporadic goitre, which may however be met with at all ages. The sex incidence of goitre is about equal in childhood, but, after puberty, females are more often affected than males—about 8 to 1.

Pathology.—The smooth diffuse goitres may be divided into the parenchymatous and the colloid, although both histological features are not infrequently present in the same gland. The parenchymatous goitres often show degenerative changes in the epithelial cells, and areas of fibrosis. The colloid goitres contain low cuboidal epithelium lining vesicles, filled with colloid. Nodular goitres usually contain multiple capsulated adenomas, which may show cystic or hæmorrhagic change. Occasionally there is a single adenoma, which may be of colloid type or of parenchymatous type. In the latter case,

it is thought by some to arise from solid masses of embryonic cells that may be seen in normal glands, and for this reason is termed "Foetal adenoma."

The above pathological changes occur both in endemic and sporadic goitres.

Symptoms.—When goitre is associated with hyperthyroidism, the symptoms may be those either of Graves's disease or of secondary thyrotoxicosis (which see). When associated with hypothyroidism, the clinical picture is that of cretinism or myxœdema.

In all varieties of goitre, including those which are endocrinologically inactive, pressure symptoms may be the major manifestations, especially so in the case of nodular goitres, and when goitres are low down in the neck or behind the sternum (intra-thoracic), pressure symptoms may be the only indication apart from that given by radiological examination. Pressure on the trachea may produce difficulty in breathing, irritating cough, alteration in voice, and stridor. For mechanical reasons, the dyspnœa is worse on lying down, and attacks of dyspnœa with cyanosis may be fatal. The voice is also affected by paralysis of the recurrent laryngeal nerve, this, however, being rarely bilateral. Pressure on veins may produce dilatation of those of the head and neck, with cyanosis, and in the case of intrathoracic goitre, dilated veins may be evident over the chest. Œsophageal pressure and resulting dysphagia are rare, as also are bradycardia due to vagus involvement, and mydriasis and sweating from cervical sympathetic stimulation.

Complications.—Malignant change is said to supervene in 1·6 per cent. of all goitres, and in 2·7 per cent. of nodular goitres. It is usually only after some years that malignancy develops, and clinical indications are a rapid increase in size and hardness of the goitre over a period of weeks or months, and sometimes with fixity to the trachea. In cases in which malignant changes supervene, 35 per cent. are correctly diagnosed before operation, 30 per cent. at operation, and the remainder only on histological examination. The capsule of the adenocarcinoma is frequently intact, but histology shows, in places, solid masses of columnar cells invading blood vessels. Occasionally a malignant goitre is so small as to be unsuspected, and the first sign is multiple metastases, especially in bones.

Course.—A goitre may remain symptomless and innocent throughout life, but at any time toxic symptoms of hyperthyroidism or hypothyroidism may become manifest.

Diagnosis.—This is usually obvious on inspection. Intra-thoracic goitre may be simulated by thymus or mediastinal tumours. Sometimes auricular fibrillation in a middle-aged or elderly person may draw attention to a small pre-existing goitre which has been symptomless for years. Pressure symptoms on the trachea may simulate asthma, perhaps with the complication of bronchitis, and some of these cases are not diagnosed for years.

Treatment.—In Switzerland the addition of iodine to all salt sold, 1 part in 100,000, has enormously reduced the incidence of endemic goitre; but in Derbyshire the results of a similar experiment have not been so convincing. In areas of endemic goitre in France, 1 minim of Lugol's iodine daily, has been employed, and in America iodised salt, 1 : 10,000, both with varying and on the whole satisfactory results. As might have been anticipated, the results are best if iodine has been administered to the mother throughout the pregnancy, but even when first given in childhood, the in-

cidence of goitre is considerably reduced. It is to be pointed out that in the case of symptomless endemic goitre, especially of the nodular variety, the use of iodine is not free from the danger of inducing thyrotoxicosis. This is also true in the case of sporadic goitre, although the writer believes that in simple diffuse goitre the risk is insignificant. At the same time, it is to be remembered that some symptomless endemic goitres become hyperactive apart from any treatment. Marine advocates, as an alternative to iodine, the use of thyroideum, B.P. 1 to 2 gr. daily, for simple sporadic goitre. This method of treatment, while logical and safe, is rarely curative.

Radiation therapy is beneficial in smooth goitres but less so in nodular ones. When in nodular goitre there are pressure symptoms or toxic manifestations, early operation is advisable.

If in goitre hypothyroid symptoms are present, thyroid is, of course, indicated. (See Cretinism, Myxœdema.)

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DISEASES OF THE PARATHYROID GLANDS

The parathyroids are four in number, and are usually situated symmetrically in the posterior aspect of the thyroid gland. They secrete a hormone, parathormone, which gives protein colour reactions, is soluble in water and 80 per cent. alcohol, but insoluble in ether or acetone. The chief function of the glands is the regulation of calcium and phosphorus metabolism. Excess of the hormone leads to the clinical entity of osteitis fibrosa diffusa, and deficiency to tetany.

HYPERPARATHYROIDISM

Synonyms.—Generalised Osteititis Fibrosa Cystica; Von Recklinghausen's Osteitis Fibrosa; Osteitis Fibrosa Diffusa.

Definition.—A disease due to the excessive secretion of parathormone, and manifested clinically by hypercalcæmia, negative calcium balance, muscular atony, weakness and wasting, and decalcification of bones resulting in deformities and fractures.

Ætiology.—The disease, which is rare, is due to a neoplasm or hyperplasia of the parathyroid glands. The latter may be secondary to a pituitary stimulus, but parathyrotrophic hormone has not been demonstrated in the blood. The malady affects women twice as frequently as men. The average age incidence is about 40, but it also occurs in childhood and old age.

Pathology.—A circumscribed adenoma of one parathyroid gland is the commonest lesion, the remaining three glands being normal or hypoplastic. There may, however, be general hypertrophy and hyperplasia of all glands, which is usually obvious to the naked eye, and may even be of extreme degree, *e.g.* one weighing 5 grams compared with a normal of 60 mg. The cause of the hyperplasia is usually indeterminate; but occasionally it appears to be secondary to chronic renal disease and associated phosphorus retention. In the latter case there is a diffuse hyperplasia, without gross

enlargement, of the cells, whereas in idiopathic hyperplasia the cells are greatly enlarged and the cytoplasm is highly vacuolated. The essential skeletal changes are softening, replacement of bone marrow by fibrous tissue, rarefaction of the cortex, and the presence of numerous osteoclasts and osteoblasts, with osteoclastic giant cells and cyst formation. Deposits of calcium as fine granules may be present in all the viscera, especially the kidneys, lungs and arteries.

Symptoms.—These are all the direct or indirect result of excessive calcium mobilisation and excretion. The long bones may be bent and deformed, with perhaps osteoclastic tumours, and in some cases pathological fractures. The vertebrae are compressed, and not infrequently height is diminished by several inches. Osteoclastic swellings may deform the jaw. The shape of the skull is rarely distorted clinically. The bones and osteoclastomatous swellings are often tender, especially on pressure. The teeth are not decalcified. The muscles show atony, fatigueability, and atrophy. Gastro-intestinal symptoms are nausea, vomiting, constipation, abdominal pains and cramps. Polyuria and polydipsia are associated with the increased calcium excretion. Urinary symptoms are common. The calcium may be deposited diffusely, giving rise to the presence of chronic nephritis and renal insufficiency, or even multiple renal calculi, the latter consisting chiefly of calcium and phosphorus. Renal colic and pyelocystitis are complications.

Metabolic changes.—The calcium and phosphorus are mobilised from the bones, and excreted in excess in the urine and to a much less extent in the fæces. The serum calcium is usually raised, *e.g.* 15 mg. per cent. (normal 10 mg.), and the plasma phosphorus is diminished, *e.g.* 2 mg. per cent. (normal 3·5 mg.). In the presence of advanced renal disease, however, there may be phosphorus retention and a raised serum phosphorus. The plasma phosphatase is raised, *e.g.* 10 units compared with a normal of 2 units, and is a measure of osteoclastic activity. There is also an increased excretion of sodium and chloride.

Diagnosis.—Radiography shows generalised osteoporosis, with granular mottling in the skull. Rarely, bone changes may not be present until a later stage, and diagnosis may then depend on the raised serum calcium and increased urinary calcium excretion. In the absence of bone changes the serum phosphatase will not be raised. Some undoubted cases of primary hyperparathyroidism, cured by removal of a parathyroid adenoma, have had normal serum calcium values, but the urinary calcium has always been considerably increased. If the kidneys have been severely damaged by calcium deposition, the plasma phosphorus may be raised instead of being low.

When urinary symptoms are prominent, the underlying primary hyperparathyroidism may be unsuspected in the absence of metabolic investigation. Rarely, hyperparathyroidism of severe degree occurs secondary to chronic nephritis of long standing, and, in such patients, although the total urinary and fæcal calcium excretion is above normal, the serum calcium is normal or slightly less than normal and the phosphorus raised. Nevertheless, apart from the time sequence, ultimate diagnosis may depend upon histological examination of the parathyroid glands (see pathology above).

Gout and arthritis may be simulated, especially if there are tender deposits of calcium in the joints, and some patients are treated for vague

rheumatic pains or lumbago. In Paget's osteitis deformans, a disease of middle or old age, there is great deformity of the skull, normal calcium and phosphorus metabolism, but an increased serum phosphatase. Osteomalacia, or *adult* rickets, is very rare in England and America, and is due to deficient intake of vitamin D or lack of sunshine. The bones are soft and deformed, the plasma phosphatase is raised, and the plasma phosphorus is low, but the serum calcium is never above normal and is often below.

Albright has described a syndrome of multiple bone cysts and areas of rarefaction, segmentally distributed in relation to nerve roots, with corresponding patches of pigmentation. The disorder is found mostly in girls and in them is associated with sexual precocity, a feature not present in the male. There are no metabolic changes.

Prognosis.—In the absence of surgery, the course of the disease is progressive deterioration, and death occurs within a few years. Weakness, wasting and deformities compel the patient to take to bed. Intercurrent respiratory infection may terminate life, while others die from uræmia or pyelonephritis.

Treatment.—Primary hyperparathyroidism can only be adequately controlled by removal of a parathyroid adenoma or, in the case of hyperplasia, of two or more parathyroid glands. Deep radiation is usually ineffective, and a high calcium and phosphorus diet is only mildly beneficial and not without danger in the presence of renal insufficiency. If at operation no adenoma is discovered, the exploration should be continued above and below the thyroid region, behind the œsophagus and into the upper mediastinum, for a parathyroid tumour is sometimes found in such aberrant positions. Tetany, sometimes of severe degree, may occur within a few days after operation but is sometimes delayed for some weeks. It may be avoided by removing five-sixths of a large adenoma instead of the whole, the problem here being analogous to thyroidectomy in Graves's disease. If tetany does occur and can be controlled medically for a period of weeks or months, it often disappears completely, probably due to subsequent hyperplasia of the remaining parathyroid glands. The detailed treatment of tetany is discussed under that heading, but post-operative tetany is more logically treated by intravenous, intramuscular or oral calcium than by solution of parathyroid, U.S.P. (parathormone), as the bones are already dangerously decalcified. Following parathyroidectomy, the general symptoms, *e.g.* pains, weakness, anorexia, improve almost at once, but the bones may take several months to become normally calcified. The serum calcium immediately falls to normal or below normal, but the phosphatase tends to remain high for some months, being an indication of osteoblastic activity. The sudden change from high to low serum calcium may cause transitory visual and mental disturbances with some degree of apprehension.

HYPOPARATHYROIDISM

Synonym.—Parathyroid Tetany.

Definition.—A disease characterised by an irritability of the neuromuscular system due to a subnormal concentration of serum calcium, the latter being the result of deficient secretion of parathormone. All forms of

tetany are due to subnormal concentrations of calcium, or of ionised calcium, in the serum, but this is not necessarily the result of parathyroid hypofunction.

Ætiology.—Idiopathic hypoparathyroidism occurs sporadically, as does myxœdema, and may do so at any age, but it is a rarity. Most cases follow thyroidectomy when the surgeon has removed some or all of the parathyroid glands at the same time. Other cases follow removal of a parathyroid tumour and the remaining glands appear to be temporarily hypoplastic; or when two or more hyperplastic parathyroid glands are removed in osteitis fibrosa diffusa. Parathyroidectomised animals show decreased urinary phosphorus excretion and rise in plasma phosphorus before changes in calcium metabolism are apparent. Later, however, there is a fall in serum calcium and a decreased excretion of calcium, with resulting tetany which may be fatal. Parathormone injections will prevent or correct the initial changes in phosphorus metabolism and the later calcium ones. Tetany occurs in conditions other than hypoparathyroidism if the concentration of calcium in the blood falls below normal. Thus in rickets, osteomalacia and steatorrhœa there is a deficient absorption and utilisation of calcium. The increased demands for calcium in pregnancy and lactation may render a latent tetany manifest. Tetany may be found in alkalosis, the total serum calcium being normal, but the ionised fraction below normal; alkalosis may result from excessive vomiting, hysterical hyperpnœa, or alkaline medication.

Pathology.—In idiopathic hypoparathyroidism, the parathyroid glands may be atrophic; in post-operative parathyroid tetany, too much parathyroid tissue has been removed.

Symptoms.—Following thyroidectomy and parathyroidectomy, symptoms may appear within the first 48 hours or may be delayed weeks or months. There is often a general irritability, nervousness and apprehension in addition to weakness. Paræsthesias, and muscular cramps and stiffness are common in the hands, especially on the ulnar aspect, but may also occur in the feet. These symptoms may be followed by, or from the first be associated with, muscular contractions of the hands and feet, giving the classical picture of carpo-pedal spasm. The so-called obstetric hand is produced by flexion at the metacarpo-phalangeal joints, extension at the interphalangeal joints, and adduction of the thumb. Spasm of the laryngeal muscles may produce hoarseness and stridor, and, if the bronchial muscles are also involved, respiratory distress and cyanosis result, sometimes with fatal convulsions or coma. Tetanic muscular spasms are not infrequently painful and may cause the patient to cry out in distress.

In chronic cases, ectodermal defects become apparent, *e.g.* brittleness and ridging of the nails, loss of hair, transverse ridging of the decalcified teeth. Blurring of vision, perhaps leading to blindness, is due to opacity of the lens (cataract), and minor degrees of the latter may be detected by slit lamp technique even in the absence of ocular symptoms. Muscular spasm may involve ocular muscles.

Diagnosis.—Although in most cases diagnosis is obvious, mild degrees of hypoparathyroidism with general irritability, weakness and paræsthesias and only slight ectodermal deficiencies, may be unsuspected. The following classical signs may be of diagnostic value. Chvostek's is the production of contraction of facial muscles by tapping the facial nerve below the zygoma; Trousseau's is the production of carpal spasm by a sphygmomanometer band

on the arm at a pressure just above systolic ; Erb's is an exaggerated muscular contraction in response to minimal electrical stimuli. The failure to elicit one or more of these signs does not exclude the diagnosis. Biochemical evidence is often conclusive. In hypoparathyroidism the serum calcium is always below the normal value of 10 mg. per 100 c.c. (*e.g.* 6 mg.) and the plasma phosphorus is above the normal 3·5 mg. (*e.g.* 7 mg.) ; there is decreased urinary excretion of phosphorus and calcium. In a doubtful case, an experimental high phosphorus diet will depress the serum calcium and produce neuro-muscular symptoms, but this does not occur with normal parathyroids. It is interesting to note, however, that in cattle there is a form of tetany, which is the result of excessive phosphorus in the diet.

Treatment.—The logical treatment of hypoparathyroidism is solution of parathyroid, U.S.P. (parathormone), which acts by primarily increasing the excretion of urinary phosphorus and secondarily mobilising calcium from the bones and raising serum calcium. This form of treatment, however, has several disadvantages. Thus, it is useless in acute tetany because subcutaneous or intramuscular injections may take 8 or more hours to be effective and are variable in time and degrec of effect. While intravenous injection is quicker it takes a few hours to act and, moreover, by this route there is a danger of a protein shock like reaction in some patients. Four hourly injections of 1 c.c solution of parathyroid (20 units) intramuscularly or subcutaneously may, however, be effective after the initial latent period ; and, rarely, overdosage results in nausea, vomiting, diarrhœa, failing circulation, dehydration, increased viscosity of blood, coma and death. With controlled serum calcium estimations, however, overdosage is a rarity and it is more probable that 40 units daily may not be adequate to control the disorder. Even when solution of parathyroid is effective at first, a refractory state sets in after some weeks. The latter is probably not due to the production of anti-hormonic substances in the blood, as in the case of other hormones, but to local tissue immunity since an intravenous injection of solution of parathyroid may be still effective. Nevertheless, this refractory state renders prolonged therapy with solution of parathyroid an impracticable scheme.

The immediate treatment of acute tetany is the intravenous or intramuscular injection of calcium gluconate, 20 c.c. of a 10 per cent. solution, the effect being rapid and dramatic, but only lasting some hours. The injections must be administered slowly, but a little leakage from a vein has not the local deleterious effects of calcium chloride. It is obviously necessary to follow this emergency injection by large doses of calcium gluconate or lactate by mouth, *e.g.* 12 gms. daily in divided dosage. Calcium chloride is less pleasant to take, and in practice the theoretical value of the resulting acidosis is not appreciable. This is perhaps less true of the addition of 3 gms. of ammonium chloride, daily, in 1 gm. capsules. In many cases calcium gluconate or lactate by mouth is sufficient to control the tetany. If not, there should also be given vitamin D, which acts by increasing calcium absorption from the intestine and secondarily by increasing phosphorus excretion in the urine. The dosage of vitamin D, or calciferol, should be high ; 50,000 to 200,000 units daily may be required. In severe cases these measures may still be ineffective, and then a derivative of irradiated ergosterol, called dihydrotachysterol, or A.T. 10, is of great value. It is not antirachitic, probably because it also causes considerable excretion of phosphorus from the

urine, but it produces a great increase in calcium absorption from the intestine and a rise of serum calcium to normal or above normal. Like vitamin D it is of no use in emergency, the effect not being produced for some 24 to 48 hours. It is, however, cumulative in action, and the dosage should be controlled by periodic serum calcium estimations if hypercalcæmia (nausea, vomiting, calcium deposition in kidneys, albuminuria, etc.) is to be avoided. The urinary test of Sulkowitch is a useful indication of dosage, apart from serum calcium. The reagent consists of oxalic acid and ammonium oxalate in glacial acetic acid, and equal amounts of urine and reagent are mixed. If no precipitate occurs, the serum calcium is probably below 7·5 mg. per 100 c.c., as the renal threshold for calcium varies between 7·5 and 9; if there is a fine white cloud, the serum calcium values are probably normal, about 10; if the precipitate looks like milk, the values are pathologically high. Using this technique Albright gives 3 c.c. of dihydrotachysterol a day by mouth until calcium appears in the urine, after which 1 c.c., 3 to 5 times a week is usually adequate. Dihydrotachysterol is prepared in an oily solvent containing 5 mg. of the drug per c.c., and is administered by the oral route.

Diet in hypoparathyroidism is a matter of some controversy. High calcium diets (milk, cheese, egg yolk) have the serious disadvantage of also being high phosphorus diets. It is better, therefore, to have a normal diet, or preferably a low phosphorus diet, and supply the extra calcium as calcium lactate or gluconate. The keynote of a low phosphorus diet is to eat less of milk, cheese, egg-yolk, meat and nuts, and more of fruit, vegetables, carbohydrates, fats, and white of egg.

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DISEASES OF THE SUPRARENAL GLANDS

The suprarenal glands consist of two parts, cortex and medulla, which are separate organs in the lower species. The cortex is of mesoblastic origin, while the medulla is ectodermal. The cortex is composed of lipoid containing epithelial cells, arranged from without inwards in three zones, zona glomerulosa, z. fasciculata and z. reticularis. The inner portion of the latter is characterised by brightly staining granules (pigment zone). The medullary cells have an affinity for chromic acid stains, and are termed chromaffin cells. The adrenal glands are supplied by sympathetic nerves from the splanchnic and coeliac ganglia, but they are cholinergic.

The medulla secretes adrenaline (orthodioxyphenylethanomethylamine), and although this substance is sympathomimetic and, on injection, can produce vasoconstriction, an increase of blood pressure, cardiac rate, blood sugar, and of the basal metabolic rate, and dilatation of the coronary arteries, and of the bronchial tubes, etc., the medulla is not essential to life, and in animals may be destroyed by cautery without obvious changes resulting. Further, it is even doubtful if there is a continuous secretion of adrenaline in normal circumstances, although certain that it is secreted under abnormal circumstances, *e.g.* exposure to severe cold, during fright or emotion, during infections, and in hypoglycæmia.

The adrenal cortex is essential to life, and bilateral adrenalectomy results in death within 7 to 10 days. The following hormones have been isolated from the cortex: androsterone (androgenic), œstrone, progesterone, corticosterone, and desoxycorticosterone. The last appears to be an essential life-saving hormone, and has been synthesised from cholesterol. Corticosterone has only a fraction of the activity of desoxycorticosterone but this also is life-maintaining. The other hormones have no such action. Their sex influence is manifested under certain pathological, or experimental, conditions, although whether so under normal conditions is less certain. It is thought that the androgenic hormone is secreted by special cells which constitute a broad inner zone at birth, but soon after undergo involution, although they may become hyperplastic in virilism and pseudo-hermaphroditism. The zone has been termed the androgenic zone, and stains deeply with the Ponceau-fuchsin dye.

The chief function of desoxycorticosterone is the regulation of sodium metabolism, with an associated influence on water balance, chloride and potassium metabolism. After bilateral adrenalectomy, there is an increased excretion of salt and water, with a retention of potassium, and a corresponding fall in the serum values for sodium and chlorine, and a rise in serum potassium. (The normal values are sodium 320, chlorine 355, potassium 20 mg. per 100 c.c.). There is also a shift of fluid from the plasma to the viscera, especially the liver, and the muscles. The blood becomes viscous, and the plasma volume is seriously decreased. Desoxycorticosterone injections will produce a return to normal. The action of desoxycorticosterone on carbohydrate metabolism is, however, feeble compared with that of cortical extract. The latter will completely correct the depletion of hepatic glycogen and fall of blood sugar that occur in the adrenalectomised animal. Corticosterone is even more potent than cortical extract in its influence on carbohydrate metabolism.

ADDISON'S DISEASE

Synonym.—Hypocorticalism.

Definition.—A disease due to destruction and hypofunction of the adrenal cortex, and manifested by pigmentation, weakness, myasthenia, anorexia, loss of weight and hypotension. It was first described by Thomas Addison in 1849.

Ætiology.—The disease is found among all races, and in all climates. Males and females are affected about equally. It is commonest between the ages of 20 and 40, and rare in childhood and old age. Tuberculosis is the most frequent cause, but any infection or toxicosis may be ætiological.

Pathology.—In the case of tuberculous lesions, both the medulla and cortex are usually destroyed, except for small islets of surviving tissue. The gland is replaced by fibro-caseous tuberculous tissue with areas of fibrosis, giant cells and lymphocytes. There may be associated tuberculosis elsewhere, rarely pulmonary. A history of gland or bone tuberculosis in childhood or in other members of the family is not uncommon. The next most frequent cause is atrophy of the cortex, of unknown origin, the medulla being scarcely

affected. The cortex is almost entirely replaced by connective tissue and dilated capillaries, with infiltration of lymphocytes, plasma cells and leucocytes. The picture is more like a toxic necrosis than a simple atrophy. Rare causes are syphilis, amyloid disease, hæmorrhage, infarction, and malignant growth. The last may apparently produce the disease even when it involves the sympathetic nerve supply only, and not the actual glands.

Symptoms.—Weakness, loss of appetite, loss of strength, and pigmentation are the usual presenting features.

The onset is often gradual. Occasionally the patient may not be seen by a physician before a grave crisis has developed. This is especially so when pigmentation is not a conspicuous feature, in which connection, it is to be noted that pigmentation may be even absent in fair-skinned people and in acute cases. Usually the patient complains of feeling not well in a vague sort of way. He (or she) may be languid, lacking in strength, and easily tired. Appetite is poor, and there may be a special aversion to fatty foods. In more severe insufficiency, nausea and even vomiting are distressing features, while abdominal pain, rarely sufficiently severe to simulate an acute abdomen, is occasionally present. Pain and tenderness may be limited to the loin region above and internal to the kidney, or pain may be referred to the scapula or shoulder region as the result of irritation of the diaphragm by the diseased suprarenal. The absence of any pain is quite compatible with the disease, and in fact is even more usual. Constipation is common, but there may be intermittent attacks of diarrhœa, either spontaneous or following purgatives, and these may precipitate a crisis. Hiccups and yawning are symptoms which may be very intractable, and which indicate incipient deterioration. There is progressive loss of weight, myasthenia and general weakness.

Generalised pigmentation, usually involving the mucous membranes as well as the skin, is a classical sign of the disease. The pigment deposited on the mucous membranes and skin is the normal pigment, melanin. Cutaneously, it is deposited in the basal layer of the epidermis, but in amounts greater than normal. Brown patches and streaks may be found on the inner aspects of the cheeks, the soft palate and posterior portion of the hard palate, the sides of the tongue, the gums, and the mucous surface of the lips, especially at the corners of the mouth. The distribution of skin pigmentation is partly determined by exposure to light and irritation. Thus, it is most marked on the face and neck, dorsum of the hands and forearms, waist-line, garter area, axillary folds and vulva, and in areas of skin overlying bony prominences, *e.g.* knuckles, ischial tuberosities and ankles. The palms show no evidence of increased pigmentation, except in the interphalangeal creases. Occasionally there are scattered cutaneous pigmented spots on the face and body. The nails of the hands and of the feet may be pigmented and striated. A leucodermic pattern of pigmentation is rare but authentic. Although pigmentation is a classical sign of Addison's disease, it may be inconspicuous or even absent in fair-skinned people, or when the onset is acute.

There is considerable variation as to interference with sex function. In some there is none, while in others there is amenorrhœa or impotence. Hypogonadism is certainly not an essential feature. Many patients feel the cold badly, especially in more severe insufficiency. The body temperature may be normal or subnormal, with perhaps intermittent pyrexia, and the basal

metabolism is rarely appreciably lowered, except in crisis. The systolic blood pressure is characteristically below 100 mm. of mercury, but this does not necessarily give rise to symptoms, and a normal blood pressure may persist for some time. Although in some patients the fasting blood sugar and carbohydrate tolerance curves may be normal, in others there is a chronically low blood sugar and clinical attacks of hypoglycæmia may even be fatal if unrelieved by glucose or adrenaline. There is an increased sensitivity to infections, shock, surgical trauma, hæmorrhage and drugs. Conjunctivitis is a minor manifestation, usually denoting inadequate therapy.

In crisis, the patient is collapsed, cold and restless. The latter feature may be intermittent, and stupor may be more characteristic. There is considerable irritability and intractability. The patient tends to curl up deep in the bed beneath the covering, and to resent interference. The pulse is rapid and of poor volume, and the blood pressure tends to fall acutely. Nausea, vomiting and diarrhœa may be persistent, thus adding to the dehydration that has resulted from the increased loss of salt and water through the kidneys. The veins are collapsed and the blood viscous on account of anhydræmia. Ultimately urine becomes scanty in amount, and terminally may contain casts and albumen.

Complications.—Addison's disease may be complicated by thyrotoxicosis or by diabetes but these are rarities. Other tuberculous lesions or intermittent infections, such as pneumonia, are not uncommon.

Diagnosis.—Clinically, this depends upon the classical features of pigmentation, weakness, wasting, anorexia and hypotension. Cutaneous pigmentation may also occur in other conditions, including hæmochromatosis, Hodgkin's disease, exophthalmic goitre, pernicious anæmia, arsenical poisoning, malignant cachexia, ochronosis, argyria, parasitic irritation, leucodermia and pregnancy. In Simmond's cachexia, a condition which has many features in common with Addison's disease, pigmentation is usually absent and is never diffuse, or marked. It is important to note that pigmentation of the mucous membranes is practically pathognomonic of Addison's disease. It is said by some to occur very rarely with pernicious anæmia, malignant cachexia and arsenical poisoning. Of the first, I wish to record that two authorities on pernicious anæmia have never met with pigmentation of the mucous membranes in this disease. In people of the negro race, or in those with an antecedent negroid admixture, pigmentation of the mucous membrane may occur normally.

If the serum sodium and chlorine are in low concentration (*e.g.* 295 and 330 compared with normal 320 and 355 mg. per 100 c.c. respectively), the diagnosis of Addison's disease is confirmed. Normal values at any one time on the other hand do not contraindicate the diagnosis. The serum potassium is rarely raised above the normal, 20 mg. per 100 c.c., except in an incipient crisis. A raised blood urea or low blood sugar is supporting evidence, but both of these may be normal. The Cutler diagnostic test consists in measuring the renal excretion of sodium chloride on a low salt diet, with the addition of potassium citrate in a daily dose of 42 mg. per pound body weight. On the first day, unrestricted fluids are given; on the second, 40 c.c. fluid per kilo body weight; and on the third, 20 c.c. per kilo body weight. The urine collected from 8 a.m. to 12 noon on the third day is assayed for chlorine. In

normal subjects an average of 50 mg. of chloride per 100 c.c. of urine is excreted, whereas in Addison's disease at least 200 mg. of chloride per 100 c.c. were excreted. The results, however, are not always so unequivocal, and Dryerre finds that the urinary sodium values are a better indication.

When tuberculous lesions of the adrenal glands have become calcified, radiology may be of diagnostic help by revealing calcareous shadows in the corto-vertebral angle.

Prognosis.—In the absence of treatment, there is progressive deterioration and death within months or years. With adequate substitution therapy, life may be prolonged, but the sensitivity to intercurrent infection is always a danger. Occasionally there is a spontaneous recovery sufficient to permit the cessation of substitution therapy.

Treatment.—As in other hormone deficiencies, the essential treatment is substitution. Until recently cortical extract (cortin, eucortone, eschatin) was employed, usually by intramuscular injection, and the daily dosage varied between 5 c.c. and 20 c.c. The most severe cases, however, required 30 c.c. or even 40 c.c. daily, and in these circumstances cost and mechanical difficulties rendered the maintenance of life precarious and painful. The cortin was standardised on adrenalectomised dogs or rats. A considerable advance was made by Loeb's discovery of the value of salt therapy. The dosage of sodium chloride is 3 teaspoonfuls, or some 12 grams, daily, taken in water, milk, porridge, or lime-juice, according to taste. In some patients the salt treatment produces nausea and vomiting as in the case of normal people, so that it must be discontinued, but others can tolerate it quite well. Mild cases need no other special treatment, but in the more severe cases cortin must be administered as well, though the salt permits a reduction in the dosage of cortin.

More recently Reichstein has isolated from the adrenal cortex and also synthesised from cholesterol a substance called desoxycorticosterone, which appears to be an essential hormone of the adrenal cortex. It is prepared in ampoules of 5 mg. in 1 c.c. sesame or arachis oil (doca, percortin, cortiron), and is injected intramuscularly. It would appear that 5 mg. of desoxycorticosterone is equivalent to 10 or more c.c. of cortical extract, and the acetate of desoxycorticosterone is normally employed for a more gradual action. Usually the injections are painless but some patients react with red hot lumps at the site of injections, and owing to a local tissue immunity they fail to do well with the synthetic hormone. There are, however, alternative methods of using desoxycorticosterone acetate. Thus, 100 mg. tablets may be inserted in the subcutaneous fat, under local anæsthesia. Four to 8 such tablets are necessary, according to the severity of the disorder, and the effect lasts from 4 to 6 months, or even longer, and the treatment may then be repeated. The tablets are sterilised at 100° C. in an autoclave. Desoxycorticosterone acetate is also effective by cutaneous inunction when dissolved in benzyl alcohol (20 mg. in 1 c.c. being equivalent to 5 mg. by injection), but this preparation is not yet on the market. Whatever route of administration of desoxycorticosterone is employed, cases are occasionally met with in which the response to treatment does not appear to be as satisfactory as with cortical extract. In such cases, the latter should be used instead of, or as supplementary to, desoxycorticosterone therapy. Whether cortical

extract or desoxycorticosterone acetate is used, it is important to remember that infection always calls for increased dosage. This is also true of the inserted subcutaneous tablets, since the rate of absorption does not vary with needs, but depends upon physical laws. It is doubtful whether a low potassium diet is worth the bother of preparation, although some report favourable results.

In crisis the treatment is on similar lines but more intensified. Thus, 20 c.c. cortin or 10 mg. desoxycorticosterone acetate would be given intramuscularly every 4 hours. It is rarely necessary to administer intravenous saline and dextrose, as was previously advocated, and, moreover, this procedure is not infrequently followed by allergic reactions and rigors. If, however, the patient is "in extremis," it is justified and such risk may be taken. Rectal saline by drop method is an adjuvant but not essential.

The treatment of the underlying tuberculosis, when the presence of such is established, is carried out on general lines, but the writer has not seen appreciable benefit resulting from tuberculin injections. Injections of the adrenotrophic hormone of the pituitary gland have been advocated, but here too the writer's experience has not been favourable. A graft of the adrenal glands of an infant, born dead because of mechanical difficulties and from healthy parents, can be effectively grafted into the rectus abdominis. If the graft is successful, beneficial effect will result, but the glands are gradually absorbed and rarely does the benefit last more than 6 months. It is not a method of treatment which can rival modern chemical therapy.

ACUTE SUPRARENAL DEFICIENCY

Apart from Addison's disease, there is some clinical and pathological evidence that acute adrenal insufficiency occurs with certain infections, such as meningococcal septicæmia, diphtheria, typhoid fever, and pneumonia. At autopsy, the suprarenals may show congestion, œdema, hæmorrhage, and necrosis. The onset is sudden. Malaise, restlessness, headache, vomiting, fever, cyanosis, scattered petechæ, and stupor or coma, are characteristic features of the malady. When the underlying lesion is acute bilateral suprarenal hæmorrhage, the term Waterhouse-Friderichsen syndrome has been applied to the clinical condition. This syndrome is usually associated with meningococcal septicæmia, and is more frequently met with in infants than in adults.

Acute suprarenal insufficiency may also complicate surgical shock and severe burns, the biochemical changes in the blood resembling those found in the more severe phases of Addison's disease.

Diagnosis.—The diagnosis of acute suprarenal insufficiency as a complication of infections, surgical shock, and burns, is often a matter of assumption, based on experimental evidence. That of the Waterhouse-Friderichsen syndrome is only occasionally made in life.

Treatment.—Treatment is similar to that described for Addison's disease, and there is some evidence that crude extract of suprarenal gland is more efficient than the synthetic desoxycorticosterone. Experimentally, the synthetic hormone corticosterone is of greater value than desoxycorticosterone.

HYPERCORTICALISM

In speaking of hypersecretion of the adrenal cortex one usually refers to hypersecretion of those cells concerned with sex function, but in some types of sexual precocity the abnormal muscular strength of the individual suggests also a hypersecretion of the life-maintaining hormone desoxycorticosterone. The sex hormones elaborated by the adrenal cortex in hypercorticalism are androgenic and œstrogenic hormones. The clinical conditions resulting are virilism, feminisation, pseudo-hermaphroditism and sexual precocity. The pathological basis is neoplasm or hyperplasia of the adrenal cortex, but in the two last conditions the hyperplasia may be a concomitant rather than a primary cause. As sexual precocity is frequently due to causes other than adrenal cortical hyperfunction it is considered in the gonad section.

VIRILISM

Synonym.—Adreno-genital Syndrome ; Cushing's Syndrome (part of).

Definition.—Virilism is said to occur when a female at any time after puberty fails to menstruate and also develops a male distribution of hair. Adiposity is often a third feature of the triad of the adreno-genital syndrome. (For Cushing's syndrome, see Pituitary Section.)

Ætiology.—The immediate cause is hypersecretion of androgenic hormone by the adrenal cortex. There appears to be a greater incidence among Jewish and Mediterranean people. There is, however, no sharp dividing line between milder cases of the disorder and accepted normality.

Pathology.—The lesion is an adenoma, a carcinoma, or a bilateral hyperplasia of the adrenal cortex. The cells have an affinity for the ponceau-fuchsin stain, and are thought to arise from the inner androgenic zone of the cortex. There is also a general lymphoid hyperplasia, and a large thymus. The ovaries tend to be atrophic.

Symptoms.—The changes usually begin at or soon after puberty, but may not become prominent until the late teens, or sometimes in the twenties, or later. The essential feature is an excessive growth of hair on the side of the face, the upper lip and chin, the forearms, thighs and legs and on the trunk. The last may be only slightly affected in the form of a linear growth of hair extending from the usual feminine horizontal upper limit of pubic hair upwards along the linea alba to the umbilicus; or the hair may cover the abdomen and chest, and tufts of hair surround the nipples. Menstruation may cease altogether, or may be only scanty and at long intervals. Sometimes menstruation is normal in the presence of a high degree of hirsutism, but such cases do not strictly come within our definition. The uterus may become small or may fail to develop, but more usually there is no gross change in its size. The clitoris may be normal or appreciably enlarged, sometimes resembling a small penis. The breasts may be atrophic or undeveloped, but with adiposity this fact is obscured. An increase of weight due to adiposity is usual, fat being deposited on the face and neck, breasts, abdomen and pubis, and upper parts of the arms and thighs ; the legs and forearms may be quite thin and graceful. There is a group of cases character-

ised by absence of fat, and with considerable muscular development and strength, and broad shoulders and narrow hips, as in the masculine build.

There may be other features approximating to the Cushing syndrome (which see), and intermediate types are met with.

Complications.—Some degree of pigmentation around the eyes is common and less frequently other features of Addison's disease are met with, while even death from adrenal insufficiency has been recorded. It would appear that hyperplasia of the "sex cells" in the adrenal cortex encroaches upon and destroys the cells that secrete desoxycorticosterone. Psycho-neurosis and psychosis, with loss of heterosexual desire and homosexual tendencies, may be complications. A complete feminine mentality, however, may be associated with virilism, and the fear of sex conversion and of feminine inadequacy is poignant.

Diagnosis.—A combination of hirsutism and amenorrhœa makes diagnosis obvious. A tumour should be suspected if the disease has started after the twenties in a person hitherto quite normal, and in no case can be excluded without investigation. Considerable enlargement of the clitoris is more common with a tumour, but may be present with hyperplasia. Intravenous injection of uroselectan combined with radiography may demonstrate a neoplasm. A more certain method, though not without danger, is perirenal insufflation of 450 c.c. of air, the neoplasm being shown surrounded by air in the radiogram. Ovarian tumours (arrhenoblastoma) may produce virilism; they are not always palpable on vaginal examination, and may be revealed by laparotomy.

Androgenic hormone is usually secreted in excess in virilism. Normally some 40 international units per diem are found in the urine, but with an adrenal tumour ten times this amount may be present. It is rare, but not unknown, for such large amounts to be met with in hyperplasia; more commonly, however, 100 to 150 units are present. The assay is done by measuring comb growth enlargement in injected capons.

Prognosis.—In the case of hyperplasia the condition may be stationary or only slightly progressive for many years. Sterility is the rule, but one child may be born. The successful removal of an innocent tumour may produce a reversion to normal. Carcinoma of the adrenal cortex is very malignant, and metastases or recurrences are the rule.

Treatment.—A tumour should be removed surgically. It is important to give cortin or desoxycorticosterone for a few days before and after the operation, since the opposite adrenal may be atrophic and the patient may die from acute adrenal insufficiency before this adrenal has had time to undergo hypertrophy. For bilateral hyperplasia, unilateral adrenalectomy is advocated, but although the operation may be followed by some return of menstruation it is, in the writer's experience, rare for the hirsutism or the adiposity to be appreciably affected. Large doses of œstrin by injection or by local inunction have been indicated, but here too the writer's experience is disappointing. X-ray treatment of the hirsutism has various disadvantages (burns, scars). This is less true of electrolysis, which may be helpful.

There are many instances of hirsutism without any disturbance of menstruation. In such cases, also, it is very important to try and give some philosophical or psychological comfort, though not an easy task. Since in actual fact we are here dealing with a variety of normality, it is to be

wondered to what degree intersexuality will ultimately be commonly accepted by the non-medical world. It is, after all, a reality.

FEMINISATION

This condition is a rarity compared with virilism. It is due to a tumour of the adrenal cortex in the male, usually malignant. There is a loss of libido and sexual potency, with a general increase in fat deposition and a hyperplasia of the glandular tissue of the breasts. The latter become enlarged, the nipples pigmented and the superficial veins dilated. There may even be some secretion, which can be expressed from the nipples as in incipient lactation. The patient usually dies from malignant metastases, but in one case successful removal of the tumour led to a return to normality. The testes on section show atrophy.

PSEUDO-HERMAPHRODITISM

Definition.—Pseudo-hermaphroditism is a condition in which there is only one type of gonad, testis or ovary, but in which the external genitals are a mixed representation of male and female characteristics, or characteristic of the opposite sex to the gonads. Strictly the term should be applied only to those cases in which the condition is present from birth, and not to those instances of virilism or feminisation which appear in later life. It is also not intended to include under this heading sexual precocity in the female due to an adrenal tumour and associated with hirsutism. Classification according to the type of gonad is the simplest, *i.e.* testicular pseudo-hermaphroditism and ovarian pseudo-hermaphroditism.

Ætiology and Pathology.—Gross hyperplasia of the adrenal cortex occurs in only 14 per cent. of pseudo-hermaphrodites, but it may well be that hyperplasia of the sex cells (androgenic zone) could be detected in a far greater proportion by the ponceau-fuchsin stain. It is certainly possible to produce symptoms of pseudo-hermaphroditism in the experimental animal (rat, guinea-pig, fish) by injecting large doses of androgens or œstrogens into the young animal or into the pregnant mother. Nevertheless, it is probable that the hyperfunction of the adrenal cortex is a mechanism, essential or concomitant, but primarily determined by genetic or chromosomal factors.

The seminiferous tubules are not completely developed, and spermatogenesis is usually absent, but the interstitial cells may be normal or hyperplastic. The ovaries are hypoplastic, fibrotic or cystic.

Symptoms.—(A) Testicular Pseudo-hermaphroditism.—The commonest and most easily understood type is the male in whom the formation of the external genitals is incomplete, the two scrotal folds remaining ununited (cf. hare lip), and enclosing a vagina-like cavity, one or more inches in depth. The penis may be incomplete, or hypospadias of varying degree may be present, or the penis may be so inadequately developed as to represent a clitoris. The patient is then brought up as a girl, until the appearance of masculine hair at puberty and the failure to menstruate lead to further investigation. The vagina is found to be false, the uterus absent, and the gonads testicles. The last, being retained in the abdomen, have the char-

acteristics of cryptorchid testicles, namely, absence or destruction of the spermatic tubules, and increase in the interstitial cells. Nevertheless, the secretion of male hormone may be deficient, and the patient be of eunuchoid type. Chapple has described the case of a young, beautiful woman, with no hirsutism, with a female figure, well-developed breasts, and normal feminine libido, who in spite of a short vagina had satisfying intercourse with males. She came under observation for painful lumps in the groin, which were found to be testicles. No uterus could be detected. It is more usual, however, for the testicular pseudo-hermaphrodite to have hirsutism and other secondary male sexual characteristics. Although the testis secretes as much œstrone as the ovary (and the female about as much testicular hormone as the male), it is difficult to understand why, of two pseudo-hermaphrodites with testes and female external genitals, one should have male hair and bodily form, and another be a beautiful female. Obviously the genetic factors may be more important than the endocrine. As regards the sexual organs other than the gonads there is a considerable variation, with the following possibilities in the case of a testicular pseudo-hermaphrodite: hypospadias only; with a vagina; with a vagina and Fallopian tubes; with a vagina, uterus and tubes. The testes may be in the pelvis, the inguinal canals, the labia, or in the scrotum.

(B) Ovarian Pseudo-hermaphroditism.—The female pseudo-hermaphrodite possesses ovaries, but has a masculine configuration, with the external genitals simulating those of the male. The basis of the condition is difficult to explain unless it is assumed that it is comparable to the adrenal virilism of the adult, and due to hyperfunction of the adrenal cortex commencing in fœtal life. Although to be within our definition such cases should show abnormalities at birth, these may not be gross until later childhood and may be further accentuated at puberty. The psychic and sexual behaviour of the pseudo-hermaphrodite varies in different individuals, and is often independent of the physical or endocrine basis. Thus the hirsute, testicular pseudo-hermaphrodite may be essentially feminine in outlook and libido, and capable of functioning to complete satisfaction of herself and partner in coitus. Some are ambisexual. Apart from indisputable pseudo-hermaphrodites, it is obvious that a number of people have the physical characteristics (apart from genitals), emotional reactions and libido of the opposite sex.

Diagnosis.—The recognition of the condition of pseudo-hermaphroditism is not difficult, although it may not become evident to the lay person until late childhood or puberty. The elucidation of the underlying pathology may, however, be impossible unless laparotomy is undertaken. Many patients present themselves with lumps in the inguinal canal, and it is only after removal and section of these gonads that the real sex can be determined.

Prognosis.—From the nature of the disorder it is unreasonable to expect a fundamental improvement, with or without treatment. The latter may ameliorate the condition.

Treatment.—If help is not sought before adult life, treatment should depend upon the sexual inclinations of the patient. If these are female, the clitoris should be amputated and, if necessary, the vagina enlarged. The removal of testes will diminish the hirsutism. In the child the removal of testes would prevent hirsutism, but in view of some testicular pseudo-hermaphrodites having beautiful feminine configuration without hirsutism

and the fact that the testis does secrete œstrogens, it is considered by some better to wait until puberty gives an indication of what is likely to develop. When the outlook and libido are masculine, a plastic operation can repair or create a scrotum and abolish the hypospadias. With ovarian pseudo-hermaphroditism the question of unilateral adrenalectomy arises, or the more drastic procedure of two-thirds resection of both adrenal glands. Good results have been reported, but the value of the procedure is still *sub judice*. Laparotomy may reveal that an apparent instance of pseudo-hermaphroditism was in fact the rarer condition of true hermaphroditism. Experience shows that it is unwise to speculate too much in the absence of laparotomy.

HERMAPHRODITISM

True hermaphrodites have both male and female gonads, namely, one testis and one ovary, or an ovo-testis in one organ. They are extremely rare, and it is probable that up to the present time not more than 20 cases have been described. Hermaphroditism is normal for some of the lower species, *e.g.* the worm, and is not a rarity among pigs and goats. In the hen, the right gonad is rudimentary, but if the left ovary is removed the right gonad becomes a testis and the hen grows a comb. Further, any remnant of the left ovary that is left behind may grow into testicular tissue, since the medulla of the ovary is the homologue of the testis. The change of sex in the hen may be so complete that the mother of chicks may become the father of chicks. In man the external genitals may give no indication of the internal genitals. Young, in 1933, described what he regarded as the twelfth case of true hermaphroditism on record. A young "male," tall and athletic, with penis and scrotum, and masculine hair, came to operation for undescended left "testicle." On opening the left inguinal canal, it was found to contain a uterus, Fallopian tube and functionary ovary. A portion of the right gonad in the scrotum was excised, and a section showed normal testicular tissue.

Although the adrenal cortex is frequently hyperplastic in true hermaphroditism, there is no evidence that this is the principal ætiological factor. On the contrary, the cause of true hermaphroditism would appear to be genetic, and the inherent mechanism gonadal. The importance of the genetic factor is well illustrated by the bullfinch, which may have a testis on the right and an ovary on the left, with masculine plumage on the right half of the body and feminine plumage on the left half. Huggins, Cohen and Harden reported another type of true hermaphroditism in which the patient was brought up and behaved as a woman, and one gonad was a testis and the other an ovo-testis, both removed from the inguinal canal and examined histologically. The patient was athletic and slightly hirsute. She had a normal vagina and uterus, and began to menstruate at the age of 14, at which time the clitoris became grossly enlarged and assumed the size of a small penis.

TUMOURS

Tumours of the cortex and of the medulla of the suprarenal gland are met with. They may be benign or malignant. Endocrine manifestations

are usual but not invariable. Tumours of the adrenal cortex may produce virilism, or the complete Cushing's syndrome (see above).

Tumours arising from the chromaffin cell of the suprarenal medulla are termed phæochromocytomas or paragangliomas. Such a tumour contains large quantities of adrenaline, and the latter is secreted into the blood paroxysmally, producing hypertensive crises. Thus, a previously healthy young adult may develop attacks of hypertension, palpitation, pallor, nausea, vomiting and cyanosis of the extremities; the systolic blood pressure may rise from 130 to 300 mm. of mercury, the change in the diastolic usually being much smaller. During the temporary rise of blood pressure, the patient may complain of agonising headache, and a sense of constriction in the chest with, perhaps, angina-like pain. There may be transitory hyperglycæmia and glycosuria, and albuminuria. The pallor and coldness of the skin, especially of the extremities, may be associated with, or followed by, profuse perspiration. Shivering, cramps of the calf muscles, mydriasis and pyrexia are other features.

These paroxysmal attacks may recur at increasingly frequent intervals, and the symptoms of hyperadrenalism may persist in lesser degree between the paroxysms.

Hypertrophy and degeneration of the arterioles are found in the more chronic cases, and the kidneys may show ischæmic fibrosis.

Removal of a medullary tumour will result in abolishing the symptoms, if the operation is done early enough.

Occasionally, bilateral tumours are met with.

THE SEX GLANDS

The testis secretes a hormone, testosterone, which has been isolated and synthesised, and is available commercially for substitution therapy. It is excreted in the urine in a slightly modified form, as androsterone. The ovary secretes two hormones, œstradiol and progesterone. The former can be obtained from ovarian follicular fluid, and the latter from the corpus luteum. Both hormones have been isolated and synthesised, and are available commercially for substitution therapy. Œstradiol is excreted in the urine as œstrone, and progesterone is excreted as pregnandiol. The action of both testosterone and œstradiol is prolonged by their esterification, so that, in practice, the propionate and benzoate respectively are employed. It is to be remembered that the sex hormones do not stimulate the gonads to increased activity, but they produce the same hormonal effects as the normal gonads do. Thus, testosterone produces increased libido, penile erections, growth of the immature penis and of the scrotum and prostate, hair on the face, and deepening of the voice. Œstradiol therapy results in growth of the mammary duct tissue, and a proliferative hyperplasia of the uterine mucous membrane. Progesterone has a further effect on the uterus, producing a secretory, or pre-gestational, mucous membrane. It thus prepares the uterus for the imbedding of the fertilised ovum, and therefore a deficient secretion results in sterility, or abortion. Progesterone also

reduces the hypersensitivity of the uterus to the posterior pituitary stimulus to uterine contraction.

The failure of gonadal function may be primary, or secondary to pituitary insufficiency. It has already been noted (see Pituitary Section) that there are two pituitary, or pituitary-like, gonadotrophins, A and B. The former stimulates the seminiferous tubules of the testis, and produces follicle maturation in the ovary. The latter acts on the interstitial cells of the testis, and produces luteinisation of the ovarian follicles. These physiological effects can be demonstrated in rats and rabbits, but not in man. Nevertheless, such experimental results constitute the basis of therapy.

THERAPEUTICS OF TESTOSTERONE PROPIONATE

The preparation may be given intramuscularly, the dose being 25 to 50 mg., three times a week. It may also be administered by inunction, the dosage by this route being four times as much.

A.—IN THE MALE

1. Eunuchism and Eunuchoidism.—Testosterone propionate will produce an increase in the size of the penis, scrotum and prostate, increased libido, and increased growth of hair on the face, on the pubis, and in the axillæ. Potency will be restored to normal. In the complete castrate, however, there is little or no ejaculatory fluid at the time of the orgasm, and spermatozoa are absent. There is a gain in muscular strength and weight; and a retention of fluid and of nitrogen.

2. Impotence.—In the majority of cases, impotence is psychogenic and does not respond well to testosterone therapy. The latter, however, is very effective in organic hypogonadism.

3. Male Climacteric.—The existence of a male climacteric is not generally accepted. Nevertheless, some men over fifty do complain of hot flushes, anxiety, inability to concentrate, and loss of libido, and all these symptoms may disappear with testosterone therapy.

4. Enlarged Prostate.—Testosterone has no effect on the objective signs produced by an enlarged prostate, but it does appear to ameliorate symptoms. Such benefit, however, has also been obtained by injections of inert oil.

B.—IN THE FEMALE

Testosterone propionate has been used with success in menorrhagia, with or without fibroids, in chronic mastitis, and also to stop lactation. If the therapy is continued for more than a few weeks, it may result in a growth of hair on the face, deepening of the voice, enlargement of the clitoris, and acne. These untoward effects tend to disappear after ceasing therapy.

THERAPEUTICS OF ŒSTRADIOL BENZOATE

This may be administered in the form of intramuscular injections of 1 c.c., containing 50,000 units, twice weekly, or as tablets by mouth, 1000 to 10,000 units daily, or by inunction.

1. AMENORRHŒA.—In primary amenorrhœa, uterine bleeding may be produced by one million units, given over a period of 4 weeks, and repeated if necessary. The effect is more physiological if the œstradiol is followed by 20 mg. progesterone. The resulting menstruation, or pseudo-menstruation, will not recur if therapy ceases. In secondary amenorrhœa, or in scanty menstruation, the normal rhythm and quality of menstruation may be restored after a few months' therapy, and may then continue normally without further treatment.

2. DYSMENORRHŒA.—When this is due to poor development of the uterine musculature, œstradiol benzoate may be beneficial. It is best prescribed in the first 2 weeks after each menstruation.

3. STERILITY.—Œstradiol benzoate will cause an infantile uterine musculature to develop. It also produces hypertrophy of the Fallopian tubes, and increases the patency of these tubes when they have been previously occluded. Pregnancy may follow such treatment.

4. CLIMACTERIC.—The climacteric in the female is a definite clinical entity, of which the menopause is only one feature. Although the constitutional disturbance in some patients is negligible, others suffer from nervousness, anxiety, hot flushes, general pruritus, pruritus vulvæ, vulval kraurosis and other symptoms. Œstradiol benzoate has a remarkable beneficial effect, but it may be necessary to continue this specific therapy over a period of months or years. The dosage varies with different individuals, and may be as little as 1000 units daily, or as much as 50,000 units daily.

THERAPEUTICS OF PROGESTERONE

1. ABORTION.—Progesterone may be administered prophylactically during the first 4 months of pregnancy, 5 mg. twice weekly by intramuscular injection. In threatened abortion, 5 mg. is given daily until all bleeding has stopped, and then twice weekly.

2. MENORRHAGIA.—Progesterone is sometimes useful in menorrhagia, 5 mg. being given daily for 5 days before menstruation is anticipated. It can also be administered during the bleeding if the latter is severe or unduly prolonged.

THERAPEUTICS OF GONADOTROPHINS

1. UNDESCENDED TESTICLE.—If there is no mechanical obstruction to the descent of the testicles, this condition will respond to gonadotrophin B. The dose is 500 units twice weekly, for 2 to 3 months. Since a large proportion of undescended testes migrate to the scrotum spontaneously at puberty, therapy is often delayed until the age of 11 years. Some children, however, develop an inferiority complex if the condition is left untreated.

2. MALE STERILITY.—If spermatozoa are absent or scarce, gonadotrophin A sometimes increases their number, but it is rare for fertility to result.

3. MENORRHAGIA.—Menorrhagia, especially at puberty or at the climacteric, may respond to gonadotrophin B, 500 units given twice weekly, or, if the condition is severe, daily.

HORMONE TESTS FOR PREGNANCY

The Ascheim-Zondek test and its Friedman modification depend upon the fact that there is a large amount of luteinising gonadotrophic hormone in the urine of pregnant women. It is usually positive within a week of a missed period. A morning specimen of urine is injected, in divided doses, into mice (Ascheim-Zondek) or rabbits (Friedman). A positive test is indicated by the resulting formation of blood spots, or of corpora lutea, in the ovaries.

SEXUAL PRECOCITY

Synonyms.—Pubertas Præcox ; Macrogenitosomia.

Definition.—The attainment of sexual maturity in childhood some years before the normal time of puberty.

Ætiology and Pathology.—Sexual precocity may be due to a variety of causes, which ultimately belong to one of three groups, primary gonadal ; or primary adrenal ; or primary pituitary or hypothalamic-pituitary. Thus the underlying lesion may be an adenocarcinoma of the testis, a granulosa cell tumour of the ovary, an adenoma or adenocarcinoma of the adrenal cortex, a pineal tumour (which probably acts by stimulating the hypothalamic-pituitary mechanism), encephalitis, internal hydrocephalus, or a third ventricle tumour. There is also an idiopathic familial type of sexual precocity. Whatever the mechanism, the result is a hypersecretion of androgenic or œstrogenic hormone.

Symptoms.—In boys, the sexual precocity is shown by enlargement of the penis and sometimes of the testicles, development of hair on the pubis and to some extent on the face, and often considerable strength. The latter, vividly described as the Hercules type, was thought to be characteristic of adrenal tumours, but may also occur with hypothalamic or third ventricle tumours. The boys will show obvious sexual behaviour, even running after and attacking adult women, masturbating against their legs, which they may clasp with great strength and may bite with anger if frustrated. Seminal emission is rare, and fertilisation not recorded. The precocity may begin in very early childhood.

With girls, there are clinically two main types. When the condition is due to ovarian hyperactivity, either primary or secondary to a hypothalamic-pituitary stimulus, it is manifested by qualitatively normal sexual development, pubic hair, well-formed breasts, menstruation, and even pregnancy, the last having been recorded as early as 6 years of age. With adrenal tumours, menstruation is usually absent, the clitoris is enlarged, the voice is deep, and hirsutism occurs on the face and body, as in virilism. These manifestations are due to the secretion of androgenic hormone by an adrenal tumour.

In both sexes, the sexual maturity is associated with premature dentition, and early union of the epiphyses. Rapid growth occurs, both with pituitary and adrenal tumours, suggesting that in the latter case the pituitary must also be involved (growth hormone). Although the instincts may be adult, the intellectual activity is usually infantile.

Diagnosis.—In girls, an enlarged clitoris and hirsutism suggest an

adrenal tumour, whereas homosexual precocity suggests an ovarian tumour. In both sexes, but especially in boys, the cause of the sexual precocity is often obscure. Radiograms of the adrenal area, after uroselectan or perirenal air insufflation, and abdominal laparotomy are justifiable. Pineal tumours are associated with ocular palsies, disturbance of vision, somnolence and increased intracranial pressure. The skull should always be radiographed.

Prognosis.—Idiopathic or familial sexual precocity may proceed to a normal adult state. Adrenal and testicular tumours are usually malignant, whereas ovarian tumours are generally not so. Intracranial lesions may be mechanically fatal. Removal of adrenal or gonadal tumours tends to produce a reversion to normal in the absence of metastases.

Treatment.—Surgical removal of the adrenal or gonadal tumour is indicated. In the former case, desoxycorticosterone is given for 1 week before and for 2 weeks after operation. Intracranial lesions offer technical difficulties. Unilateral orchidectomy is not helpful, and complete castration should not be lightly undertaken.

PRESCRIBING AND ADMINISTRATION OF HORMONE PREPARATIONS

The increasing number of commercial firms producing hormone preparations and the variety of trade names employed tend to create a state of chaos. In my opinion, the only solution is prescribing the hormone by its scientific name and, if so desired, writing the name of the manufacturing firm in brackets after it. It is to be noted that the esters of the hormones are employed to give a more prolonged action.

ŒSTRADIOL BENZOATE

This œstrogenic hormone is the one usually used, and it is prepared by the conversion of crystalline œstrone, obtained from pregnant mare's urine, into œstradiol benzoate by hydrogenation and esterification. It can be given by intramuscular injection, by mouth, by cutaneous inunction, or in the form of vaginal or rectal suppositories. By injection the dosage is about one-fourth of that required by the other routes. For injection, œstradiol benzoate is prepared in ampoules of 1 c.c. oily solution containing 1000, 10,000, 20,000 or 50,000 international units. One mg. of œstradiol benzoate is equivalent to 10,000 international units. Tablets are prepared in strengths of 1000, 3000 and 10,000 international units. Vaginal or rectal suppositories contain 1000 and 10,000 international units (*i.e.* 0·1 mg. and 1 mg. respectively). Ointment containing 0·5 mg., 1 mg. or 2 mg. per gram, is put up in tubes of 18 or 25 grams. Standardisation of œstrogenic hormones is now by weight. Biological assay is by the production of œstrus in ovariectomised rats and mice.

Œstradiol is a natural occurring hormone obtainable from ovarian follicular fluid, but other œstrogenic hormones, which do not occur naturally, can be synthesised. Of these, stilbœstrol is prepared in 1 c.c. ampoules of oily

solution, containing 1 or 5 mg., and in tablets of 0·1, 0·5, 1 and 5 mg. One mg. is equivalent to 10,000 international units. Stilbœstrol is cheaper than œstradiol and equally efficacious, but it has the disadvantage of producing nausea and vomiting, and even skin rashes, in a small proportion of patients. Hexœstrol, a similar preparation, used in comparable doses, is apparently less toxic. Stilbœstrol ointment is also available in concentration of 0·1 mg. per gram of lanoline base.

PROGESTERONE

This hormone can be obtained from the corpus luteum, but is now generally prepared by synthesis. One mg. of progesterone is equivalent to 1 international unit. It is usually given by intramuscular injection, and is prepared in 1 c.c. ampoules of oily solution containing 1, 2, 5 or 10 mg. A further synthesis produces a compound of progesterone active by mouth, but the dosage by this route is four times that by injection. It is called anhydrohydroxy-progesterone, or pregneninolone, and is prepared in 5 and 10 mg. tablets. Standardisation is now by weight. Biological assay is by the production of secretory endometrium in young rabbits.

TESTOSTERONE PROPIONATE

Testosterone can be obtained from the testes, but it is prepared commercially by synthesis from cholesterol and subsequent esterification to the propionate. It is available for intramuscular injection in ampoules of 1 c.c. of oily solution containing 5, 10 and 25 mg. (1 mg. is equivalent to 50 international units). It is also effective by subcutaneous inunction (four times the intramuscular dosage), and for this purpose is prepared in tubes of 25 grams of ointment containing 2 mg. per gram, or in more concentrated form in tubes of 2 grams of ointment containing 25 mg. per gram. Methyl testosterone in 5 mg. tablets has been employed experimentally by the oral route, but is not yet available commercially. The dosage is some four times that by injection. Standardisation is by weight. Biological assay is by measurement of the increase of comb growth in capons.

GONADOTROPHIC HORMONE

The problem of scientific prescribing offers some difficulty in the case of the gonadotrophins, since the essential hormones have not been isolated, crystallised or synthesised. Gonadotrophin A is obtained from pregnant mare's serum, and its preponderate action in lower animals is follicle ripening; Gonadotrophin B is obtained from human pregnancy urine, and its preponderate action is that of luteinising. Both are given by intramuscular injection and are prepared in ampoules containing powder to be dissolved in 1 c.c. solvent, with the exception of one preparation, antuitrin S, which is in liquid form. Standardisation is by measuring the increase in weight of the ovary of immature mice, or by the production of œstrus in immature rats.

Gonadotrophin A: Antostab (Boots), 100 units per c.c.; Gestyl (Organon), 400 units per c.c.; Gonadyl (Roussel), 40 units per c.c.; Prolan (Bayer), 100, 500 and 2000 units per c.c.; Serogan (B.D.H.), 200, and 1000 units per c.c.

Gonadotrophin B: Antuitrin S (Parke, Davis & Co.), 100 and 500 units per c.c.; Gonan (B.D.H.), 100 and 500 units per c.c.; Physostab (Boots), 100 units per c.c.; Pregnyl (Organon), 100, 500 and 1500 units per c.c.

ADRENAL CORTEX HORMONES

The essential hormone, desoxycorticosterone acetate, is prepared by synthesis from cholesterol, and is available for intramuscular injection in 1 c.c. ampules of oily solution containing 5 mg. One c.c. ampoules of benzyl alcohol, containing 20 mg. of desoxycorticosterone acetate, may be used for cutaneous inunction, but are not yet commercially available. Cortical extracts are also prescribed as solutions for intramuscular injection, and are labelled in rat units, dog units, or according to the weight of crude cortex. Generally speaking, they do not differ from one another in relative potency. Such preparations are Cortin (Organon), Eschatin (Parke, Davis & Co.), and Eucortone (Allen & Hanburys, Ltd.), usually prescribed in rubber-capped bottles of 10 c.c. They are standardised by their maintenance of adrenalectomised rats, or dogs, or by measuring the muscular contraction of the gastrocnemius muscle of adrenalectomised rats, before and after the injection of the cortical extract.

GROWTH HORMONE

This is prepared by Parke, Davis & Co., and called Antuitrin Growth. It is available in rubber-capped bottles of 10 c.c., each c.c. containing 10 rat units. Organon have a similar preparation (Crescormon) in powder and solvent ampoules, each containing 120 rat units. Growth hormone is standardised on hypophysectomised rats by measuring the increase in body weight and the increase in length of the tail vertebræ seen radiologically.

PROLACTIN

This lactogenic hormone is presented in 15 c.c. rubber-capped vials containing 60 Riddle units per c.c. (Physolactin-Glaxo); or 30 Riddle units per c.c. (Prolactin-Organon). It is standardised by the increase in weight of the crop gland of an injected pigeon.

S. L. Simpson.

SECTION IX

DISEASES OF THE DIGESTIVE SYSTEM

DISEASES OF THE MOUTH

ORAL SEPSIS[1]

Oral sepsis is the condition in which excessive bacterial activity occurs in the mouth. Apart from actual infection associated with the teeth and gums, it develops whenever insufficient attention is paid to the cleanliness of the mouth. Thus particles of food may stagnate between the teeth, under bridges, and in connection with badly fitted dental fillings, crowns and plates which are not removed and washed with sufficient frequency.

The mouth should be thoroughly examined in every patient, from whatever condition he may be suffering, but with special care in all digestive disorders and in those conditions which will be presently described as possible sequels of oral sepsis, even if the patient says he has never suffered from toothache and that he regularly visits his dentist. In patients who wear tooth-plates the mouth should be examined both before and after their removal. Each tooth and the gum surrounding it should be carefully inspected. The presence of tartar and red swollen gums indicates that some infection is present. In doubtful cases the patient should be sent to a dentist for an expert opinion, and if no obvious disease is found, radiographs should be taken, as they alone can show with certainty the existence of septic foci under apparently well-fitting crowns and fillings and at the roots of teeth which are otherwise perfectly healthy, and they make it possible to determine with great accuracy the extent of any periodontal infection.

Dental Hygiene

Dental sepsis does not occur if the teeth are always kept free from food between meals. The teeth should be thoroughly cleaned every morning and evening by brushing in one direction only—from the gums towards the teeth.

Normally the gums completely fill the spaces between the teeth, but when they begin to recede, as in pyorrhœa, the spaces are no longer filled and food collects between the teeth. As this food cannot be removed by a tooth-brush, the brushing must be followed at night by the use of a metal tooth-pick, bent at an angle so that it will pass readily between the molar teeth. Patients with inflamed gums or pyorrhœa should also massage the gums with the forefinger and thumb from the gum towards the teeth after

[1] I am indebted to Mr. A. L. Spencer-Payne for help in revising this section.

using the brush, and the dried gum margin should be painted with tincture of iodine applied on a small swab of wool held by curved dental tweezers.

Artificial teeth should be kept in antiseptic at night, and should be thoroughly scrubbed with a brush and soap and water, if possible after every meal.

Children should be given some food at each meal which requires thorough mastication. Soft food, which can be swallowed without chewing and with the production of little or no saliva, is likely to cause stagnation of sticky carbohydrate material between the teeth. Mouth-breathing should be corrected by direct treatment of nasal obstruction and by respiratory exercises.

At the end of every meal some fluid should be drunk, or some fresh fruit, the acid of which excites the flow of saliva, should be eaten in order to keep the teeth clean.

The dentist should be visited twice a year, even when there is no reason to suppose that anything is abnormal, so that tartar can be removed, early caries dealt with, and pyorrhœa alveolaris recognised and treated in its earliest stage.

(1) Pyorrhœa Alveolaris; Chronic Periodontitis

Ætiology and Pathology.—Stagnation of food mixed with pyogenic organisms between the teeth leads to inflammation of the edge of the gums —marginal gingivitis. The attachment of the muco-periosteum to the neck of the tooth is destroyed, and a pocket develops between the tooth and the gum. The margin of the alveolar process is then slowly eroded as a result of rarefying osteitis, until it may finally be replaced by granulation tissue. Stagnation of infective material in the pocket leads to gradual extension of the disease and aggravation of the gingivitis. Pus is produced, the condition at this stage being commonly known as pyorrhœa alveolaris.

Symptoms.—In marginal gingivitis the edge of the gum of one or more teeth is red and swollen and bleeds with abnormal ease when brushed, the first part to be affected being usually the interdental papillæ. When pyorrhœa alveolaris has developed, pockets are present round the teeth, and pus can generally be seen exuding from the edge of the gum; even when none is seen on first examining the mouth, beads of pus appear if the edges of the gum are pressed. In chronic cases the teeth are often loose. Reflex salivation occurs, and an excessive quantity of mucus is secreted by the small mucous glands of the mouth. This is a common cause of aërophagy. The accumulation of decomposing food, debris and pus in the pockets round the teeth produces an unpleasant taste in the mouth, most marked on waking in the morning, and is a common cause of foul breath. There is no pain, and the slight discomfort which may be present is generally insufficient to induce the patient to consult a dentist.

Treatment.—In early cases the disease can be arrested by sealing and treatment of the pockets with strong antiseptics. When the supporting bone has been destroyed to more than half the depth of the root, extraction is necessary. In intermediate cases the gum should be cut away in order to eradicate the pockets. This should be followed by correct brushing, and massage by the fingers of the outer and inner surfaces and by wooden toothpicks between the teeth.

(2) Dental Caries

Ætiology and Pathology.—Foods containing a relatively high content of vitamin D promote the calcification of teeth, whilst cereals, especially oatmeal, contain a substance which hinders calcification. When vitamin D is abundant in the diet its calcifying power is strong enough to counteract the effect of cereals and of a relative deficiency of calcium. Dental caries occurs when the diet is deficient in vitamin D, especially when this is associated with excess of cereals or deficiency in calcium. The organic acids produced by fermentation of carbohydrate foods is an additional factor.

Symptoms.—Carious teeth are tender, and their presence renders mastication painful. The patient therefore avoids using the affected teeth, and this favours the deposit of tartar and the stagnation of food. If many teeth are affected the food is bolted, so that indigestion is likely to occur owing to insufficient mastication, quite apart from possible infection of the alimentary canal caused by swallowing septic material from the mouth. The irritation produced by the decomposition of stagnant food around the teeth gives rise to marginal gingivitis and pyorrhœa alveolaris. Oral sepsis produced in this way is of much more importance than that caused by the caries itself, as the quantity of decomposing material and bacteria swallowed from dental cavities is comparatively small, and no local absorption of toxins or bacteria can occur so long as the pulp cavity is not reached. When the latter becomes infected, absorption of toxins is likely to lead to enlargement of the cervical glands, especially in children, and the chronic inflammation produced in this way is a common precursor of tuberculous infection of the glands, and probably also predisposes to lymphadenomatous changes. Inflammation of the pulp spreads to the periodontal membrane and may finally produce an alveolar abscess.

Dental caries is the most common cause of toothache, and pain is often referred to various situations more or less remote from the teeth.

Treatment.—" A relatively high vitamin D content of the food can do much to diminish the incidence of caries in children if the vitamin is given during the development of the teeth; a beneficial effect may be obtained if it is given at a fairly late stage of development; and even when it is given after the eruption of the teeth the onset and spread of caries is delayed." [1] The chief source of vitamin D is milk, and, when necessary, cod-liver oil or synthetic vitamin D (calciferol) should be given in addition.

Dental cavities produced by caries should be filled at the earliest possible moment, but if this cannot be efficiently done the teeth should be extracted, as tender teeth which prevent proper mastication are a much greater source of danger than the absence of teeth, even in very young children. Removal of all the milk-teeth in children may cause narrowing of the dental arch and consequent crowding of the permanent teeth, but this can be easily remedied by treatment, whereas the septic condition of the mouth caused by extensive caries may lead to permanent ill-results.

(3) Apical Infection

Ætiology.—Infection of the apex of the root of a tooth can occur only if the pulp is dead, except in rare cases of extensive caries.

[1] Medical Research Council, Special Report, No. 211, 1936.

Symptoms.—Apical infection may be acute or chronic. In the former an alveolar abscess forms; this gives rise to the usual symptoms and signs of inflammation. Chronic apical infection, on the other hand, frequently gives rise to no pain or discomfort, and no signs recognisable on ordinary examination. It can then be recognised only in a good radiograph.

Treatment.—In cases of only moderate severity the pulp canal should be opened and sterilised with ammoniacal silver nitrate followed by formalin, or by ionization with zinc chloride, and the root should be filled to its apex with an impervious material. In more advanced cases, and in all in which secondary symptoms are present, extraction should be performed without delay and the socket should be curetted.

Results of Oral Sepsis

The inflamed condition of the gums often leads to general stomatitis and sometimes to chronic pharyngitis and tonsillitis. Infection of teeth in the upper jaw may spread directly to the antrum and lead to sinusitis. Inhalation of septic material from the mouth may lead to infection of the bronchi and lungs, the danger of pulmonary complications after general anæsthesia being greatly increased if the mouth is in a septic condition. Chronic bronchitis and bronchiectasis often improve rapidly when oral sepsis is overcome.

Most of the pus which is constantly forming round the teeth in pyorrhœa alveolaris is swallowed; the amount is often considerable, as the ulcerated area round each tooth may be as great as half a square inch. During the day the infected pus is so diluted by what is eaten and drunk that it cannot do much damage, most of the bacteria being destroyed by the hydrochloric acid in the stomach. During the night, however, when no hydrochloric acid is secreted and nothing is eaten or drunk, the pus and organisms which are constantly swallowed with the saliva may infect the stomach and intestines. Pyorrhœa alveolaris is thus an important factor in the production of chronic gastritis, especially in individuals with hypochlorhydria and achlorhydria. In those with constitutional hyperchlorhydria it may help to prevent the healing of a chronic gastric or duodenal ulcer. The danger of infecting the small intestine and, through it, the colon, and of ascending infection of the gall-bladder and appendix is greatly increased in the absence of the normal bactericidal action of the gastric juice in achlorhydria.

The local reaction in pyorrhœa and in apical infection may be sufficient to prevent the passage of toxins and organisms into the circulation. In many cases, however, toxins are absorbed. Non-hæmolytic strep[illegible] found in the blood immediately after the extraction of teeth in 75 [illegible] cases if chronic gum infection is present, and less frequently with a[illegible] infection. The trauma caused by "rocking" a tooth during its removal increases the liability to a severe degree of bacteriæmia. The bacteriæmia generally lasts only ten minutes, but occasionally subacute streptococcal septicæmia follows, and, if the heart valves are already abnormal, subacute infective endocarditis may develop.

Apart from bacteriæmia the toxæmia caused by chronic dental infection may give rise to general ill-health, which may be accompanied by septic anæmia and slight chronic pyrexia. Predisposed individuals may develop rheumatoid arthritis, fibrositis, neuritis, and less frequently iridocyclitis.

Other forms of joint disease, such as gout and osteoarthritis, may be aggravated by the toxins resulting from oral sepsis. Various disorders of the skin, such as chronic eczema, urticaria, rosacea and erythema, may also occur, and angioneurotic œdema is generally secondary to dental sepsis. The causal connection between these conditions and dental sepsis is shown by their temporary aggravation after an overdose of autogenous vaccine and in some cases after extracting the teeth.

Treatment.—When dental extraction is required in patients with old valvular disease of the heart, great care should be taken to eliminate gross infection as completely as possible before the operation, and manipulation of the infected teeth during the extraction should be reduced to a minimum. In any case teeth should not be extracted until pockets have been thoroughly cleansed or sterilised by the electric cautery. With more local infection and in the presence of general disease the patient should be desensitised by giving two or three doses of an autogenous vaccine, the last about five days before the first extractions. If many teeth are infected, two or three should be extracted at intervals of about five days in order to reduce the risk of a severe reaction.

Although the masticatory power of artificial teeth is only about one-fifth of that of normal teeth, indigestion is unlikely to result if care is taken to avoid tough meat and hard food. Even in the absence of artificial teeth no disturbance of digestion follows if only soft food is eaten.

The removal of the teeth does not result in the complete eradication of the disease unless care is taken to remove at the same time the diseased parts of the supporting alveolus, as radiograms may still show small areas of rarefying osteitis, from which it is possible to obtain cultures of streptococci, which continue to give rise to general symptoms. Curetting the diseased bone after incision of the gum, followed by the use of an autogenous vaccine, is the most satisfactory treatment for such residual foci of infection.

STOMATITIS

Catarrhal Stomatitis

Ætiology.—Catarrhal stomatitis is common in ill-nourished children during dentition and in association with gastro-intestinal disturbances. In adults it may result from excessive consumption of alcohol or highly-seasoned food, or excessive smoking. It is sometimes present in the specific fevers, and may also be caused by septic teeth and a dirty or badly-fitting plate. It develops rapidly in very ill people whose mouths are not kept clean, especially if they sleep with the mouth open.

Symptoms.—The gums and lips are often affected alone; in other cases the whole mouth, including the tongue, is involved. The mucous membrane is red and dry, but excess of mucus may be secreted by the small buccal glands. The tongue is swollen and furred.

The mouth is uncomfortable, and occasionally actual pain is present, especially on mastication. The patient complains of a nasty taste, especially on waking, and fetor oris may be present. The general health is unaffected.

Treatment.—The teeth should be cleaned with special care, and the

tongue kept as free as possible from fur by scraping. A mouth-wash should be used after each meal, and glycerin of borax should then be applied to the inflamed parts.

Ulcerative Stomatitis

Ætiology.—Ulcerative stomatitis is not a specific disease, but is, like catarrhal stomatitis, produced by the action of various irritants. It can develop from neglected cases of catarrhal stomatitis, and is a prominent symptom of mercurial poisoning and scurvy. The following are special varieties of the condition:

(*a*) Recurrent Ulceration in Adults.

Single or multiple superficial ulcers may occur on the mucous membrane of the cheeks, lips, tongue and gums. They have a grey surface with a red, but not raised, border, and the intervening mucous membrane is generally healthy. In severe cases, however, the ulcer is deeper and its base bright red. Each ulcer generally lasts only a few days, but a patient may have one or more in his mouth for months, or even years, without an interval. They are often very painful, especially on chewing, and it may be impossible to take any acid food. Their ætiology is most obscure; the condition is aggravated by oral sepsis and ill-fitting plates, and some ulcers may begin as abrasions produced by the careless use of a tooth-brush, but it appears to depend primarily upon some obscure constitutional defect. It is not associated with any disturbance in digestion or with any special form of gastric secretion. The saliva is not acid and the ulcers do not appear to be infective in origin.

No treatment beyond scrupulous attention to oral hygiene and the application of silver nitrate to each ulcer as it appears is, as a rule, of any use. A severe recurrent case, associated with colitis, in a girl of seven, completely recovered after adding liver to the diet.

(*b*) Aphthous (or Vesicular) Stomatitis.

Ætiology.—Aphthous stomatitis occurs especially in children under three, either alone or associated with some febrile or digestive disorder.

Symptoms.—The aphthæ consist of small slightly raised vesicles, each surrounded by a red areola. Within 24 hours the vesicles rupture, leaving grey ulcers, 2 to 4 mm. in diameter, with bright red margins. The ulcers heal rapidly. They occur especially on the inner surface of the lips, the edges of the tongue and the inside of the cheek; in severe cases the pillars of the fauces may be affected.

The mouth feels sore, and the child is unwilling to take food. Salivation is frequently present.

Treatment.—The mouth must be carefully washed after meals with potassium chlorate solution (10 grs. to 1 fl. oz.). In severe cases the ulcers may be treated with silver nitrate.

(*c*) Follicular Stomatitis.

Ætiology.—Follicular stomatitis may occur at any age, but especially in nursing women.

Symptoms.—The mucous follicles of the lips and cheeks become inflamed

and swollen; the epithelium over them breaks down, and ulcers, 3 to 5 mm. in diameter, result. They may cause no trouble, but more commonly they give rise to a considerable amount of pain on taking food and to reflex salivation.

Treatment.—The ulcers heal rapidly after being touched with silver nitrate.

(*d*) Mercurial Stomatitis.

Ætiology.—Stomatitis may occur when large doses of mercury are taken, especially in individuals already suffering from oral sepsis. Some people are especially susceptible to mercurial poisoning and develop stomatitis after taking a comparatively small dose.

Symptoms.—The gums become sore, red, swollen and finally ulcerated; mastication is painful. Salivation occurs, and the salivary glands may be enlarged, tender and painful. The tongue is swollen, and the neighbouring lymphatic glands are often enlarged. The breath is foul, and the patient complains of a metallic taste. Formerly, when mercury was given for syphilis more frequently and with less care than at present, the teeth often became loose and the pharynx affected, but these complications are now rare.

Treatment.—The administration of mercury should at once be discontinued. The bowels should be wel lopened by giving salts in order to facilitate the elimination of the mercury present in the body.

(*e*) Ulcero-Membranous Stomatitis.

Ætiology and Pathology.—Severe ulcero-membranous stomatitis is a contagious disease, which occurred in epidemic form among the troops in England and France during the War of 1914–1918, and it is by no means rare in civilians. It appears to be caused by infection with the same spirilla and fusiform bacilli which cause Vincent's angina.

Symptoms.—All parts of the mouth and pharynx may be involved, but the margins of the gums are specially liable to be affected. The stomatitis is similar to that caused by mercury, and the gums may be so swollen and bleed so readily that scurvy is simulated. The breath has a characteristic fetid odour, and the tender gums may make mastication painful.

The disease is sometimes acute, but more often runs a chronic course and is often followed by pyorrhœa alveolaris. It generally gives rise to but little constitutional disturbance.

Treatment.—The pockets and interdental spaces should be packed with a paste of zinc oxide and cloves on strands of cotton-wool, which is left for at least a week. After removal the teeth should be scaled and any suspicious areas treated by leaving liquor arsenicalis in contact for 15 minutes. Sodium perborate should be used as a tooth-powder and hydrogen peroxide as a mouth-wash. Treatment must be maintained for at least a fortnight after all signs of stomatitis have disappeared.

(*f*) Gangrenous Stomatitis.

Synonyms.—Cancrum oris; Noma.

Ætiology.—This rare disease occurs in children, especially girls between the ages of two and five, who live under very insanitary conditions. It

generally develops during convalescence from an acute fever, especially measles, and less frequently scarlet and typhoid fever. It also forms part of the clinical picture of agranulocytosis (p. 800).

Symptoms.—A sloughing ulcer develops in the inside of the cheek or on the gums; it rapidly spreads and leads to brawny induration of the skin of the cheek. Occasionally it heals spontaneously, but more frequently it perforates the cheek or spreads to the tongue, chin, jawbone or eyelid and eye.

Cancrum oris is accompanied by severe constitutional symptoms, the patient being prostrated with a high temperature and rapid pulse; diarrhœa or broncho-pneumonia frequently follows, and death generally occurs between seven and ten days on the onset.

Treatment.—The only adequate treatment for cancrum oris in children is to destroy the diseased part as completely as possible with the cautery. For the treatment of agranulocytosis *vide* p. 801.

Thrush

Ætiology.—Thrush is most common in weak, emaciated infants with gastro-intestinal symptoms, who have been fed with an unsuitable diet, and whose mouths have not been kept clean. Acid fermentation of food remnants leads to catarrhal stomatitis, and this is likely to be followed by thrush. Thrush occurs in epidemic form in badly-managed institutions, being spread by dirty feeding-bottles. The disease may also occur in enfeebled adults in the late stages of tuberculosis, cancer and diabetes, and in severe febrile infections.

Pathology.—Thrush is caused by infection with *Oidium albicans*—a fungus, the filaments of which form a dense felt-work in the superficial epithelial layer of the mucous membrane.

Symptoms.—Thrush generally appears first on the tongue, and then on the cheeks, lips, hard palate, tonsils and pharynx. In rare cases the entire buccal mucous membrane is covered, and the infection may even spread to the vocal cords, œsophagus and stomach. It begins as slightly raised, pearl-white spots, which gradually grow and then coalesce. The white material can be readily detached, leaving either intact mucous membrane, or, in more severe cases, a bleeding and ulcerated surface.

Diagnosis.—Adherent milk curds may superficially simulate thrush. In aphthous stomatitis the white patches are at first vesicles and then definite ulcers, and salivation is present in contrast to the dry mouth in thrush. A definite diagnosis can be made only with the aid of the microscope.

Treatment.—Thrush should be prevented by keeping the mouth clean and babies' bottles sterilised. It is important to improve the patient's general health as well as to give local treatment. The mouth should be washed with sodium sulphite solution (60 grs. to 1 fl. oz.), after which the fungus can be easily scraped off.

Arthur F. Hurst.

DISEASES OF THE SALIVARY GLANDS

PTYALISM

Ætiology.—The flow of saliva is increased by reflexes originating in the mouth and also in more distant situations. Thus all pathological conditions in the mouth and its neighbourhood, such as stomatitis, epithelioma of the tongue and carious teeth, especially if associated with pain, are accompanied by salivation. Trigeminal neuralgia, whatever its cause, is frequently associated with a reflex flow of saliva. Mechanical irritation of the œsophagus caused by the passage of a tube into the stomach or by the impaction of a foreign body causes salivation, which is a common symptom in achalasia of the cardia and in simple and malignant ulceration of the œsophagus. Reflex salivation is the cause of waterbrash associated with the hyperchlorhydria of duodenal ulcer.

The salivation which may occur during menstruation and in the early months of pregnancy is also probably reflex in origin. Salivation is a common and sometimes very distressing symptom of paralysis agitans and post-encephalitic parkinsonism. Ptyalism may result from excessive smoking. It is also caused by the specific stimulating action of certain drugs, such as pilocarpine, and by drugs such as the iodides and mercury, which are partially excreted by the salivary glands.

Salivation due to any of the causes already described may be exaggerated or perpetuated by auto-suggestion (hysterical ptyalism).

Symptoms.—Every time saliva is swallowed some air passes with it into the stomach, which may therefore become distended with swallowed air. In neurotic individuals with ptyalism a spitting or swallowing tic may develop; the latter is always accompanied by aërophagy and the patient consequently complains of severe flatulence (p. 574). Excessive salivation may also cause waterbrash (p. 572).

Treatment.—In order to cure ptyalism the primary cause must be discovered and removed. As purely symptomatic treatment, belladonna should be given: 5 minims of the tincture, taken three times a day, half an hour before meals, is sufficient in the majority of cases, but occasionally much larger doses are required. The drug has the additional advantage of diminishing the secretion of gastric juice when gastric hypersecretion is the primary cause. Hysterical ptyalism can be cured by psychotherapy.

XEROSTOMIA

Ætiology.—The dry mouth, which is constantly present in fevers, is due mainly to deficiency in the psychical, chemical and mechanical stimuli to salivary secretion. The associated toxæmia probably also exerts some direct inhibitory action on the gland-cells. Depressing emotions and the loss or perversion of taste, which may occur when the tongue is furred, result in diminution in the psychical secretion. The paralysis of the secretory nerve-endings produced by belladonna, stramonium and their alkaloids

sets the limit to the dose of these drugs which can be administered. The secretion of saliva is also diminished when excessive quantities of fluid are lost by other channels, as in severe diarrhœa. Diseases of the salivary glands themselves, such as mumps, result in diminished secretion. Severe xerostomia occasionally develops without any obvious cause. Xerostomia is also a common result of sleeping with the mouth open.

Symptoms.—Deficient secretion of saliva causes the mouth to become dry and septic, as particles of food remain between the teeth, where they undergo bacterial decomposition. The tongue is furred and there is often an unpleasant taste in the mouth. It is difficult to chew food sufficiently, and the appetite is impaired as a result of the condition of the mouth and the difficulty in tasting. The insufficiently chewed food is likely to irritate the stomach. In severe cases dysphagia occurs and speech becomes difficult. The loss of the digestion of starch by the ptyalin of the saliva is of no importance owing to the amylolytic activity of the pancreatic juice.

Treatment.—A diet should be chosen which stimulates the flow of saliva; acids are most active, then salt and bitters, whilst sweet substances have very little action. The food should be given in as appetising a form as possible and masticated very thoroughly. If the saliva is only slightly deficient, dry biscuits should be taken at each meal. The taste of a bitter mixture taken immediately before meals may directly stimulate the flow of saliva, and pilocarpine may be tried, but it is rarely of much use, as a dose sufficiently large to increase the flow of saliva generally produces unpleasant symptoms, such as excessive sweating. It is, however, valuable in the treatment of paralysis agitans and post-encephalitic parkinsonism, as it counteracts the xerostomia (and also the paralysis of the intrinsic eye muscles) often caused by hyoscine and stramonium, without diminishing their effect on the tremor of paralysis agitans and the rigidity following encephalitis. Great care should be taken to keep the teeth clean, and the mouth should be washed after each meal.

SPECIFIC PAROTITIS (MUMPS)—(see p. 163)

PAROTITIS

Ætiology.—Parotitis is almost always due to infection ascending Stenson's duct from the mouth. This is particularly apt to occur in the acute parotitis that not infrequently follows operations on the alimentary tract, when the mouth has become septic owing to dehydration, the absence of chewing and normal salivation. It may follow obstruction by a stone in Stenson's duct. Subacute parotitis commonly occurs without obvious cause in persons with healthy mouths. Infection presumably ascends in these cases from the mouth, but may occur by direct spread from the tonsils, through the lymphatics draining an infected middle ear, or possibly by blood stream infection. This subacute or recurrent type of infection is relatively common in children and occurs more frequently in women than in men. An ascending infection may be limited to Stenson's duct, not involving the gland itself, and therefore giving rise to a condition of sialodochitis.

Symptoms.—In acute parotitis following operation both glands are

generally affected, except in mild cases when the condition is often unilateral. The glands are enlarged and tender, the skin over them stretched and shiny. In severe cases suppuration takes place, the neighbouring lymphatic glands enlarge, the temperature is high and constitutional symptoms are present. The mouth is dry and difficult to keep clean; the tongue is covered with a thick, dry fur. The mouth of Stenson's duct is everted and forms a small, red nodule from which a bead of pus can sometimes be squeezed. In milder cases the inflammation gradually subsides; rarely the condition becomes chronic, the parotid glands remaining permanently enlarged and secreting no saliva.

In the subacute form swelling of one or both glands may occur on a single occasion or repeatedly at intervals of weeks or months, sometimes over a period of many years. The swelling usually lasts for several days, but may persist for months. Fluctuation in the size of the swelling takes place, an increase usually accompanying or following mastication. The inflamed gland is painful to touch and the overlying skin may be reddened and hot. Firm pressure over the gland often causes expulsion of pus or turbid saliva from the reddened orifice of Stenson's duct. In recurrent cases the saliva is clear and free from debris between attacks. X-ray examination of the ducts after injection of lipiodol frequently shows bead-like dilatation of the terminal acini. In severe cases there may be irregular dilatation of the main and branch ducts.

Microscopical examination of the parotid saliva shows degenerated leucocytes, epithelial cell debris, and organisms. Streptococci and pneumococci are most commonly found.

Treatment.—The mouth should be kept clean with the greatest care and the flow of saliva promoted by means of chewing gum. In the acute cases, if suppuration occurs, the gland must be incised. In subacute cases, firm massage over the partoid swelling from the ear towards the angle of the mouth, especially at meal times, assists drainage. Local application of heat relieves pain and congestion. In chronic cases, the injection of 1 per cent. mercurochrome into the duct has proved helpful. Deep X-rays are also of value in chronic cases, but should be employed with care in the case of children.

NON-INFECTIVE RECURRENT SWELLING OF THE PAROTID GLANDS [1]

Ætiology.—This condition may occur at all ages. Its pathogenesis is unknown, but the frequent association with conditions, such as asthma, hay-fever and eczema, in the patient himself and in his relatives has led to the suggestion that in some cases an allergic process may be responsible. This theory is supported by the presence of eosinophil cells in the parotid saliva of some cases.

Symptoms.—Eating may precipitate attacks, especially when the food is acid in character, and in some patients the parotid glands become swollen whenever they take food over a period of years. Exposure to cold sometimes has the same effect. The swellings are more often bilateral than unilateral. They develop rapidly and are present for a short time only, often subsiding within half an hour and seldom persisting for more than 24 hours. Single

[1] I am indebted to Dr. R. S. Bruce-Pearson for this article.

isolated attacks may occur, but owing to their brief duration and the absence of after-effects such cases are seldom seen, and cases presenting themselves for treatment are usually recurrent. Signs of inflammation are absent, the parotid saliva contains no pus, and the swellings are seldom painful.

In some patients it is impossible to obtain saliva by pressure during attacks. In others the saliva differs from normal parotid saliva, as it contains globules of jelly-like mucus which obstruct Stenson's duct and may be expressed from it, to be followed by a flow of 2 or 3 c.c. of clear saliva. It is in this type of case that eosinophil cells are sometimes observed both in the mucous plugs and the pent-up saliva; the saliva is always sterile, but secondary infection may occur.

Sialography often reveals no abnormality, but it may show changes resembling those seen in the infected cases. Gross fusiform dilatations of the main and branch ducts are found in long-standing cases of mucous obstruction. Infective parotitis, and a stone in Stenson's duct, a rare condition, must be excluded before a definite diagnosis is made.

Treatment.—Massage over the gland is of value, especially when mucous obstruction is present. In some cases injection of adrenaline subcutaneously leads to subsidence of the swelling.

UVEO-PAROTID SYNDROME (HEERFORDT'S DISEASE)[1]

Definition.—Heerfordt drew attention in 1909 to the association of enlargement of the parotid glands with uveitis and facial paralysis, sometimes with lesions of other cranial nerves and a slight intermittent pyrexia.

Pathology.—The uveo-parotid syndrome is probably a special expression of that form of reticulo-endotheliosis, known as sarcoidosis. Cases have been described in which the uveo-parotid syndrome has been found associated with the skin, pulmonary and bone lesions characteristic of sarcoid. The tuberculin skin reaction is frequently negative, but a number of cases have come to autopsy in which miliary tuberculosis has been the cause of death. Sections of the parotid gland and iris removed during life show granulation tissue of fibrosing type with epithelioid and giant cells but little or no tendency towards caseation. The appearance of the nodules which occur on the iris in about a third of the cases is said to be characteristic of tuberculosis if syphilis and leprosy are excluded. It seems certain that at least one group of these cases is definitely tuberculous.

Symptoms.—The essential features are swelling of the parotid glands and inflammation of the uveal tract. In about half the cases there is in addition facial paralysis on one or both sides. Swelling of the lachrymal, submaxillary or sublingual glands is sometimes present, lymph glands may be generally enlarged, and the spleen may be palpable. Peripheral neuritis with loss of vibration sense, paræsthesia, anæsthesia, weakness of the limbs, and absent knee and ankle jerks, and paralysis of the cranial nerves other than the seventh have been described. Some fever is frequently present.

The parotid swellings are almost invariably bilateral, though one side may precede the other. They are firm and painless, often nodular, and sometimes confined to one part of the gland. They do not vary in size with

[1] I am indebted to Dr. R. S. Bruce-Pearson for this article.

the secretion of saliva. The orifices of Stenson's ducts and the sialographic appearance of the ducts are normal. The parotid saliva is clear, but may be diminished, leading to dryness of the mouth. The uveal lesions most commonly take the form of iridocyclitis, but choroido-retinitis and optic neuritis may be present; vitreous hæmorrhages have been described, and glaucoma and cataract may develop. Skin lesions, including erythematous rashes, indurated erythematous patches on the extremities, and erythema nodosum occur in approximately 20 per cent. of cases; some of these lesions are almost certainly due to skin sarcoid.

Diagnosis.—In the presence of bilateral uveitis, with swelling of one or both parotid glands, the diagnosis is not difficult. In some cases, however, the uveitis or parotid swellings may precede one another by an interval of some weeks. In the latter case subacute parotitis can be excluded by the absence of tenderness over the gland and of pus cells in the parotid saliva. Cases in which there is swelling of the lachrymal glands fall into the group included in the Mikulicz syndrome. A radiograph of the thorax occasionally reveals evidence of tuberculosis, or the nodular deposits of sarcoid. The small bones of the hand may also show the radiological appearance (" shot holes ") of the latter.

Prognosis.—The parotid swelling, uveitis and nerve palsies usually undergo apparently spontaneous cure in the course of some months or even after a period of two years. Recurrences may occur, either of the original lesion, of sarcoid elsewhere in the body, or of frank tuberculous infection. The uveitis is often followed by the development of posterior synechiæ, and vitreous opacities giving rise to impairment of vision are not uncommon. The facial palsy almost invariably recovers completely. In a small proportion of cases death resulted from tuberculosis.

Treatment.—General treatment as for tuberculosis, and the usual treatment of uveitis should be adopted. Tuberculin injections are dangerous on account of the severe focal reactions that may follow. Deep X-ray treatment of the parotid glands has been employed successfully.

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DISEASES OF THE TONSILS

ACUTE TONSILLITIS

Tonsillitis has been classified as superficial, follicular or lacunar, and parenchymatous, according to the degree in which the various parts of the gland bear the brunt of the inflammation; the distinction, however, is not a definite one, as the entire organ is necessarily inflamed.

Ætiology.—The disease is rare in children below the age of 5 or 6, and after middle age; and it is commonest in spring and autumn. It is predisposed to by general ill-health, overwork and a polluted atmosphere; the escape of sewer-gas from defective drains is a probable cause, and the infection may be carried by water or milk. It occurs as a regular symptom of scarlet fever, measles and diphtheria. There is a very close connection between rheumatism and tonsillitis, and it was formerly believed that tonsillitis was of

rheumatic origin; but it is now generally recognised that both acute rheumatic fever and chronic rheumatic pains in joints and muscles are frequently caused by septic infection through the tonsils. Unhealthy conditions of the tonsils due to previous inflammation strongly predispose to further attacks by causing adhesions in the crypts or supratonsillar fossæ, and between the tonsils and the pillars and plicæ, thus promoting the retention of secretion; previous partial removal acts in the same way.

Symptoms.—The symptoms are those of a feverish attack, together with a sore throat; the former often appears before the latter, and only examination of the throat reveals the cause of the disturbance. The temperature may rise to 103° or 105° F., and there is a variable degree of malaise, backache, headache and pain in the limbs. The soreness of the throat radiates to the ear, and is increased by attempts to swallow; the voice becomes thick, the breath foul, and the submaxillary and upper cervical glands are tender and swollen.

The tonsils are swollen, and their purple-red colour extends to the pharynx, palate and uvula—the latter frequently being œdematous. The surface of the tonsils is usually spotted over with yellowish masses of secretion which have exuded from the crypts; sometimes this secretion becomes confluent on the tonsils and occasionally, though rarely, it spreads beyond their surface—it is soft and readily wiped away. The tongue is coated, and the fauces covered with tenacious mucus. There is usually constipation, and the urine is scanty and high-coloured, but not ordinarily albuminous. Albuminuria is, however, an occasional complication, as are pericarditis, endocarditis and suppurative otitis media.

Diagnosis.—The diagnosis from diphtheria is important, and sometimes difficult. The latter is more gradual and asthenic in onset, with less pain, less fever and a more rapid pulse, and the urine frequently contains albumin. The membrane of diphtheria is greyish-white rather than yellowish, and frequently spreads to the pillars and soft palate; whereas the exudation of tonsillitis rarely spreads, and never to any great extent, beyond the surface of the tonsils. The diphtheritic membrane is adherent and, when detached, leaves a raw bleeding surface, while that of tonsillitis is readily removed and more often discrete. In cases of doubt a bacteriological examination should always be made, and an injection of antitoxin should be given while waiting for the result.

Treatment.—The patient should be kept in bed in a warm well-ventilated room, an initial dose of calomel, 2 to 4 grains, should be administered and followed by a saline aperient. Externally, warmth is usually more comforting than cold, and a hot fomentation applied to the neck and covered by a large pad of cotton-wool gives some relief. Internally, especially if the fauces are clogged with tenacious mucus, a warm alkaline lotion, such as Dobell's solution (see p. 1086), may be used with advantage, either by means of a spray or a rubber ball-syringe; but, if the inflammation is so severe that the patient is unable to open the mouth without pain, the lotion should only be used as a mouth-wash; gargling is, of course, only possible in mild cases. Lozenges containing potassium chlorate, guaiacum or formalin may be employed. Of internal medication, sodium salicylate holds the favourite place in doses of 15 grains every 3 hours, and later three times a day; or aspirin, 10 grains, may be used instead; potassium chlorate in 15-grain doses, three or four times daily, appears to be helpful, especially in the

follicular variety; and guaiacum, in the form of mistura guaiaci, was at one time in high repute. The patient must be encouraged to absorb as much nourishment as his dysphagia permits, and he will usually find that soft semi-solids are easier to swallow than liquids; there is room for ingenuity and resource in the provision of a suitable diet, such as junket, baked custard, ice-cream, meat jellies and soups thickened with corn-flour or arrowroot. An iron and quinine mixture may be given when the acute symptoms have subsided.

PERITONSILLAR ABSCESS OR QUINSY

Ætiology.—This is an acute affection due to the formation of an abscess outside the tonsil caused by septic secretions in the supratonsillar fossa or in the depths of a crypt bursting through the thin capsule of the tonsil into the surrounding loose areolar tissue. This process is favoured by adhesions obstructing the mouth of the supratonsillar fossa or the crypts, and, therefore, previous tonsillitis and imperfect surgical removal are predisposing causes. The abscess is usually situated above and external to the tonsil, but in rare cases is behind it.

Symptoms.—The affection is unilateral; but sometimes the opposite side is attacked as the first recovers. It begins with a feeling of malaise, fever, often a rigor, and severe pain radiating from one side of the throat up to the ear and into the neck; the cervical glands are enlarged and tender, and the neck stiff. Dysphagia is intense, the tongue thickly coated, and the breath foul. The mouth cannot be opened widely, and a good light is required for examination, when the typical large deep-red swelling is to be seen bulging one side of the soft palate. Pus forms in 2 to 4 days and, if left alone, will eventually burst, usually through the soft palate; relief is then immediate, but occasionally the opening closes prematurely and the abscess refills.

Complications.—Although one of the most painful and distressing of acute diseases, complications are uncommon, and death is very rare; it has occurred from rupture of the abscess, and inspiration of the pus, during sleep. Severe hæmorrhage may take place after spontaneous or surgical evacuation of the abscess when, as the blood may come from the internal carotid or from a branch of the external carotid artery, ligature of the common carotid is called for. The swelling has been known to spread to the larynx, and to necessitate tracheotomy. Suppuration of the cervical glands is a rare complication, as are pneumonia, septicæmia and pyæmia.

Treatment.—The general treatment is the same as that of severe acute tonsillitis, and the pain sometimes calls for an occasional injection of morphine. Pus is probably present as soon as the swelling has assumed a well-defined rounded form, still more so if there is a boggy area in the centre. The abscess should be opened without delay, for this cuts short the attack and diminishes the risk of complications; but it does not always give immediate complete relief when there is marked cellulitis of the surrounding tissues. After the application of cocaine, a narrow sharp-pointed knife is introduced with the cutting edge upwards and the blade held in the sagittal plane; it is made to puncture the swelling at its most prominent part, and to enlarge the incision by cutting upwards as it is withdrawn. The knife should not be passed to a depth exceeding about $\frac{3}{4}$ inch; if pus is not struck, a sinus-forceps is intro-

duced into the wound and pushed backwards until the pus is found, when it is opened widely to assist the evacuation. After the disease has subsided, removal of the tonsil is advisable, in order to prevent recurrence.

CHRONIC TONSILLITIS

Chronic inflammation of the tonsils may, from the clinical point of view, be divided into two groups: Chronic Parenchymatous Tonsillitis or "enlarged tonsils," and Chronic Follicular Tonsillitis.

Chronic Parenchymatous Tonsillitis

Enlarged tonsils in children are nearly always associated with adenoids; but adenoids are often found in children whose tonsils are not enlarged.

Ætiology.—This is similar to that of adenoids. The condition occurs chiefly in children between the ages of 5 and 15; but it frequently persists into adult life, although normal healthy tonsils atrophy about puberty and hypertrophy seldom takes place *de novo* after that age. The affection may be the result of repeated colds or a sequela of scarlet fever, diphtheria, measles or whooping-cough.

Symptoms.—The symptoms are not easy to separate from those caused by the concomitant adenoids, but it is certain that chronic inflammation of the tonsils can affect the ears, and that gastro-intestinal disturbances and appendicitis are produced by the septic secretion squeezed out of the tonsils during deglutition. Recurrent attacks of acute tonsillitis are common; and the cervical glands are frequently enlarged, may break down and suppurate, or may become tuberculous.

The objective appearances are very various, and it is extremely difficult to estimate the healthiness of a tonsil by inspection. Slightly enlarged tonsils may be prominent and may readily meet on gagging, while big tonsils are often largely buried in the palate or hidden beneath the plica triangularis —in which case a bulging can be seen at the side of the soft palate corresponding to the site of the upper pole.

Treatment.—For children with slight degrees of tonsillar hypertrophy, palliative measures may be tried; an open-air, country life, preferably at the seaside, with cod-liver oil, malt, or iodide of iron, and a nasal lotion for the accompanying adenoids; paints are of doubtful utility, Mandl's solution (iodine, grs. 6, potassium iodide, grs. 12, peppermint oil, min. 3, glycerin, 1 fl. oz.) is perhaps the best.

The tonsils should be removed when there have been repeated attacks of tonsillitis, after a quinsy, with any affection of the middle ear, when there is chronic enlargement of the cervical glands, and when rheumatic fever or chorea has occurred. When chronic cervical adenitis is present, and is not due to some other obvious cause, such as pediculosis or dental caries, the tonsils should be removed whether they appear diseased or not; in these cases about one-third of the tonsils are tuberculous, and this latent tuberculosis cannot be recognised by inspection, many of these tonsils, indeed, being quite small.

The reader is referred to surgical works for details of the operation, but

it may be said here that, if a tonsil requires removal, it must be removed completely in its capsule, for the deeper portion of a diseased tonsil is quite as unhealthy as the superficial; trouble in the remaining portion is very common, and the previous operation only adds to the surgeon's difficulties. In cases where operation is inadmissible, the tonsils may in adults be treated by diathermy, or by application of a caustic, "London Paste," which consists of equal parts of caustic potash and unslaked lime made up into a stiff paste with absolute alcohol. A general anæsthetic is not required, but repeated treatments are necessary, which are not free from pain, and all the tonsillar tissue can only be extirpated by unusual perseverance.

Chronic Follicular Tonsillitis

In older subjects, when fibrosis has followed the hypertrophy, the stenosed crypts become filled with yellowish-white caseous masses. The patient complains of an offensive taste, foul breath, often of recurrent attacks of sore throat, and of gastric disturbances. Not infrequently various forms of chronic toxæmia, such as fibrositis or osteo-arthritis, are induced by absorption from these septic foci. In many cases the tonsils are quite small; they may look healthy, but pus can be squeezed out of the crypts on applying pressure at the anterior pillar by means of a flat instrument.

Treatment.—The treatment in the more marked cases is removal. There are, however, a good many patients who have only a few unhealthy crypts in the tonsils; these may often be cured by passing a fine galvano-cautery point down to the fundus, several applications being usually necessary. The patient may also be shown how to clean out the secretion with a cotton-wool mop on a fine wooden applicator, and to paint the inside of the crypt with Mandl's solution.

VINCENT'S ANGINA

Ætiology.—This affection is believed to be due to two organisms, the bacillus and spirillum of Vincent growing in symbiosis; these organisms may be found in many ulcerative conditions of the mouth and throat, but their constant presence in this affection points to their specific character. The invasion of the throat is frequently secondary to periodontal infection of the gums. It occurs especially in debilitated persons and under insanitary conditions and, though rather rare in civil life, was common during the War of 1914–1918 in some camps and barracks.

Symptoms.—The attack begins insidiously, with malaise, general pains and a temperature of 100° to 101° F. The pain in the throat is slight, but the glands on the affected side become enlarged and tender, and the breath is usually offensive. The affection is nearly always unilateral.

At first there is a patch of soft, yellowish detachable membrane on the affected tonsil which, in a day or two, comes partially away, exposing an ulcer with a well-defined margin. By the end of a week the membrane ceases to form, and the ulcer begins to heal. The ulceration may be quite deep in severe cases, but is ordinarily limited to the tonsil, and very seldom spreads to any distance from it.

Complications are very rare.

Diagnosis.—The disease is particularly interesting by reason of its liability to imitate diphtheria in its early stage, and syphilitic ulceration later. In both cases the discovery of numerous spirilla and fusiform bacilli in smear-preparations—they are difficult to cultivate—will help the physician to the correct diagnosis; but these organisms may also be found in tertiary ulceration, and the Wassermann reaction is occasionally positive in Vincent's angina. The subacute onset, the raised temperature and the tenderness of the glands aid the differentiation from syphilis; and from diphtheria the milder constitutional symptoms, the extremely localised lesion, the soft friable character of the membrane and the absence of the Klebs-Loeffler bacillus.

Prognosis.—Death hardly ever occurs.

Treatment.—Topical application of weak solution of iodine was recommended by Vincent. Liquor arsenicalis and vinum ipecacuanhæ in equal parts, or neoarsphenamine in the strength of 20 grains to the ounce, are effective; these should be firmly applied on a swab, with due regard to their poisonous nature. Intravenous administration of one of the arsphenamine group of drugs is a valuable measure in the more severe cases. Attention should be paid to the condition of the gums and teeth.

HAROLD S. BARWELL.

DISEASES OF THE PHARYNX

DIVERTICULA (see p. 550)

ACUTE CATARRHAL PHARYNGITIS

This is not a very well-defined affection, and is usually accompanied by acute rhinitis on the one hand, and by laryngitis on the other; the tonsils also often participate in the inflammation.

Ætiology.—The affection is generally due to catching cold; it is also caused by traumatism of any kind and by the irritation of hot fluids, corrosives or chemical vapours, and it forms a part of various acute infectious fevers, such as measles, German measles, scarlet fever, influenza and typhoid.

Symptoms.—The discomfort varies from a tickling sensation, or the feeling of a lump in the throat, to severe dysphagia. The voice is husky and thick, and the cervical glands tender and somewhat enlarged. There is slight fever and general malaise.

The pharynx is to a varying degree red and swollen, especially at the sides behind the posterior faucial pillars, where the swelling forms the so-called "lateral bands." The palate is swollen and relaxed, and the uvula elongated. The posterior wall is often covered by a film of tenacious mucus.

Treatment.—The patient should stay in a warm room and avoid the irritation of smoking, talking, alcohol or irritating foods. Calomel, 2 to 4 grains should be given, and followed by a saline aperient. Aspirin, or sodium salicylate, is helpful, and, as the naso-pharynx is involved, the nose should be syringed with a warm saline lotion which may also be applied to the pharynx as a spray.

ACUTE SEPTIC PHARYNGITIS

This term includes a series of severe infective inflammations, erysipelas of the throat, œdematous, phlegmonous and gangrenous pharyngitis and laryngitis, and angina Ludovici. Any classification must necessarily be a clinical one, based on the severity of the symptoms and their localisation, for they can be produced by a variety of micro-organisms, though they are usually caused by a streptococcus. These severe inflammations are fortunately uncommon, and most often, though by no means invariably, occur in debilitated or alcoholic persons.

Symptoms.—These vary greatly with the severity of the infection, which ranges from a mild inflammation to the most severe septic intoxication. They include malaise, sore throat, dysphagia, hoarseness and dyspnœa. The temperature in some cases rises to 105° or 106° F.; but in many of the worst cases it is hardly raised at all, and may be subnormal. Pleurisy, pneumonia and pericarditis may ensue, or death may result from asphyxia; but the worst cases die from general toxæmia and heart failure, even within 24 hours of the onset of the disease.

The objective appearances, also, are very variable. The pharynx and palate are of a deep purplish-red, and there may be sloughy patches or pseudo-membrane. The entire mucosa may be enormously swollen, and the œdema may involve the upper aperture of the larynx and produce asphyxia. The sublingual region is sometimes occupied by a peculiar brawny swelling, of a hardness like wood, which spreads downwards into the neck to a variable extent, and is known as "angina Ludovici."

Treatment.—The patient must be in bed and well nursed, and every care must be used to ensure that he takes as much nourishment as possible. Polyvalent anti-streptococcic serum is sometimes very successful, and should be given early in a large dose (40 to 50 c.c.). Hot fomentations to the neck and inhalations of steam are comforting. Œdema of the upper aperture of the larynx should be treated promptly by scarification; free incisions should be made with a curved bistoury guided by the finger, and tracheotomy under local anæsthesia must not be delayed, if dyspnœa be severe or not relieved by scarification. For angina Ludovici a deep incision should be made in the middle line, as all anatomical landmarks have disappeared, and an attempt should be made to find pus with the finger or a director. Sulphanilamide, or one of its congeners, is now indicated in this as in other forms of streptococcal infection.

RETRO-PHARYNGEAL ABSCESS

There are two forms—(1) Acute, and (2) chronic.

1. The acute form occurs in children up to the age of 3 or 4, but is far more frequently met with in the first 12 months. It is due to suppuration in the prevertebral glands, situated behind the posterior pharyngeal wall, which retrogress and disappear in later life. The abscess results from absorption of sepsis from the nares, naso-pharynx, or fauces, and is sometimes secondary to an infectious fever.

Though rare, the condition is an important one, for it may easily remain unrecognised in a young infant, and it is usually fatal if left unopened. The symptoms are fever and restlessness, a hoarse cry and croupy cough, with difficulty in swallowing and dyspnœa. Such symptoms should arouse a suspicion of retro-pharyngeal abscess, which may be seen on inspection as a rounded swelling of the posterior pharyngeal wall. The abscess is often very large, and must be freely opened in such a way as to avoid aspiration of the pus, without an anæsthetic, and with the child firmly held, either on the side with the face directed somewhat downwards, or on the back with the head hanging almost vertically. Recovery is rapid, and no after-treatment is required beyond attention to the enfeebled general health.

2. The chronic form, also, is found most frequently in children, but generally after the third year. It is of tuberculous origin, and is due either to tuberculosis of the prevertebral glands, or to caries of the cervical spine. The latter should be carefully excluded, for this abscess should on no account be opened through the mouth, as septic infection of the diseased bone will occur. The chronic glandular abscess, however, may be successfully opened and curetted by this route, though some surgeons prefer to treat them all by an incision behind the sterno-mastoid.

CHRONIC PHARYNGITIS

(Pharyngeal Hyperæsthesia)

The symptoms of discomfort in the throat in the conditions grouped as chronic pharyngitis bear little relationship to the intensity of the changes seen on examination. Many people, especially heavy smokers, complain of no discomfort, in spite of showing decided chronic inflammation; whereas others, in particular dyspeptic or anæmic women or those at the menopause, suffer great discomfort, with no apparent local abnormality. Indeed, in many cases the condition is better described as pharyngeal hyperæsthesia.

Ætiology.—The causes of chronic pharyngitis are most often found in nasal disease, which produces inflammation of the pharynx by causing mouth-breathing, and by the irritation of discharges; incorrect production of the voice is an important factor which is often in its turn dependent on nasal obstruction. Unhealthy conditions of the teeth or tonsils are further causes, as are the inhalation of irritating dust and vapours in various occupations, tobacco smoke and over-indulgence in alcohol. A long list of constitutional affections is active in the ætiology, such as gout, rheumatism, dyspepsia, anæmia, cardiac disease, cirrhosis of the liver, chronic bronchitis and pulmonary phthisis.

Symptoms.—The discomfort may take the form of aching, fullness, or feeling of a lump, a hair, or a pricking. The voice has a dead tone, and there is usually much hawking and frequent swallowing. The sufferer often becomes depressed, and fears that he has cancer of the throat. The unpleasant sensations are markedly lessened after a meal.

The mucosa of the pharynx and palate is thickened, and there is a loss of the finer modelling of the faucial pillars; the uvula is elongated, often slightly œdematous at its edges and tip, and fails to retract on phonation.

The posterior wall is covered by a film of mucus, which puckers up and becomes more obvious on touching it with a probe or swab. The wall of the pharynx is traversed by enlarged venules, and sometimes it is set with slightly raised pink lenticular nodules of lymphoid tissue, constituting a variety known as *granular pharyngitis*. In other cases two elongated masses of lymphoid tissue appear behind and parallel to the posterior pillars; these are the "lateral bands," and this form is called *lateral pharyngitis*. *Pharyngitis sicca* is a dry glazed condition usually dependent on rhinitis sicca or atrophic rhinitis, and occasionally the crust formation of the latter disease extends to the pharynx, causing a genuine *atrophic pharyngitis*.

Treatment.—The most important part of the treatment consists in the detection and alleviation of the cause, and should begin with a careful examination of the nasal passages. Cases of pharyngeal hyperæsthesia without obvious local changes are often harmed, rather than helped, by local treatment which directs attention to their trouble. Tobacco should be given up, and alcohol in concentrated forms, indeed the latter should be abandoned completely in plethoric patients and where the pharynx is congested; condiments and highly seasoned food should be avoided; this type of patient is benefited by a morning dose of sulphate of soda or magnesia, a teaspoonful in a glass of hot water while dressing, or by one of the natural mineral waters. When the pharynx is dry, or covered with tenacious mucus, an expectorant mixture gives relief, such as tinctura ipecacuanhæ, min. 12, vinum antimoniale, min. 5, potassium iodide, grs. 3, syrup of tolu, min. 60, water, 1 fl. oz., three times a day. The throat may be sprayed with a warm alkaline saline lotion, and the same may be, with greater advantage, syringed through the nostrils. Of local applications in the form of paints, iodine is the most generally useful, and may be applied daily by the patient as Mandl's solution; iodine, grs. 6, potassium iodide, grs. 12, peppermint oil, min. 3, glycerin, 1 fl. oz.; a 5 to 10 per cent. solution of resorcin in glycerin may be employed, or, if a more astringent effect is desired, iron-alum gr. 60, in glycerin, 1 fl. oz.; or the physician may himself apply, once or twice a week, nitrate of silver, grs. 10 to 30 to the ounce of water. In many cases, the galvano-cautery is of great value; it acts as a counter-irritant and astringent, and should be applied lightly and with caution. Prominent granulations may be destroyed and enlarged venules obliterated by this means, but deep eschars should not be produced, and only a few applications should be made at one sitting.

KERATOSIS PHARYNGIS

In this condition a number of sharply defined projecting white or yellow nodules occupy the surface of the tonsils; they also occur, though less profusely, scattered over the lingual and naso-pharyngeal tonsils and on any lymphoid granules in the pharynx. They occur at any age after childhood, and usually in persons in a poor state of health. The causation is unknown; the nodules consist of heaped-up epithelium and detritus containing numerous micro-organisms of the kind ordinarily present in the mouth. They sometimes disappear quickly, in other cases they remain for many months, or they may frequently recur. They produce no symptoms, or at most a slight discomfort, and are of interest chiefly because they are frequently mistaken

for the exudation of chronic follicular tonsillitis. Once seen they can, however, be recognised at a glance, for they are hard and adherent, discrete and prominent, and occur beyond the limits of the tonsils, on the pharynx and base of the tongue. They are usually discovered accidentally by the patient, who is naturally alarmed at their appearance. They are quite harmless, and local treatment is useless, for they are removed with difficulty and usually recur; it is wise to reassure the patient by telling him these facts and, if any treatment be required, to trust to attention to the general health, a holiday and change of air.

SYPHILIS

The *primary* chancre occurs on the fauces, occasionally on the pillars, palate or pharyngeal wall, but usually on the tonsil. In this situation the disease is apt to pass unrecognised, for the symptoms are usually slight and the lesion masked by the general inflammation of the tonsil; the typical induration is often absent, but there is always a characteristic bubo behind the angle of the jaw.

Secondary Syphilis

Secondary manifestations in the fauces are a part of the normal course of the general disease and are intensely contagious.

Symptoms.—The subjective disturbances are usually limited to dryness and discomfort. Objectively there are two types of lesion, erythema and mucous plaque. The former is a patchy, dusky red rash, with well-defined margins, somewhat symmetrical, and affecting especially the anterior pillars and soft palate. It is particularly associated with the early secondary symptoms; whereas the mucous patch may be present at the same time or may be found later, together with tertiary manifestations. The mucous plaque occurs on the soft palate, tonsils and pillars; in appearance it is a dusky, slightly-raised patch, with a sharply defined red margin, the surface is covered by a delicate milky-white layer of superficial necrosis resembling a "snail-track" or, if rather thicker, looking as if it had been touched with nitrate of silver.

Diagnosis.—The appearances just described are so characteristic that they are of great help in the diagnosis of the general affection; if their nature should be misinterpreted, other secondary symptoms nearly always co-exist to establish the correct diagnosis.

Treatment.—General treatment quickly cures these secondary lesions, though they may reappear during the first two or three years. Of local treatment, abstinence from tobacco and alcohol is important, as are the careful use of a tooth-brush after every meal and the employment of a mouth-wash, such as peroxide of hydrogen or potassium chlorate.

Tertiary Syphilis

Tertiary lesions usually occur about the third or fourth year after infection but may rarely be found within a few months or may make their appearance at any later time throughout the patient's life.

Symptoms.—Two principal forms may be described—(1) superficial ulcer, and (2) gumma.

1. The *superficial ulcer* may attack any part of the fauces, the posterior wall, tonsils, pillars or palate, a favourite site being the junction of the uvula with the edge of the soft palate. It has a flat base, with a smooth yellowish necrotic surface and a well-defined red margin, devoid of swelling or infiltration, and has a peculiar "serpiginous" contour as though marked out by segments of a series of circles.

2. A *gumma* is a localised infiltration which rapidly breaks down and exposes a deeply excavated circular ulcer covered with a thick yellow slough. One favourite site is on the posterior pharyngeal wall above the level of the palate, and another on the upper surface of the soft palate; in the latter situation nothing is seen from the mouth except a general dusky swelling of the palate until perforation suddenly occurs and irremediable damage has been done. After severe gummatous ulceration the resulting cicatricial contraction may bind the palate to the pharyngeal wall and partly or completely shut off the naso-pharynx from the mouth.

Of subjective symptoms, dysphagia may be very severe; nasal obstruction is present when the naso-pharynx is occluded by swelling or scarring; the voice is altered to a dead tone when there is nasal obstruction, or to the characters of a cleft-palate articulation if a perforation of the palate has occurred.

Diagnosis.—From an ulcerating malignant growth the diagnosis may be a matter of difficulty, especially as in syphilis the dysphagia may produce marked cachexia and loss of weight. The gummatous ulcer is excavated, covered by a dirty yellow adherent slough, its margin only moderately thickened, often overhanging, and surrounded by an area of deeply congested mucous membrane; the base of an epitheliomatous ulcer presents a nodular "cauliflower" aspect, and its edge is thick and everted; palpation with the finger is of great value, for the peculiar hardness of an epithelioma is highly characteristic. The superficial tertiary ulcer is usually easily distinguished from lupus, the ulcerations of which are surrounded by and dotted over with the characteristic granules, and the lesions of which occur on a pale mucous membrane, while manifestations of lupus are to be found elsewhere. Tuberculous ulceration of the fauces is superficial, but is more intensely painful than the superficial syphilitic ulcer, and is a terminal event in advanced pulmonary tuberculosis. Vincent's angina may closely resemble syphilitic ulceration of the tonsil, but is distinguishable by its more acute onset, raised temperature and tender glands. Actinomycosis, when it attacks the region of the tonsil, closely resembles an ulcerating gumma, especially as it improves under administration of iodides; the detection of the characteristic yellow granules will lead to their microscopical examination and recognition.

Treatment.—The most energetic general treatment may be called for to prevent perforation of the palate or severe cicatricial deformity. Local treatment consists chiefly in the use of antiseptic mouth-washes and gargles. Orthocaine (orthoform) by insufflation is helpful when there is dysphagia. The daily application of 3 grains of calomel, sublimed by a spirit-lamp and insufflated from a glass tube, is to be recommended in severe cases of ulceration.

LUPUS AND TUBERCULOSIS

Lupus occurs most frequently in young women. It usually shows evidence of having spread from the nasal passages, and attacks first the uvula and soft palate, whence it spreads to the faucial pillars. It appears as a patch made up of minute reddish nodules, each containing the typical "apple-jelly" centre; the surrounding mucosa shows no sign of inflammation. A progressive superficial ulceration gradually occurs, and may cause destruction of the uvula and part of the soft palate, while elsewhere scarring becomes evident and may finally result in considerable deformity. The subjective symptoms are limited to a feeling of stiffness and discomfort. The diagnosis is generally easy from the characteristic appearance, the chronicity, and the presence of lupus in the nares and on the skin. Syphilis is more rapid and does not spare the bony palate, which is never attacked by lupus. Lupus in the pharynx is far more amenable to treatment than in the nose, and may be expected to improve under the general anti-tuberculous régime of good food and open air; arsenic in full doses is very valuable, beginning with 5 minims of liquor arsenicalis three times a day, and increasing the dose gradually to 15 minims. Tuberculin has proved disappointing. Of local measures multiple puncture with a fine galvanocautery point is most useful, and massive patches of infiltration may be curetted.

Apart from the latent tuberculosis of the tonsils associated with cervical adenitis, which has been referred to under chronic tonsillitis, tuberculous disease of the pharynx is a rare affection; it occurs as a late and terminal complication of advanced consumption. The onset is acute; the affected parts, especially the soft palate and faucial pillars, are covered with numerous tiny grey tubercles on a bright red mucosa which soon break down to form multiple superficial ulcers with a flat greyish-yellow base. Pain is intense and swallowing becomes well-nigh impossible; treatment must be directed to alleviating the distress with insufflations of orthocaine, lozenges of cocaine or morphine, hypodermic injections of morphine or diamorphine, and saline and nutrient enemata.

INNOCENT TUMOURS

Papillomata are fairly common on the uvula, soft palate and faucial pillars and tonsils. They are small pedunculated warty growths and are easily removed. A flat sessile papilloma in this region must be regarded with suspicion as a possible early epithelioma and should be promptly excised by an elliptical incision around the site of origin.

Angiomata occur in the soft palate. Removal by the knife is a formidable matter and must be performed by incisions wide of the tumour. Diathermy excision, electrolysis, or cautery or diathermy puncture are preferable methods of treatment.

Dermoid cysts, teratomata and *mixed tumours*, resembling those found in the parotid, are occasionally observed.

MALIGNANT TUMOURS

Epithelioma attacks the tonsils, soft palate or pharynx; the lower pharynx behind the cricoid plate is often affected in females and at a younger age than is usual in cancer. Sarcoma usually originates in the tonsil and the cervical glands are secondarily involved, though generally somewhat late in the disease. In the earlier stages, malignant tumours of the tonsil resemble simple hypertrophy and may easily escape attention; in many cases enlargement of the cervical glands is the first symptom, and in such the tonsil should always be remembered as a possible site of the primary disease; palpation with the finger is of great service in its detection, the firm hard feel of a tumour distinguishing it from simple enlargement. Very early malignant tumours of the tonsil and palate may be removed through the mouth, and tumours situated low down in the pharynx may be reached by the operation of lateral pharyngotomy. The cervical glands should be cleared out. The final results of surgical extirpation of cancer of the tonsil are very bad, and radiotherapy may now be said to offer a better prospect of cure. Of palliative measures, diathermy may be used to remove the mass of the tumour, check fungation, and relieve symptoms. Oral hygiene, including the removal of all unhealthy teeth, antiseptic sprays and insufflation of orthocaine and benzocaine (anæsthesine) for dysphagia, will do much to relieve the severity of the symptoms. Palliative tracheotomy or gastrostomy, if required, should not be too long deferred.

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DISEASES OF THE ŒSOPHAGUS

DYSPHAGIA

Dysphagia, or difficulty in swallowing, is generally the first symptom in diseases of the œsophagus. Owing to the fixed position of the œsophagus localisation of abnormal sensations is very accurate, and a patient generally points to the exact level of obstruction. In some cases, however, reflex achalasia or spasm occurs at the pharyngo-œsophageal sphincter simultaneously, so that the patient experiences difficulty in initiating the act of swallowing as well as feeling the obstruction in the passage down the œsophagus caused by the primary disease.

The causes of dysphagia can best be considered according to whether the difficulty is experienced at the upper extremity, near the middle, or at the lower extremity of the œsophagus; the last is the most common.

(*a*) *Pharyngo-œsophageal dysphagia.*—This is most commonly a result of neuro-muscular inco-ordination associated with atrophy of the glosso-pharyngeal mucous membrane and with anæmia (Paterson's syndrome). A similar inco-ordination is the cause of hysterical dysphagia, and difficulty in the initiation of the act of swallowing may occur in progressive bulbar paralysis, myasthenia gravis, and in the paralysis of the soft palate caused by diphtheritic neuritis. In comparatively rare cases epithelioma may

develop in this situation, and still more rarely dysphagia at the upper end of the œsophagus is caused by a pouch.

(*b*) *Mid-œsophageal dysphagia.*—This is almost always caused by epithelioma. External pressure by an aneurysm or mediastinal tumour rarely causes dysphagia. This is the situation of congenital strictures and strictures following injury caused by the impaction of foreign bodies, and I have seen mid-œsophageal strictures caused by cicatrisation of an ulcer following broncho-pneumonia and by syphilis.

(*c*) *Lower œsophageal dysphagia.*—Dysphagia at the lower end of the œsophagus is most frequently caused by achalasia of the cardia and by epithelioma of the œsophagus. Next most frequent is the dysphagia caused by spasm secondary to peptic œsophagitis and œsophageal ulcer, and by carcinoma of the fundus of the stomach. Lastly, the dysphagia may be due to cicatricial stenosis secondary to peptic ulcer or to the phlegmonous œsophagitis resulting from the swallowing of boiling water or corrosive poisons.

Upper Dysphagia with Anæmia

(Paterson's (so-called Plummer-Vinson) Syndrome)

Pathology.—In the voluntary initiation of swallowing the food is thrown to the back of the pharynx. The sphincter formed by the lower division of the inferior constrictor muscle of the pharynx (the "crico-pharyngeus muscle") at the junction of the pharynx and œsophagus, which is normally closed, then opens and allows the bolus to enter the œsophagus, along which it is carried by active peristalsis. In this syndrome, which occurs almost exclusively in middle-aged women, there is inco-ordination of the muscles concerned, and the sphincter fails to relax (achalasia) and may even contract spasmodically. As it is always associated with atrophic inflammation of the mucous membrane of the tongue, which spreads to the upper end of the œsophagus, it seems reasonable to suppose that the inflammation involves the myenteric (Auerbach's) plexus in the region of the sphincter, exactly analogous to what occurs in achalasia of the cardia. Both the atrophy of the mucous membrane and the anæmia are probably nutritional in origin, as most of the women affected have for long periods been living on an insufficient diet.

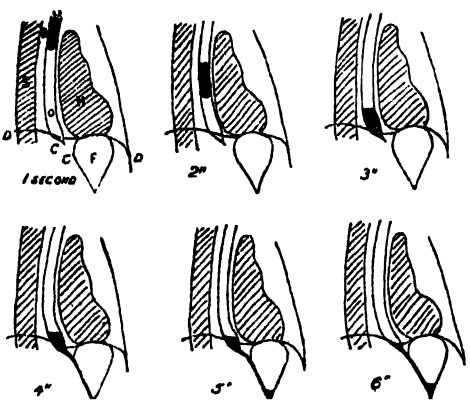


Fig. 14.—Diagrams of normal swallowing as seen with the X-rays in successive seconds. OO, œsophagus; B, bolus of food; CC, cardiac sphincter; DD, diaphragm; S, spine; H, heart; F, gas-containing fundus of stomach.

Symptoms.—The patient, who is generally an edentulous woman who has been in poor health for a long period owing to the presence of simple microcytic anæmia (*vide* p. 775), gradually finds difficulty in initiating the

act of swallowing, especially of solids. Sometimes, however, the dysphagia begins quite suddenly, and it may occur intermittently. It is frequently so slight that its presence is discovered only on cross-questioning a patient suffering from the other symptoms of the syndrome. The dysphagia is associated with atrophic inflammation of the mucous membrane of the tongue, which extends back to the entrance to the œsophagus. An atrophic condition also involves the lips, which are thin and inelastic with cracks at the angles of the mouth. Achlorhydria is frequently, but not always, present, and the spleen is enlarged in about 20 per cent. of cases. The nails are often thin, brittle and spoon-shaped (*koilonychia*).

The X-rays reveal no abnormality, and the œsophagoscope shows nothing more than an atrophic inelastic condition of the mucous membrane in the neighbourhood of the pharyngo-œsophageal sphincter.

The atrophic glosso-pharyngitis predisposes to epithelioma. About 50 per cent. of women with cancer of the mouth and a still larger proportion of those with cancer of the hypopharynx and upper end of the œsophagus give a history suggestive of the syndrome. The fact that the latter is almost confined to women probably explains why 80 per cent. of cases of cancer of of the upper end of the œsophagus occur in women, whereas at least 80 per cent. of cases of cancer of the middle and lower end occur in men.

Treatment.—A mercury bougie should be introduced into the œsophagus and passed from time to time until the dysphagia disappears. The anæmia responds to treatment with large doses of iron ; liver is without effect, except in the rare cases in which it is Addisonian. The atrophic condition of the mucous membrane also responds to iron therapy even if there is no anæmia.

Achalasia of the Cardia (so-called Cardiospasm)

Ætiology.—Achalasia of the cardia may begin at any age, but most commonly in adults, and males and females are equally affected.

Pathology.—The hypertrophy of the muscular coat of the œsophagus, which is always present in this condition, indicates that violent efforts must have been made to overcome some obstruction. As no organic obstruction is ever found after death it was at first thought that the spasm of the cardiac sphincter was present and the condition was called *cardiospasm*. As the symptoms may be present without intermission for many years before death, a considerable degree of hypertrophy of the cardiac sphincter would result from the long-continued spasm. In very few autopsies, however, has there been any hypertrophy, and in several cases in which the cardiac sphincter,



Fig. 15. - Drawings from a case of dilated œsophagus secondary to achalasia of the cardiac sphincter. (*a*) Dilated œsophagus filled with a 7-inch column of opaque food; sphincter closed. (*b*) Opaque food passing into stomach through sphincter which has opened after additional food has raised column in œsophagus above 7-inch height. (*c*) Return to condition of (*a*) after excess of food over the 7-inch column has entered stomach.

which is normally about one inch long and corresponds with the whole of the abdominal œsophagus, was exposed by operation, the muscle was found to be unusually thin. I believe that the obstruction is caused not by spasm but by achalasia (α, not; χαλάω, I relax), or absence of the normal relaxation of the cardiac sphincter, which should occur when each peristaltic wave reaches it (Figs. 14 and 15). Food stagnates in the œsophagus, which dilates as more and more collects in it; the distension of the œsophagus acts as a powerful stimulus to peristalsis, which is excessively violent and continues at intervals throughout the day. This is the cause of the hypertrophy.

Further evidence that the condition is due to achalasia and not to spasm is afforded by the fact that, although strong peristaltic waves are unable to overcome the obstruction, the weight of an indiarubber tube filled with mercury is sufficient to cause it to drop through the cardia into the stomach, the actual passage through the cardia being often inappreciable to the hand which holds the mercury bougie, which can be withdrawn with equal ease; it is not gripped, as the finger is gripped when it enters or is withdrawn from a spasmodically contracted anal sphincter.

The achalasia is a result of degenerative changes in the myenteric (Auerbach's) plexus between the circular and longitudinal muscular coats of the lower end of the œsophagus (Rake). The vagi themselves are unaffected. The degeneration is a sequel of inflammation, which spreads from the mucous membrane from a primary œsophagitis, or results from blood-borne infection or toxæmia and possibly from vitamin-deficiency.

The dilated œsophagus may be able to hold as much as two pints, and its circumference may exceed 6 inches.

Symptoms.—Achalasia of the cardia generally develops gradually, a slight attack, lasting for a day or two, being followed by a period of freedom for a few days or even several weeks or months. Attacks then occur at gradually shorter intervals, until finally the condition becomes permanent. The patient feels as if the food "sticks." He often recognises that the obstruction is beneath the lower end of the sternum, but sometimes the sensation is felt in the upper part or middle of the chest. Sometimes actual pain is produced. Salivation occurs in every case.

As a rule the patient voluntarily relieves his discomfort within a few minutes of finishing a meal by bringing up the greater part of what he has eaten mixed with saliva. He realises that this comes from his chest and not his abdomen, and, unlike true vomiting, it is not associated with nausea.

The weight of the column of food in the dilated œsophagus after a meal is sufficient to force a small proportion of the fluid present through the cardia as a very narrow stream; but as soon as the height of the column falls below a certain point, generally about 7 inches, or the individual lies down, the pressure becomes insufficient and the flow ceases (Fig. 15). Consequently, stagnating food mixed with mucus is always present in the œsophagus, and a considerable quantity can be removed from it even after a fast of 24 hours. No regurgitation occurs on lying down as the pharyngo-œsophageal sphincter is always, as in normal people, closed except during the act of swallowing.

The œsophagoscope shows that the entry to the cardiac sphincter, which is generally at the level of the diaphragm but may be within the thorax or within the abdomen, is completely closed. The mucous membrane may be

normal, but it is often red and inflamed, especially in the lowest part of the œsophagus, and there may be superficial erosions, which are secondary to the stasis.

The general health at first remains good in spite of the fact that weight is rapidly lost. After a certain amount of weight is lost, a condition of equilibrium develops; though extremely small quantities of food reach the stomach, the patient loses no more weight, and though he is less strong than formerly, he may continue to live in this condition for many years and attain old age.

Diagnosis.—The patient's description of his symptoms is generally so characteristic that a diagnosis of œsophageal obstruction can be made with a considerable degree of probability. This is confirmed by means of an X-ray examination, which must in the early intermittent stage be made during an attack, when the situation of the obstruction at the cardiac sphincter is at once apparent. It is next necessary to ascertain whether this is due to achalasia or to cancer, or to spasm associated with œsophagitis or a simple œsophageal ulcer, which may also give rise to a fibrous stricture. The intermittent character of the early attacks, the absence of serious constitutional symptoms in spite of rapid loss of weight, the comparatively early age at onset with many patients, and, in cases in which an early diagnosis has not been made, the long duration of the illness and enormous dilatation of the œsophagus point to achalasia rather than to growth. Occult blood is present in the stools in cancer, but never in achalasia of the cardia. In achalasia the shadow of the dilated œsophagus narrows abruptly and ends at the entry into the sphincter, either on a level with the diaphragm or a short distance above or below it. As each additional quantity of food is swallowed, a narrow and uniform channel is seen for a moment to join the œsophagus with the stomach before the sphincter closes again. In simple ulcer of the lower end of the œsophagus the sphincter remains open, but a narrowing is seen just above as a result of spasm with or without cicatricial contraction, and the round crater of the ulcer may be recognisable. In the cicatricial obstruction which follows caustic poisoning the obstruction extends for some inches upwards instead of being confined to the sphincter. In carcinoma the lumen of the cardiac sphincter is replaced by an irregular channel which extends a varying distance up into the œsophagus, the unaffected part of which is rarely as dilated as in achalasia. Further evidence pointing to achalasia is the ease with which a mercury tube passes through the cardia in contrast with the complete obstruction offered to its passage by a growth.

Prognosis.—If the condition is recognised at the onset of symptoms, a permanent cure often results from treatment, but if treatment is instituted only after the obstruction has become continuous and the œsophagus greatly dilated, cure as distinct from mere relief of symptoms is less likely to be obtained. In the absence of treatment death has occurred at an early stage in very acute cases; but more often the patient survives for a considerable period, even for 40 years. In rare cases a diverticulum may form in the lower end of the dilated œsophagus or cancerous degeneration of a wart developing on the chronically inflamed mucous membrane may occur.

Treatment.—The simplest and most effective treatment is by means of a series of mercury bougies, the smallest of which is 24- and the largest 34-gauge. They are made of rubber tubes closed at the top and with a

rounded lower end, and are half-filled with mercury. The whole series can generally be passed at the first sitting, which should be done with the guidance of the X-rays. Afterwards only the largest bougie which the patient can himself pass should be used. It drops easily through the cardia and requires no pushing. It is kept in position for a quarter of an hour on each occasion at first, but later it can be withdrawn directly after it has entered the stomach. The patient feels relieved and realises that "the passage is clear" as soon as it is withdrawn. It should be passed immediately before meals; the food then enters the stomach without difficulty. In very early cases the tube may only need to be passed once. Generally, however, the tube has to be passed before each meal at first, then once a day, and gradually less often, till finally it is only used at rare intervals when the patient feels that some slight obstruction is returning. In chronic cases, which are always associated with secondary œsophagitis, the diet for the first 2 or 3 weeks of treatment should consist of nothing but a pint of milk taken three or four times a day immediately after the passage of the bougie; half a pint of water should be drunk 10 minutes later. In the very rare cases in which a mercury bougie cannot be passed owing to the kinking caused by great elongation in addition to dilatation of the œsophagus, the cardiac sphincter should be stretched by the fingers inserted through an opening made in the stomach after laparotomy.

DIVERTICULA OF THE PHARYNX AND ŒSOPHAGUS

Ætiology and Pathology.—Diverticula may develop from the anterior wall of the middle third of the œsophagus by the traction resulting from adhesions between inflamed glands near the bifurcation of the trachea and the wall of the œsophagus; these "traction diverticula" are generally less than an inch in depth and rarely give rise to symptoms.

A diverticulum, which has given rise to no symptoms, is occasionally discovered at the lower end of the œsophagus during a routine X-ray examination. Its origin is generally obscure, but in one of the three cases I have seen it was associated with achalasia of the cardia.

Pressure diverticula are rare, but of considerable clinical importance. They occur only in adults, especially elderly edentulous men who habitually swallow lumps of unchewed food. They develop at the muscular gap on the posterior wall of the pharynx between the upper and lower divisions of the inferior constrictor of the pharynx at the level of the cricoid cartilage. They are really diverticula of the pharynx and not of the œsophagus, though they are generally described as œsophageal. The lower division of the inferior constrictor of the pharynx (the crico-pharnygeus muscle) forms a sphincter surrounding the entrance to the œsophagus. It is closed at rest, but opens during each act of deglutition the moment the food reaches it. When, as a result of a neuro-muscular inco-ordination, it fails to open (achalasia), the food is forced against the weak spot on the posterior wall of the pharynx immediately above the sphincter. A pouch of mucous membrane may thus be formed; it becomes progressively larger towards one side, generally the left, owing to the accumulation of food in it, until it may finally measure as much as 5 inches in depth and be large enough to contain over a

pint of fluid, in which case it may extend into the posterior mediastinum. Its wall is formed of mucous membrane and submucous tissue without any muscular covering.

Symptoms.—Diverticula of the pharynx sooner or later cause progressive dysphagia, but this may be preceded by irritation of the throat and increased secretion of mucus. The patient complains of obstruction in the neck when he swallows, and a small quantity of food is regurgitated at varying intervals after meals. As the sac increases in size, the symptoms become more marked owing to obstruction of the œsophagus by the distended diverticulum, which finally forms a prolongation of the pharynx, the œsophagus opening as a transverse slit in its anterior wall. Increasing quantities of food are brought up, mixed with a large amount of mucus, and food eaten several days before may be recognised. The patient becomes steadily more emaciated. Distension of the sac often causes pain, which is relieved when it is emptied. An irritable cough is often present, and dyspnœa may result from pressure on the trachea. A large diverticulum containing food may form a visible tumour in the neck, generally on the left side, which can be emptied by pressure, the food returning into the pharynx, but in most cases there is no palpable tumour.

The size, shape and exact position of the diverticulum can be recognised with the X-rays after a barium meal.

Treatment.—The only satisfactory treatment is excision. Whilst waiting for operation the patient should be fed through a catheter, which is introduced over a string swallowed when the sac is empty; if no fluids are taken for 5 or 6 hours the string always reaches the stomach.

ŒSOPHAGITIS

Two distinct forms of œsophagitis occur, both of which may be either acute or chronic. In one the irritants which cause it are either hæmatogenous or swallowed. In the other form, which, unlike the first, is often associated with ulceration, the essential factor is the presence of acid gastric juice in the œsophagus.

A. Simple Œsophagitis

(*a*) *Acute*

Ætiology.—Acute simple (non-acid) œsophagitis is a rare complication of various acute infections and toxæmias, such as scarlet fever. It may also complicate cancer of the œsophagus and spread from acute pharyngitis. In 5 per cent. of fatal cases of diphtheria the inflammation spreads from the fauces into the œsophagus, and in very rare cases the membrane extends as far as the cardia. The impaction of a foreign body in the œsophagus may cause local suppuration. Acute inflammation results from swallowing boiling water or corrosive poisons, taken by accident or in attempted suicide; owing to the obstruction to the passage of the œsophageal contents caused by the narrow cardiac sphincter the lower end is the part most affected, the upper extremity being next most seriously injured.

Symptoms.—In mild cases there may be no symptoms, but more or less dysphagia is generally present; in severe cases deglutition is so painful that the patient may be afraid to swallow his saliva or relieve his urgent thirst by drinking. There may also be constant pain beneath the sternum. Attempts to swallow often prove unsuccessful owing to reflex spasm and the food is immediately rejected. Mucus is expectorated, together with blood and pus in severe cases.

Treatment.—In severe cases nothing should be given by mouth, but saline solution must be injected into the rectum or intravenously. Morphine is required for the pain. When the pain begins to subside a tablespoonful of olive oil followed by 5 oz. of milk can be given in every 3 hours. Solid food should not be given until swallowing no longer causes pain. Complete obstruction necessitating gastrostomy is likely to occur in severe cases following corrosive poisoning.

(*b*) *Chronic*

Ætiology.—Chronic œsophagitis results from the constant swallowing of irritants, the most important of which are strong alcoholic drinks, and from septic conditions of the teeth and nasopharynx. It is also a common sequel of the stasis of food in the dilated œsophagus in achalasia of the cardia (p. 548).

Symptoms.—As the condition is frequently associated with chronic pharyngitis and gastritis, it is generally impossible to isolate the symptoms of one of these from the others. The morning vomiting of alcoholics is to a great extent caused by œsophageal catarrh.

Treatment.—The œsophagitis quickly disappears when the sources of irritation are removed. The patient should become teetotal, and all septic foci in the mouth and pharynx should be treated.

B. Acid Œsophagitis and Ulcer

(*a*) *Acute Acid Œsophagitis and Œsophageal Ulcer*

Ætiology and Pathology.—Acute peptic œsophagitis and œsophageal ulceration occur at all ages; the latter is one of the causes of fatal hæmatemesis and melæna in infants. It is always a sequel of severe vomiting in an enfeebled individual with low resistance. The acid gastric contents are retained in the œsophagus just above the closed cardiac sphincter, where their irritant action gives rise to inflammation, the lower end of the œsophagus being generally alone involved. In most cases the acute œsophagitis is associated with the presence of one or more acute ulcers just above the sphincter.

The majority of cases follow post-operative vomiting. Less frequently they result from the vomiting caused by pyloric obstruction secondary to a chronic gastric or duodenal ulcer. In one of my patients acute œsophagitis followed prolonged sea-sickness.

Symptoms.—The most common symptom of acute œsophageal ulcer is hæmatemesis. It may begin between 24 and 48 hours after an operation which has been followed by severe vomiting. Heartburn and occasionally a burning pain may be felt behind the lower end of the sternum, especially

on swallowing. The symptoms rarely persist for more than 10 days after an operation, but in other cases they may continue for long periods, though it is doubtful whether a chronic ulcer ever develops from this condition. Death may occur from hæmorrhage or from perforation of an acute ulcer into the pleural cavity, sometimes without any warning symptoms.

Treatment.—The patient should be kept in the erect position and given small feeds of citrated milk every 3 hours. Five minutes after each feed he should drink a few ounces of water.

(*b*) *Chronic Acid Œsophagitis and Œsophageal Ulcer*

Ætiology.—Simple chronic ulcer of the œsophagus was formerly regarded as little more than a pathological curiosity, but a recognition of its clinical features has in recent years shown that it is not uncommon. Since I became familiar with the clinical picture in 1929 I have seen about 20 cases in private patients in comparison with some 350 cases of duodenal and 70 of gastric ulcer. The incidence is greater among men than women; the majority of cases occur between the ages of 50 and 70.

Pathology.—Œsophageal ulcers have all the anatomical characteristics of chronic gastric and duodenal ulcers. In fatal cases heterotopic gastric mucous membrane has sometimes been found in the œsophagus; it probably secretes acid gastric juice, which collects in the lower end of the œsophagus immediately above the closed sphincter, and in course of time an erosion and finally a chronic ulcer develops. The condition is then analogous with the ulcers occasionally found in Meckel's diverticulum, which are always associated with the presence of ectopic gastric mucous membrane. In the majority of cases, however, the ulcer is associated with that form of diaphragmatic hernia of the stomach which is the result of congenital shortness of the œsophagus. For some unknown reason the cardiac sphincter is always relaxed in this condition, and consequently regurgitation of the acid contents of the stomach occurs on lying down and on increasing the intra-abdominal pressure by leaning forward.

Symptoms.—Discomfort or pain, often of a burning character and sometimes described as heartburn, occurs under the lower third of the sternum whilst eating solid food. The pain may also occur on leaning forward and shortly after lying down. It often radiates to the back and occasionally to the left shoulder or left side of the neck. At first the pain lasts for only a few minutes and is relieved by alkalis, but later it is prolonged and the patient may become frightened to eat. The food sometimes appears to stick at the lower end of the œsophagus before passing into the stomach. The spasm which causes the dysphagia sometimes leads to effortless regurgitation of sour material. The pain is relieved by alkalis and can generally be completely prevented by taking only fluid food. Progressive emaciation and anæmia are common in chronic cases. As with chronic gastric and duodenal ulcer, the symptoms at first occur for periods of varying duration with intervals of complete freedom.

Occult blood is always present in the stools. Hæmatemesis, which may be severe but is rarely fatal, is a common complication and may be the earliest symptom. Perforation into the mediastinum, pericardium or peritoneum is rare, but it is a more common cause of death than hæmorrhage. In very

chronic cases a fibrous stricture may develop and lead to more or less complete obstruction.

Hyperchlorhydria is generally present. The clinical picture may be confused by association with a gastric or duodenal ulcer. Excessive salivation is common. This may lead to aerophagy, which occasionally causes severe pain in the left hypochondrium owing to inability to expel the excess of gas from the stomach on account of œsophageal spasm (*aërogastrie bloquée*).

An X-ray examination during the swallowing of a barium emulsion generally shows no abnormality, though the emulsion may be held up by spasm at the lower end of the œsophagus. The œsophagus may be slightly dilated, but there is never anything approaching the characteristic mega-œsophagus caused by achalasia of the cardia. When a semi-solid opaque meal is swallowed, or if the opaque emulsion is swallowed whilst the patient is lying down, a characteristic picture is obtained. This consists of a narrowing caused by spasm near the lower end of the œsophagus; below this is a rounded shadow corresponding with the crater of the ulcer, and below this again is the normal cardiac sphincter, in which two or three longitudinal folds can often be recognised, passing to the stomach, a small portion of which is frequently above the diaphragm and separated from the rest of the stomach by a narrow neck.

It is sometimes advisable to confirm the diagnosis by œsophagoscopy, though occasionally the ulcer itself cannot be reached owing to the spasm just proximal to it. If there is any doubt about the nature of the ulcer, a fragment of its margin should be removed for microscopical examination. The ulcer is always associated with inflammation of the mucous membrane of the lower third of the œsophagus.

Diagnosis.—The diagnosis of peptic œsophageal ulcer must be made from a consideration of the symptoms, as the condition is generally missed in a routine radiological examination. The latter, however, serves to exclude achalasia of the cardia and cancer of the œsophagus, which might be regarded as the cause of the dysphagia, though substernal pain and heartburn are never present in achalasia.

Ulcer of the œsophagus is clinically indistinguishable from acid œsophagitis affecting the lower end of the œsophagus; the latter may be associated with spasm, but no actual ulcer can be recognised either with the X-rays or the œsophagoscope. I have seen two cases in which the œsophagus was divided into three distinct segments by a constant spasm at three different points, which was, however, insufficient to prevent the easy passage of an œsophagoscope.

Treatment.—A patient with œsophageal ulcer should be given a pint of citrated milk and ½ oz. strained orange juice 4 times a day without any of the thick feeds which can be safely used in cases of gastric and duodenal ulcer. He should sit up all day and have the head of his bed raised by blocks so as to prevent stagnation in the lower end of the œsophagus, and he should drink a few ounces of water a quarter of an hour after each feed so as to wash its remains into the stomach. Maximal doses of atropine and a tablespoonful of olive oil should be given a quarter of an hour before each feed in order to overcome spasm. The treatment should be continued until not only all pain and dysphagia have disappeared, but also until the X-rays show no trace of a crater and the occult blood has disappeared from the stools. If the ulcer

does not heal within a couple of months, or if, when first seen, much cicatricial narrowing with secondary stasis in the œsophagus is present, a gastrostomy should be performed without further delay. When the ulcer has completely healed, any stenosis which may be present should be treated by dilatation with graduated bougies (*infra*).

In peptic œsophagitis without ulceration the spasm can generally be quickly overcome by the passage of graduated mercury bougies. The patient should be dieted as if he had an œsophageal ulcer, but much less prolonged treatment is required.

NON-MALIGNANT STRICTURE

Ætiology.—Stricture of the œsophagus is in rare cases congenital; the middle part of the œsophagus may be represented by a fibrous cord, or the lower part may open into the trachea or into one of the bronchi. It may also be a sequel of the acute œsophagitis resulting from caustic poisoning or the impaction of a foreign body and of the healing of a chronic ulcer just above the cardiac sphincter.

Treatment.—Fibrous strictures must be dilated by the passage of bougies of gradually increasing size. They should be guided into the stomach by a piece of string, previously swallowed, threaded through a metal slide at their lower end. There is a constant tendency to recur, so a mercury bougie must be passed at regular intervals. In acquired cases in which the origin is obscure, the Wassermann reaction should be tested; if it is positive, anti-syphilitic treatment may produce much improvement, though dilatation by bougies is generally required as well.

CANCER OF THE ŒSOPHAGUS

Ætiology.—Cancer of the œsophagus occurs with about one-third the frequency of cancer of the stomach. Over 70 per cent. of all cases occur in men, but 80 per cent. of upper œsophageal growths occur in women (p. 547). Among 100 cases of cancer occurring in the alcohol trades (barmen, cellarmen, waiters and brewers) about 15 affect the œsophagus compared with 7 in men working in other trades, showing that the chronic œsophagitis caused by excessive indulgence in alcohol is a predisposing cause of cancer of the œsophagus.

Pathology.—Most growths of the œsophagus are epitheliomata. They are most common in the lower end and then at the level of the bifurcation of the trachea, these being the narrowest parts, the mucous membrane being consequently most subjected to friction by coarse food. Less frequently they occur at the upper end of the œsophagus; it is then impossible to say whether an epithelioma is a primary growth of the pharynx, from which it has spread into the œsophagus, or a primary growth of the œsophagus which has spread into the pharynx. Ulceration occurs at an early stage. Accumulation of food in the œsophagus above the obstruction leads to progressive dilatation, and the efforts of the œsophageal musculature to overcome the obstruction results

in hypertrophy, but the dilatation and hypertrophy are comparatively slight except in cancer of the lower end, as when the obstruction is higher up, vomiting occurs so quickly that very little food can accumulate.

Symptoms.—Dysphagia is almost always present, and is the first symptom in a large majority of cases. Most frequently a patient in perfect health one day experiences a slight discomfort on swallowing; soon he notices that his food seems to stick for a moment before passing on into his stomach. The difficulty becomes slowly but steadily more marked, with rare intermissions lasting for a few meals or at most for a few days. The patient often manages to swallow his food by chewing more thoroughly, by taking smaller mouthfuls, and by drinking after each mouthful; but more and more effort is required, until after a period, which is generally between 1 to 4 months but may be as long as a year, solid food ceases to pass at all and is regurgitated into the mouth a few seconds later. The patient generally localises the position of obstruction correctly, but owing to a protective reflex spasm or achalasia of the pharyngo-œsophageal sphincter he sometimes thinks that it is in the upper end when it is really in the lower third. The difficulty in swallowing continues, until after an average of 8 months there is complete obstruction to the passage of fluids as well as solids.

Pain occurs in only 40 per cent. of cases; it is most frequently absent when the growth is in the lowest third of the œsophagus. It occasionally begins a few days before or simultaneously with the dysphagia, but more commonly it is not noticed until the latter has been present for 1 or 2 months. The pain may be present only during deglutition, disappearing as soon as the food passes the obstruction. It is situated at the level of the obstruction and often passes through to the back.

Regurgitation of food almost always occurs sooner or later; it generally begins between 1 and 2 months after the onset of symptoms and is rarely delayed as long as 6 months. When the growth is situated in the upper third of the œsophagus the food is violently ejected out of the mouth or even from the nose after a coughing effort. When the middle or lower third is involved, the food regurgitates without effort into the mouth, often immediately after meals. If the œsophagus is dilated, food may be regurgitated any time up to 2 hours after being swallowed. The food is completely undigested and always contains mucous saliva, often in considerable quantity. Regurgitation of saliva alone occurs when the obstruction is sufficient to interfere with the swallowing of fluid as well as of solid food. Salivation may be continuous. The regurgitation of the contents of the dilated œsophagus gives relief to any discomfort or pain which is present at the time. The regurgitated material sometimes contains blood and pus, and may be very foul; occasionally several ounces and, in rare cases, a large quantity of blood is vomited.

Progressive emaciation occurs owing to the small amount of food which is taken, and when obstruction is complete the loss of weight is very rapid. The appetite may remain good, and hunger may be very distressing in the early stages, but this becomes less marked as the disease progresses. Severe thirst with dryness of the mouth is sometimes present, and fetid breath is common when there is extensive ulceration. In the late stages small hard glands are often felt in the neck, especially just above the inner end of the clavicle and beneath the lower jaw.

The vagus or recurrent laryngeal nerves, especially of the left side, may be involved, and one, or rarely both, vocal cords may consequently be paralysed. Pressure on the cervical sympathetic may cause contraction of the pupil with slight enophthalmos and narrowing of the palpebral fissure on the affected side. Compression of the trachea or the main bronchi by the tumour or by secondary glands may cause hoarseness, coughing and dyspnœa. Perforation into the trachea or a bronchus gives rise to a paroxysm of coughing and dyspnœa whenever food is swallowed, and death from broncho-pneumonia or gangrene of the lung is likely to occur. Perforation into the pleural cavity may produce an empyema, but a serous pleural effusion may develop without perforation.

Diagnosis.—In a large proportion of cases it is possible to make a definite diagnosis from the history and from the information obtained with the X-rays, which should always be used without delay in cases of dysphagia. Before giving the opaque meal the thorax should be examined from every direction in order to exclude an aneurysm, although in the very rare cases in which this causes dysphagia other more characteristic symptoms generally make the diagnosis clear. Occasionally a growth of the œsophagus or secondary glands throw a shadow with the X-rays, but this is rarely obvious until the symptoms have been present for a considerable time. With an opaque meal the X-rays show the position and length of any narrowing of the lumen of the œsophagus, the degree of dilatation above the obstruction and the amount of obstruction, but the latter may be in part caused by spasm. In the earliest stages, when the lumen is not much reduced, the semi-fluid opaque meal may pass down without revealing any abnormality. Some ordinary food which is known to cause pain or difficulty should then be swallowed with the opaque fluid; spasm is induced and the position and extent of the growth can be clearly recognised.

The diagnosis of a growth of the cardia from achalasia has already been considered (p. 549). The presence of hard glands in the neck makes the diagnosis of cancer extremely probable. In the rare cases in which the history and the X-rays leave the diagnosis in doubt, and especially in early cases, an examination should be made with the œsophagoscope, by means of which the nature of the obstruction can generally be recognised, and a fragment removed for biopsy, though failure to detect malignant disease in the excised fragment does not exclude the possibility of cancer.

There may be considerable difficulty in diagnosing between an epithelioma of the lower end of the œsophagus, which spreads upwards, but very rarely downwards into the stomach, and a primary carcinoma of the fundus of the stomach, which almost invariably involves the cardiac orifice sooner or later. With the former the dysphagia is the first symptom; with the latter anorexia, pain after food, loss of weight and strength, vomiting and increasing pallor may appear before the dysphagia, but this is not always the case, as dysphagia may be the only symptom. When the tumour is gastric in origin the X-rays show a filling defect, together with irregularity of the folds of mucous membrane and encroachment on the transparent arc which is normally formed by the gas in the fundus, and sooner or later a mass can be felt high up under the left costal margin.

Prognosis.—Death occurs between 2½ months and 2½ years after the onset of symptoms, the most common period being between 6 and 12 months.

It is most frequently due to broncho-pneumonia, exhaustion from starvation being the next most common cause.

Treatment.—The radical treatment of cancer of the œsophagus by excision of the growth has very rarely been successful. In recent years great advances have been made in treatment by radiotherapy. Though I have not seen any cases which could be regarded as cured, dysphagia has completely disappeared and the patient has been able to eat ordinary food and lead an active life for many months. Two different methods may be tried, and in some cases when the symptoms return after one the other can be safely used. The first is by means of maximal doses of deep X-rays given from different angles. The usual dosage is much too small, but when only just insufficient to produce anæmia and burning of the skin is given, rapid improvement follows. The other method is by the direct implantation of radon seeds through an œsophagoscope. When the growth is so long that the lower end cannot be reached, additional seeds can be implanted from below through an œsophagoscope introduced through an opening in the stomach.

With the modern forms of radiotherapy it is now rarely necessary to insert tubes, but if obstruction in the middle of the œsophagus is not overcome, a spiral metal tube should be introduced through an œsophagoscope, if necessary after preliminary dilatation of the stricture by bougies. Its lower end reaches beyond the growth, whilst the upper funnel-shaped end rests on its proximal margin. The tube can be left *in situ* until the end, but it sometimes leads to so much dilatation that it passes through the obstruction and is expelled *per anum*.

So long as any obstruction is present the food should be semi-fluid or fluid, and should be taken in small quantities at frequent intervals. Some patients are able to swallow raw eggs whole. As large a dose of atropine as possible short of producing unpleasant symptoms given half an hour before each feed and a dessertspoonful of olive oil just before often help its passage through the stricture.

Gastrostomy is required only in the comparatively rare cases in which sudden complete obstruction occurs before there has been time for radiotherapy to be applied and a tube cannot be introduced owing to the growth being at the upper or lower extremity of the œsophagus.

ARTHUR F. HURST.

DISEASES OF THE STOMACH

INTRODUCTION

I. FUNCTIONS OF THE STOMACH

Until recently little attention was paid to any of the functions of the stomach except that concerned with the digestion of proteins. It is now realised that several other functions are of equal or even greater importance from a clinical point of view.

(*a*) *Digestion.*—The pepsin of the gastric juice digests proteins in the presence of free hydrochloric acid. Its activity rapidly falls when the amount of free acid present sinks below 0·08 per cent. until it finally ceases in complete achlorhydria, even if hydrochloric acid is still present in organic combination. In spite of this digestion of proteins remains unimpaired in achlorhydria, as the trypsin of the pancreatic juice is capable by itself of digesting all the proteins consumed in ordinary meals. An increase in the free hydrochloric acid above the average normal does not lead to any increase in peptic activity.

(*b*) *Protection of the small intestine from injury.*—An important function of the stomach is to protect the small intestine from thermal, chemical and mechanical irritants. Very hot and very cold food and drink are brought to the body temperature; the gastric juice dilutes chemical irritants, such as alcohol, and softens hard particles, and the churning movements in the pyloric vestibule break up lumps of insufficiently chewed food. At the same time the stomach, like all other mucous membranes, attempts to protect its own mucous membrane from damage by secreting mucus in response to stimulation by chemical and mechanical irritants.

(*c*) *The antiseptic acid barrier of the stomach.*—The free hydrochloric acid of the gastric juice is a very efficient germicide and rapidly destroys streptococci swallowed from the mouth, throat and nose, as well as organisms present in contaminated food and drink, such as those of typhoid fever and bacillary and amœbic dysentery. It also helps to keep the reaction of the small intestine at a level which prevents its invasion by *B. coli* from the lower ileum and colon.

(*d*) *Influence on the blood and spinal cord.*—The gastric juice contains an enzyme, hæmopoietin, the "intrinsic factor" of Castle, which acts on something present in protein food, the "extrinsic factor," to produce a substance which is stored in the liver and is the normal stimulant for the formation of red corpuscles by the bone marrow. It is produced by the glands of the pyloric end of the stomach and the duodenum, but not by those of the body of the stomach, the chief and parietal (oxyntic) cells of which secrete pepsin and hydrochloric acid respectively. The gastric juice also contains an enzyme, neuropoietin, which is produced by the same glands and acts in the same way as hæmopoietin to form a substance which is essential for the nutrition of the central nervous system.

The presence of free hydrochloric acid helps the conversion of the iron contained in food into a form in which it is easily absorbed so as to become available for the production of hæmoglobin.

II. GASTRIC DIATHESES

The anatomy and physiology of the stomach of 80 per cent. of healthy people are so well adjusted to the exigencies of ordinary life that they are likely to reach old age without ever suffering from any chronic gastric disorder. Of the remaining 20 per cent. approximately one-half are born with a *hypersthenic gastric diathesis*, and most of the other half are born with a *hyposthenic gastric diathesis*, both of which are often familial. The former have hyperchlorhydria, which is often, though not invariably, associated with a short, high, rapidly emptying stomach. The latter have hypochlor-

hydria, which is generally associated with a long, low, slowly emptying stomach. Both constitutions are compatible with perfect health, but under unfavourable conditions each predisposes to the development of special symptoms and special organic diseases. The hypersthenic stomach is capable of secreting very little mucus compared with the hyposthenic stomach, whether in response to mechanical, thermal and chemical irritants or as a result of gastritis.

Complete achlorhydria is present in about 3·5 per cent. of healthy children and young adults of both sexes, but it is still uncertain whether this is congenital and a result of an inborn error of secretion—a true constitutional achylia, or whether it is acquired as a sequel of gastro-enteritis or some general infection in infants or young children with an extreme degree of constitutional hypochlorhydria.

III. CAUSES OF GASTRIC DISORDERS

A.—Organic

(i) *Mechanical, chemical and thermal irritants.*—The mouth acts as the first line of defence in protecting the alimentary tract from damage by swallowed irritants. Food and drink are brought to the body temperature, chemical irritants are diluted, lumps of food are broken up by chewing and are intimately mixed with saliva, which softens hard particles and coats insoluble ones with mucus. A man with good and sufficient teeth, who takes the trouble to use them and avoids grossly indigestible food and excess of alcohol, need not swallow anything until its thermal, chemical and mechanical properties have been so altered that it will cause no irritation when it comes into contact with the gastric mucous membrane. But many people bolt their food before it has been thoroughly masticated, whilst others have insufficient teeth and inadequate dentures, with the result that the stomach is daily subjected to mechanical, chemical and thermal irritants. It is also often damaged by excessive indulgence in alcohol, and especially by taking cocktails and spirits whilst fasting, when even a small quantity acts as a powerful irritant. Strong tea and coffee, mustard, pepper, curry, pickles, and excess of totally indigestible raw vegetable matter, taken in the mistaken idea that plenty of "roughage" is good for the health, may have the same effect. The stomach is frequently irritated by the unconscious swallowing of the "juice" of tobacco smoked in excess, especially when the stomach is empty. Many people injure their gastric mucous membrane by taking drugs, often quite needlessly, for supposed constipation, rheumatism, and other self-diagnosed complaints, quite apart from those used in the treatment of definite chronic maladies, such as aspirin, bromides, iodides, digitalis, mercury, creosote and quinine. The contents of the duodenum act as irritants when introduced into the stomach; gastritis is consequently a frequent sequel of gastro-jejunostomy and partial gastrectomy.

I have already described how the stomach acts as a second line of defence for protecting the small intestine from mechanical and chemical irritation. But it is itself liable to suffer in the attempt in spite of the mucus it secretes with the object of protecting itself from damage, especially if the first line of defence is deficient owing to bolting of food or inadequate teeth. In the

80 per cent. of people with an average type of stomach it generally proves successful. In the 10 per cent. with constitutional hypochlorhydria and achylia the second line of defence is deficient; they are consequently very likely to develop gastritis and in most cases the hypochlorhydria sooner or later gives place to achlorhydria. In the 10 per cent. with hyperchlorhydria there is ample protection against mechanical irritants, and also against chemical irritants if taken when the stomach is full. But as hyperchlorhydria is generally associated with rapid evacuation, the stomach is empty for a much larger proportion of the day and night than in the average individual, so that there is more opportunity for the mucous membrane to be damaged by alcohol, tobacco and drugs. When gastritis has once developed in an individual with constitutional hyperchlorhydria, the abnormally vulnerable mucous membrane is likely to be further irritated by the excessive acidity of the gastric juice, which is completely without effect on the normal gastric mucous membrane.

(ii) *Infection.*—Infected material is constantly swallowed by people with pyorrhœa alveolaris, infected tonsils, chronic pharyngitis and sinusitis, and by children with adenoids. In achlorhydria the antiseptic acid barrier of the stomach is lost, and streptococci from the mouth invade the stomach and irritant toxins are likely to form in the gastric contents. When gastric juice is secreted in normal or excessive quantities, and even when it is deficient in hypochlorhydria, swallowed bacteria are rapidly destroyed. When hyperchlorhydria is associated with a rapidly emptying stomach, the unconscious swallowing of infected material from the mouth, nose and throat may infect an erosion or ulcer of the gastric or duodenal mucous membrane during the many hours in which it is not protected by the presence of gastric juice.

(iii) *Hæmatogenous irritants.*—Many acute infections may be accompanied by acute gastritis, which is often followed by chronic gastritis. The gastritis is due mainly to the direct action of bacterial toxins conveyed in the blood to the gastric mucous membrane, which perhaps makes an attempt to excrete them. Possibly the toxins produced in the body tissues themselves in acute infections may be in part responsible, just as the toxins of uræmia and those produced in the skin in extensive burns may cause gastro-duodenitis and acute ulcers. The abdominal symptoms in gastric influenza are the result of acute gastritis, and acute ulcers and erosions are common in the stomach and duodenum in fatal cases of a great variety of infections.

The causes of gastritis are so numerous and so common that few people can pass through life without being subjected to one or more of them. The 80 per cent. of individuals with the average normal stomach are so well protected that they are less liable to develop gastritis as a result of these insults, but probably few of those with constitutional hyperchlorhydria and constitutional hypochlorhydria escape.

B.—Functional

Exhaustion from physical or mental overwork, insufficient sleep, prolonged residence in the tropics, insufficient food, and from the toxæmia of chronic infections, such as phthisis, and acute infections, such as influenza, has a depressing effect on all bodily functions and at the same time it tends to increase the

irritability of the visceral nervous system. This *faiblesse irritable* gives rise to symptoms in an organ, the physiological and anatomical functions of which are less efficient than the average. Consequently it is only individuals with the hypersthenic and hyposthenic gastric diatheses who are likely to develop gastric symptoms as a result of exhaustion. Their symptoms are then very similar in character to those produced by the organic diseases which may be associated with these diatheses.

Depressing emotions and the psychological factors concerned in the production of the anxiety neuroses may also give rise to similar gastric symptoms in the predisposed. They may also be important factors in the actual development of organic diseases, especially gastric and duodenal ulcer. Anxiety is a common cause of recurrences and of the sudden increased activity of ulceration which may result in hæmorrhage or perforation.

C.—Reflex

Disorders of other abdominal organs may give rise to reflex gastric symptoms in individuals with the hypersthenic gastric diathesis and, less frequently, in those with the hyposthenic gastric diathesis. Thus chronic cholecystitis, recurrent subacute appendicitis, diseases of the colon and even simple constipation may give rise to reflex gastric symptoms.

IV. EFFECT OF GASTRITIS ON GASTRIC SECRETION

The functional activity of an organ is always reduced when it is inflamed. At the onset of acute gastritis no gastric juice is secreted. In chronic gastritis the secretion is reduced to an extent which varies with the severity and the duration of the inflammation, the actual amount of free acid present in the stomach in a test-meal depending upon the constitutional type of stomach in each individual. Thus the hyperchlorhydria of individuals with the hypersthenic gastric diathesis becomes less extreme or may be replaced by a normal curve of acidity or even, in exceptional cases, by hypochlorhydria. This is well seen in the gastritis accompanying chronic ulcer: when medical treatment has resulted in the healing of the ulcer and the disappearance of the gastritis, the acidity is almost always higher than it was before.

The hypochlorhydria of individuals with the hyposthenic gastric diathesis is in most cases eventually replaced by complete achlorhydria, which can generally be overcome by treatment (p. 585). The reduction in acidity in these cases is mainly due, as it is in hyperchlorhydria, to the effect of the inflammation on the activity of the secreting glands, but it is increased as a result of the excessive secretion of mucus which accompanies the inflammation. The mucus acts partly by its mechanical action in blocking the mouths of the secreting tubules and partly by its chemical action in combining with some of the free acid. The neutralising effect is, however, slight and due almost entirely to the sodium bicarbonate it contains and not to its own buffer action, as it almost completely disappears after the salt has been separated by dialysis. When free acid does not return as a result of treatment the gastritis has presumably led to a profound degree of atrophy of the gastric mucosa.

It is clear that gastritis associated with high or normal acidity, so-called

acid gastritis, is not an early stage of gastritis associated with achlorhydria, nor is the former a result of prepyloric gastritis and the latter of fundus gastritis. Both are due to the same causes, the amount of free acid present depending upon the constitution of the individual concerned.

V. RESULTS OF HYPERCHLORHYDRIA

I have already pointed out that hyperchlorhydria tends to protect the stomach from irritation when the first line of defence is inadequate. But the deleterious effect of friction on the mucous membrane of the distal half of the stomach when hard or large pieces of food are swallowed continues, and irritation by alcohol, tobacco and drugs may occur during the many hours in which the stomach is empty. If even a mild degree of gastritis is produced as a result of this, the mere presence of hyperchlorhydria is likely to aggravate it, as, although hyperchlorhydria is not itself a pathological condition, the excessive acidity of the gastric juice is a potential danger. The healthy mucous membrane is always bathed in gastric juice and is neither digested by its pepsin nor irritated by its free hydrochloric acid. After death, however, the mucous membrane is rapidly digested. During life localised necrotic areas may also undergo digestion, and this may perhaps also occur in areas in which the circulation is temporarily arrested or very deficient before actual necrosis has occurred. As peptic digestion is no more active with 0·3 per cent. than with 0·08 per cent. free hydrochloric acid, such digestion is not specially likely to occur in the presence of hyperchlorhydria. But although the living mucous membrane even when abnormally vulnerable as a result of gastritis can never undergo peptic digestion, it is very likely to be damaged by free hydrochloric acid if present in a strength greater than the average. The likelihood of this is still greater when the hyperchlorhydria is associated with hypersecretion, as unusually strong acid continues to be secreted in the absence of food, which under ordinary conditions dilutes it and partially neutralises it. In the extreme forms of constitutional hyperchlorhydria the stomach secretes acid throughout the night, so that undiluted gastric juice comes into contact with the mucous membrane of the stomach and duodenal bulb for 9 or 10 hours. Moreover, owing to the deficient power of secreting mucus, which is a characteristic of the hypersthenic stomach, the protection against damage afforded by a layer of mucus in the hyposthenic stomach is absent. In the conditions already described, in which the failure of the first line of defence gives rise to chronic gastritis, the excessive acid in hyperchlorhydria gives the gastritis certain characteristics which are absent from that associated with hypochlorhydria and achlorhydria. Biopsies and gastroscopic investigations have shown that it is very frequently associated with minute erosions, some of which may develop into acute ulcers, which may in turn become chronic ulcers. The condition may therefore be called ulcerative gastritis. When the hyperchlorhydria is associated with the rapidly emptying, short, high stomach, which is often a feature of the hypersthenic gastric diathesis, the duodenal bulb is equally involved, the condition thus being one of ulcerative gastro-duodenitis, in which a chronic ulcer is most likely to develop in the duodenum. When, on the other hand, the hyperchlorhydria is associated with a long, low, slowly emptying stomach, the main stress falls upon the stomach : the gastritis is likely to be more severe

and a gastric ulcer may develop, whilst the duodenum is spared. At the same time the gastric stasis leads to more prolonged contact of the entire gastric mucous membrane with any irritants it may contain, so that, although the distal half of the stomach is still the part most severely inflamed, the fundus is more affected than with a rapidly emptying stomach. Consequently the power of secreting acid by the fundus glands may be directly impaired and their stimulation may be reduced owing to the deficient production of the gastric hormone by the antral mucous membrane in response to chemical stimulation. In gastric ulcer the hyperchlorhydria which is at first present thus tends to be more or less reduced, and in very chronic cases hypochlorhydria, and in rare cases even achlorhydria, may result. With treatment, however, the acidity always rises, though sufficient permanent damage may have taken place to prevent a return to the original hyperchlorhydria.

Owing to the familial incidence of the hypersthenic gastric diathesis, it is common for gastric or duodenal ulcers to occur in several members of the same family.

Chronic gastric or duodenal ulcers or scars of such ulcers are found in about 10 per cent. of all autopsies, this being also approximately the number of healthy young adults with hyperchlorhydria. It would appear, therefore, that an individual with the hypersthenic gastric diathesis is almost certain sooner or later to develop an ulcer. It is true that hyperchlorhydria may no longer be present when a test-meal is given, especially in the case of a gastric ulcer, but it was probably present when the ulcer first formed, perhaps many years earlier, and has since been masked by the coexistent chronic gastritis.

VI. RESULTS OF HYPOCHLORHYDRIA AND ACHLORHYDRIA

The incidence of achlorhydria among healthy people rises from 4 per cent. at the age of 20 (Bennet and Ryle), to 8 per cent. in the 30–39 period, and 12 per cent. in the 40–49 period, but in the next three decades taken together there is a further rise of only about 4 per cent. It can thus be concluded that all or very nearly all of the individuals with the hyposthenic gastric diathesis as well as a few with normal acidity eventually develop achlorhydria as a result of gastritis.

Gastritis with achlorhydria generally gives rise to no gastric symptoms, though it may occasionally produce a mild form of chronic indigestion, and it is a not uncommon cause of nausea.

In achlorhydria the excess of mucus is a poor substitute for gastric juice, and the consequent loss of the second line of defence leads to irritation of the small intestine, so that duodenitis and enteritis develop in addition to the gastritis. The mechanical and chemical irritation of the intestines explains why achlorhydria is a common cause of chronic and recurrent diarrhœa.

Swallowed bacteria flourish in the alkaline contents of the stomach and pass into the duodenum, which is normally sterile, but now swarms with bacteria. The increased alkalinity of the intestinal contents allows bacteria which are normally confined to the colon to ascend the small intestine as far

as the duodenum and stomach, both of which contain colon bacilli from the large intestine even more frequently than streptococci from the mouth.

Chronic cholecystitis is generally a result of a *B. coli* infection which ascends from the duodenum by way of the common bile duct and cystic duct to the gall-bladder. This is especially likely to occur when achlorhydria is present. As gall-stones are generally secondary to cholecystitis, it is not surprising that achlorhydria occurs in about 50 per cent. of cases.

Achlorhydria is also a very important predisposing cause of intestinal infections, such as typhoid and paratyphoid fever, bacillary and amœbic dysentery and cholera, the organisms of which are rapidly destroyed by the normal gastric juice, and its presence is therefore a constant source of danger in individuals residing in tropical countries.

The toxæmia which follows the intestinal infection resulting from achlorhydria is one factor in about 35 per cent. of cases of rheumatoid arthritis and in some cases of asthma, skin diseases and other conditions associated with allergy, especially in children. Flushing of the face during meals is common in achlorhydria, and achlorhydria or hypochlorhydria is generally present in rosacea.

VII. EFFECTS OF GASTRITIS ON HÆMATOPOIESIS AND THE NUTRITION OF THE CENTRAL NERVOUS SYSTEM

The absence of free acid from the gastric contents in achlorhydric chronic gastritis and the enteritis with which it is often associated may interfere with the assimilation of the iron in food, so that in individuals who take a diet, in which there is only just enough iron for the needs of the body under the most favourable conditions, a simple achlorhydric anæmia develops, which differs from pernicious anæmia in occurring almost exclusively in women and in being curable by large doses of iron, whilst liver and stomach extract are entirely without effect.

Achlorhydria is found in about 99 per cent. of cases of pernicious anæmia and of subacute combined degeneration of the spinal cord, though it is not the actual cause of it, the absence of hydrochloric acid from the gastric secretion being associated with the absence of the hæmopoietin and neuropoietin, required for the production of the natural stimulant of hæmatopoiesis, and of the substance required for the normal nutrition of the central nervous system respectively. The gastritis is the primary condition; there is consequently often a history of chronic diarrhœa or other symptoms to which it has given rise dating from months or years before the onset of anæmia or nervous symptoms, and in several cases the achlorhydria has been known to exist during this time. The frequent occurrence of pernicious anæmia and subacute combined degeneration of the cord in more than one member of a family is due to the familial occurrence of constitutional achylia gastrica and hypochlorhydria, which may depend upon a primary atrophy of the gastric mucosa. Moreover, achylia is often present without any abnormality of the blood or central nervous system in relatives of patients with these diseases.

The first function of the gastric mucous membrane to suffer in gastritis is the secretion of hydrochloric acid. Consequently in the majority of cases of achlorhydria pepsin is still secreted in normal quantity, the secretion

of mucus is actually increased, and the production of hæmopoietin and neuropoietin is unimpaired. If the exciting cause of the gastritis continues to be at work when complete achlorhydria has developed, the gastritis becomes progressively more severe. After a time the damage to the secreting tubules is so severe that they can never recover their power of secreting acid, even if all active inflammation ceases, and at the same time the secretion of pepsin becomes more or less impaired. The mucus-secreting cells take part in the general atrophic changes of the mucous membrane, so that mucus disappears from the test-meal, its absence being a sign of the severity of the process and not an indication that no gastritis is present. In this advanced stage of gastritis the production of the intrinsic factors required for the normal activity of the bone-marrow and nutrition of the central nervous system, hæmopoietin and neuropoietin, may cease to be formed, and pernicious anæmia or subacute combined degeneration of the cord develops. In a small number of cases this function of the mucous membrane is impaired at an earlier stage; thus in three of my cases of pernicious anæmia the secretion of free acid returned as a result of treatment of the gastritis, and in 1 per cent. of cases pernicious anæmia and subacute combined degeneration of the cord develop whilst free hydrochloric acid is still being secreted.

The hæmatopoietic and neurotrophic functions of the gastric mucous membrane are occasionally destroyed suddenly by an exceptionally severe attack of acute gastritis, the symptoms dating from an attack of food poisoning or an acute infection. Complete and partial gastrectomy, and very rarely the gastritis following gastro-jejunostomy, may have the same effect.

EXAMINATION OF THE STOMACH

I. Motor Functions

(*a*) *Size, shape and position.*—Inspection of the abdomen may reveal the outline of the stomach in thin patients, especially is pyloric obstruction has led to excessive peristalsis. By palpation under similar circumstances the lower border of the stomach can often be felt. Palpation may also reveal the presence of a tumour, the size, shape, position and mobility of which should be estimated. Percussion may give some idea as to the quantity of gas in the stomach, but it cannot help in the determination of its size, shape or position. Auscultatory percussion and friction have been shown by means of the X-rays to be quite valueless for examining the stomach.

The size, shape and position of the stomach can be readily and accurately determined, both in the vertical and horizontal position, by means of the X-rays after a meal of strained gruel containing 4 ounces of barium sulphate. By palpation during the screen examination its mobility can be investigated and the presence of adhesions and areas of tenderness recognised.

(*b*) *Tone.*—Splashing and succussion can be obtained in an individual with relaxed abdominal muscles and a stomach with normal tone. They give no information as to the presence of deficient tone.

Owing to the adaptation of the stomach to the volume of its contents, there is little difference in the upper level of the semi-fluid chyme as seen with the X-rays in the erect position whether the volume is 5 ounces or 2 pints,

and the greater curvature is only slightly depressed as the stomach is gradually filled. When the stomach is hypotonic, this adaptation to the volume of its contents does not occur; the food drops to the most dependent part, the upper level of the contents slowly rising and the greater curvature becoming more dependent as the volume increases. It is important to distinguish this condition from the distension without hypotonus caused by the constant presence of fluid or fluid and food in the stomach when the pylorus is obstructed. The opaque meal then appears to fall to the bottom of a large stomach, but closer investigation shows that it is really falling through a large quantity of fluid already present in the stomach, the upper limit of which can be recognised at the normal distance below the diaphragm. If the examination is repeated after emptying the stomach by means of a stomach tube, its tone and size are found to be normal.

(*c*) *Peristalsis.*—In unusually thin women normal peristalsis is occasionally visible, but in the majority of cases the presence of visible peristalsis indicates organic pyloric obstruction. The patient should be examined immediately after a meal; in doubtful cases peristalsis can be rendered more obvious by massage. At a stage preceding that in which peristalsis is visible, it may sometimes be felt as a periodic hardening if the hand is kept for some time gently pressing upon the right side of the abdomen a little above the umbilicus.

In pyloric obstruction the peristaltic waves can be seen with the X-rays to arise in the fundus instead of in the centre of the stomach and to be unusually deep at a period considerably earlier than that in which they become visible through the abdominal wall. Reversed peristalsis generally indicates organic pyloric obstruction, but I have seen it in cases of lesser curvature ulcer with gastric stasis but no obstruction. Irregular peristalsis, and especially peristalsis which begins in the normal position but disappears and perhaps reappears as it passes along the greater curvature before the pylorus is reached, is very suggestive of malignant infiltration.

(*d*) *Rate of evacuation.*—If splashing can be produced by palpation over the stomach at a time when it should be empty, gastric stasis is probably present. But there are so many possible fallacies that this is of very little value compared with the accurate results obtained with the stomach tube and X-rays. Nothing should be eaten or drunk during the 12 hours preceding a test-meal. The stomach should be completely emptied after the tube has been swallowed before the meal is given. In normal individuals it is uncommon for more than 25 c.c. of colourless or bile-stained gastric juice to be found; the reaction for starch is negative, no gross food residue is present, and even microscopically no meat fibres and only occasionally a little vegetable debris, together with a few leucocytes and bacteria derived from the mouth, are seen. In chronic gastritis a small quantity of thick alkaline fluid, consisting of gastric mucus with swallowed saliva and pharyngeal and œsophageal secretion, is present. In the continuous secretion which results from an ulcer near the pylorus, even in the absence of organic obstruction, a varying quantity of very acid fluid without any food residue is found. When an ulcer has led to organic obstruction, starch granules and vegetable debris, but no meat fibres, are present, in addition to some acid fluid containing starch; the quantity of fluid is much increased if the ulcer is still active, as hypersecretion then occurs in addition to stasis. In malignant obstruction

the gastric contents are thicker and contain debris of both vegetable and animal food; free hydrochloric acid is absent, and lactic acid, together with many bacteria, are present.

If the test-meal is completely evacuated in less than three hours, no organic obstruction can be present. If starch is still present in the 3-hour fraction, the stomach should be completely emptied: a further estimate of the degree of gastric stasis can be made from the volume of starch-containing fluid obtained.

Careful examination with the X-rays before the opaque meal is given may show that a considerable quantity of fluid is present in the fasting stomach; its upper horizontal level can be seen under the gas in the fundus, and splashing can be observed if the patient shakes himself. If the shadow of the stomach is still visible 6 hours after a barium meal, nothing having been taken in the interval, stasis is present; after 9 hours it is probably, after 12 hours it is almost certainly, due to pyloric obstruction.

It is important to remember in connection with both the test-meal and the X-rays that if the patient has a severe headache at the time, any delay in evacuation may be due to the complete cessation of peristalsis which occurs during an attack of migraine.

II. Chemical Functions

The chemical functions of the stomach can only be adequately investigated by means of a test-meal. The old-fashioned test-breakfast is less satisfactory than the modern fractional test-meal, which provides information respecting quantity and character of the resting-juice and post-prandial secretion, the secretory response throughout the period of gastric digestion, the secretion of mucus, the regurgitation of bile and duodenal contents. The patient, who should have taken no food since the previous night, swallows the tube (the best form being Ryle's modification of that introduced by Einhorn) in the morning. The resting-juice is withdrawn and measured, its bile and mucus content noted, and the free and total acidity determined; the presence of gross food residue or a positive starch reaction is diagnostic of pyloric obstruction. After withdrawal of the resting-juice the patient drinks one pint of oatmeal gruel, and small specimens of gastric contents are withdrawn with a syringe at intervals of a quarter of an hour until the stomach is empty. If starch is still present at the end of three hours the stomach is emptied, the volume obtained is measured, and the tube is withdrawn. The free and total acidity in each specimen is estimated. Topfer solution and phenolphthalein being the respective indicators customarily employed. The time of disappearance of the starch, which may precede complete emptying, is determined by adding iodine to the successive samples. The free and total acidity are plotted as curves upon a chart.

If achlorhydria is present, the resting-juice may be examined for lactic acid by Uffelman's reagent (30 c.c. 1 per cent. carbolic acid with a few drops of ferric chloride solution), which it changes from blue to a canary yellow. An ethereal extract of the gastric contents must be used, 5 c.c. of gastric contents being shaken with 30 c.c. of ether.

Microscopical examination of the resting-juice may reveal the presence of red corpuscles. The discovery of leucocytes is only of importance if their

number is obviously in excess of the number present in a specimen of spittle obtained at the same time, or if they reappear without squamous epithelial cells half an hour after thorough lavage. True excess of leucocytes indicates the presence of severe gastritis or carcinoma. When the resting-juice or some or all of the fractions of a test-meal are pink or red owing to the presence of blood, a bleeding ulcer or carcinoma is present. Specks of blood in otherwise blood-free specimens may be due to accidental contamination, but more frequently they indicate an abnormal vulnerability of the mucous membrane such as is present in chronic gastritis.

III. Gastroscopy

The introduction of the flexible gastroscope has removed the dangers from gastroscopy. The instrument can be passed without difficulty in a patient who has been prepared by a preliminary injection of morphine and anæsthetising his pharynx. All parts of the gastric mucous membrane can be inspected with the exception of the fundus and the lesser curvature of the pyloric vestibule.

The chief value of gastroscopy is in the recognition of the different forms of gastritis and of erosions and acute and subacute ulcers, which may cause hæmorrhage, but are never recognisable with the X-rays. It is often helpful in diagnosing the cause of post-operative symptoms when radiology has failed to show anything abnormal, and it affords the only reliable evidence of complete healing of a gastric ulcer (p. 593). It occasionally affords valuable evidence in the early diagnosis of cancer.

Arthur F. Hurst.

FUNCTIONAL DISORDERS OF THE STOMACH

HYPOTONUS: ATONIC DILATATION

The diagnosis of atonic dilatation of the stomach, which is still frequently made, is a survival from pre-radiological days, when it was supposed to be a common sequel of acute infections, malnutrition and neurasthenia. In a hundred consecutive cases of abdominal disorders examined with the X-rays hypotonus was present in six, and in only one of these, in which it was associated with an unusually long stomach, did it have any direct or indirect connection with the symptoms. In no case was it associated with infections, neurasthenia or malnutrition, and in all but one of 15 cases of extreme wasting due to anorexia nervosa (not included in this series) the tone was normal. Severe hypotonus never occurs except as a result of exhaustion of the hypertrophied musculature of the stomach in organic pyloric stenosis.

VOMITING

Ætiology.—(*a*) Central Vomiting.—Vomiting is only rarely under the control of the will. But a person who has vomited a number of times owing to some central, reflex or toxic cause, may suggest to himself that certain

circumstances will invariably cause him to vomit. The hysterical vomiting which results is a common sequel of vomiting due to other causes (p. 578).

Various emotions, especially those of disgust and fear, may result in vomiting, especially in neurotic individuals. It may occur as a result of incidents which subconsciously revive the memory of an emotion which on some particular occasion caused vomiting. Thus a woman who, on one occasion vomited as a result of terror in a railway carriage, subsequently vomited whenever she travelled in a train and after a time in any vehicle, and even in closed places, such as a church, from which she could not readily escape. The vomiting was associated with a vague feeling of fear, but not consciously with the incident which was the primary cause.

Certain organic nervous diseases, such as cerebral tumour and meningitis, are frequently accompanied by vomiting, which may also occur in compression and in concussion caused by injury. This is generally due to increased intracranial pressure, and in cerebral tumour the relief of intracranial pressure by trephining often leads to cessation of vomiting. A mid-cerebellar tumour may give rise to vomiting as a result of direct pressure on the vomiting centre in the floor of the fourth ventricle long before any other symptoms develop.

The vomiting in migraine is also of central origin. The cyclical vomiting of children is generally associated with a family history of migraine and is often followed by true migraine in adult life, but biochemical factors may play an important part in its pathogenesis, as it is generally controlled by the administration of glucose.

Attacks of vomiting, with or without nausea, but unaccompanied by any pain or discomfort in the abdomen, are generally of central origin. This is all the more likely to be the case if they are associated with headache.

(*b*) Reflex Vomiting.—Vomiting may result from a local or central reflex. The former is the most common of all causes of vomiting. It occurs when the gastric mucous membrane is irritated by poisons, whether introduced in the food or resulting from bacterial decomposition. Gassing was a common cause of vomiting in the War of 1914–1918, some of the irritant gas being dissolved in the saliva, which was secreted in excess and then swallowed. Overdistension with food, especially if it occurs rapidly, as when a big meal is bolted, or if it continues for an abnormally long period as a result of pyloric obstruction, has the same effect. In all these cases more or less relief to the local symptoms results from vomiting.

Painful stimulation of any afferent nerves, but particularly those of abdominal viscera, such as occurs in attacks of pain associated with gastric ulcer, in biliary and renal colic, in Dietl's crises, and in intestinal obstruction, often causes vomiting as a result of a central reflex. Tickling the fauces is a common method of inducing vomiting.

Sea-sickness and air-sickness are caused by a reflex arising from excessive stimulation of the semicircular canals. The vomiting in diseases of the ear in which the semicircular canals are directly or indirectly involved, as in Ménière's syndrome, is of similar origin. The vomiting of early pregnancy is probable reflex; when persistent, it is, I believe, always hysterical and curable by psychotherapy (p. 579).

(*c*) Toxic Vomiting.—Some emetics, such as apomorphine, cause vomiting by direct irritation of the vomiting centre. Other emetics, such as warm water containing salt and copper and zinc sulphate, act reflexly from the

stomach and are consequently only effective when they are swallowed, whilst tartar emetic, ipecacuanha and general anæsthetics, act in both ways.

Poisons produced in the body, as in uræmia, hyperthyroidism and Addison's disease, may irritate the vomiting centre. In uræmia, however, the action is partly reflex owing to the excretion into the stomach of toxins which should be excreted by the kidneys and partly a result of increased intracranial pressure. The bacterial toxins in acute infections, especially gastric influenza, often excite vomiting by their irritant action on the gastric mucous membrane. Toxic vomiting differs from central vomiting and some cases of reflex vomiting in being almost invariably preceded by nausea.

The consumption of certain foods to which a predisposed individual is sensitised may give rise to attacks of " abdominal allergy," in which vomiting is often a prominent symptom (*vide* p. 751).

Treatment.—The proper treatment of vomiting is to remove the cause. In toxic cases and in those due to reflexes from the stomach itself, complete evacuation by a stomach tube gives relief. As purely symptomatic treatment, the most useful drugs are dilute hydrocyanic acid, 3 to 6 minims of which should be given in 60 minims of water, and chlorbutol, 5 grains of which can be given in a cachet and repeated, if necessary, three or four times at intervals of 2 hours. Sea-sickness and air-sickness can generally be prevented by taking $2\frac{1}{2}$ grains each of phenacetin and soluble barbitone half an hour before and again shortly after starting on the journey.

REGURGITATION, HEARTBURN AND WATERBRASH

Regurgitation.—Regurgitation of unaltered food mixed with more or less saliva occurs with pharyngeal diverticula and in œsophageal obstruction resulting from achalasia of the cardia and simple and malignant stricture. Regurgitation of small quantities of partially digested food into the pharynx and less often into the mouth without effort and without nausea occurs in various forms of dyspepsia; its acidity produces a scalding sensation in the pharynx. Regurgitation is frequently associated with flatulence due to aerophagy, the unsuccessful efforts made by the patients to bring up wind when no excess is present in the stomach resulting in regurgitation of some of its fluid contents. The regurgitation may later give place to vomiting, both the regurgitation and vomiting being to a great extent under voluntary control.

Heartburn.—When the indigestion which gives rise to regurgitation is a result of some swallowed irritant such as excess of condiments, alcohol, tobacco or drugs, the gastritis, which is the cause of the indigestion, is likely to be associated with œsophagitis. Apart from this, constant regurgitation of acid food through the œsophagus into the pharynx or mouth leads to œsophagitis. In whichever way the œsophagitis is caused, the œsophageal mucous membrane, which is normally insensitive to dilute hydrochloric acid, becomes sensitive, so that the acid gastric contents produce a sensation of burning behind the sternum when regurgitation occurs. This burning sensation is known as heartburn, and may occur with or without regurgitation into the pharynx and mouth.

Waterbrash.—Waterbrash may occur in any of the conditions which give

rise to ptyalism (p. 529), but most commonly with duodenal ulcer. At a certain interval after a meal, which varies in different cases, but is fairly constant for each individual, an uncomfortable sensation of constriction, which may amount to severe pain, is felt deeply beneath the lower end of the sternum. This may be accompanied by profuse salivation, which is sometimes accompanied by pain in the jaws from the rapid swelling of the parotid glands. Relief occurs on bringing up a few mouthfuls of clear fluid, which is generally described by the patient as being like water, though it sometimes contains a good deal of mucus. The fluid rises into the mouth with little or no effort and without nausea. It comes from the œsophagus and not from the stomach, as even when the previous meal was large and finished less than an hour before, no food is present in the regurgitated material, which is alkaline in reaction and has all the characters of pure saliva. When the flow of saliva is excessive, it runs down the œsophagus without the patient's knowledge and without the aid of actual swallowing; the cardiac sphincter being closed, the fluid collects in the lower end of the œsophagus.

The morning vomiting of alcoholic individuals is the result of a similar process, though it is accompanied by more violent vomiting efforts. In this case the fluid consists of saliva with a considerable proportion of pharyngeal and œsophageal mucus, secreted as a result of chronic pharyngitis and œsophagitis.

Treatment.—No special treatment is required for regurgitation, heartburn and waterbrash beyond that of the primary condition. The momentary discomfort caused by regurgitation and heartburn can be overcome by drinking water or sodium bicarbonate solution, or by chewing and then swallowing an alkaline tablet.

ANOREXIA

Anorexia, or loss of appetite, occurs in a small proportion of cases of chronic gastritis and in the majority of cancer of the stomach, in which it may be the first symptom, but never in uncomplicated gastric or duodenal ulcer. It is common in toxæmic conditions, such as acute fevers and tuberculosis. It is often present when for any reason the tongue is dry or furred.

ANOREXIA NERVOSA

Ætiology.—Anorexia nervosa occurs in adolescents and young adults of both sexes, but much more commonly in females than males. There is rarely any family history of psychoneuroses or psychoses. The anorexia is in most cases at first the visceral expression of some emotional disturbance, often an unhappy love affair. Sometimes the diet is voluntarily reduced with the object of overcoming a real or imaginary tendency to get fat, or on account of some fanciful ideas concerning the effect of food in stimulating sexual activity. Whatever the origin of the condition may be, the restriction of food results in the gradual disappearance of the appetite until the patient loses all desire for food. After the anorexia has continued for some time its origin, which is never recognised by the patient without explanation, recedes into the background, and it often remains after the psychological difficulties which gave rise to it have disappeared.

The constant presence of amenorrhœa has led to the idea that the condition is the result of endocrine disorder. But there is no good evidence for this theory, and complete recovery always follows simple psychotherapy without accessory treatment of any kind. There is also no justification for comparison with Simmonds's disease, a very rare condition, caused by degeneration of the anterior lobe of the pituitary gland; this is not necessarily associated with either anorexia or emaciation, and is uninfluenced by psychotherapy.

Symptoms.—The patient has a great repugnance for every kind of food, and as even small quantities have to be forced down, they give rise to a sense of complete repletion and distension and sometimes nausea. He may learn to vomit at will, and as he realises that he can overcome his discomfort by this means, it may occur after every meal. The small intake of food leads to increasingly severe constipation, and the aperients used for its treatment increase the abdominal discomfort.

The patient rapidly loses weight and in time becomes extremely emaciated, almost all the subcutaneous fat disappearing. At first physical and mental activity are unabated, the restless energy and absence of fatigue being in striking contrast with the wasted appearance of the patient, but in the later stages the patient becomes weak and lethargic, and finally may lie in bed unable to move a limb or raise his head. In girls amenorrhœa is a constant symptom; it develops at an early stage and persists for many months after recovery is complete in all other respects. It is probably of psychical origin and not a result of malnutrition, as it develops at an early stage and may persist long after the patient has returned to a normal diet. An abnormal growth of hair is a common symptom; this is a direct result of malnutrition, as it is constantly observed in times of famine.

The pulse and temperature are normal. The X-rays show no abnormality in the alimentary tract, the constipation being due solely to the insufficient quantity of food residue, and gastric secretion is unaffected. The extremities and the nose and ears are cold and blue, the skin dry and scaly. The urine is normal.

If proper treatment is not instituted, death may result from inanition, extreme atrophy without any organic visceral lesion being found *post mortem*.

Treatment.—Except in the earliest stages, it is essential to remove the patient from his home surroundings and to allow only infrequent visits from his relations. The nature of the symptoms is explained to him, and he is made to understand that he can recover and return to his home and to a normally active life only when, as a result of eating a proper quantity of ordinary food, his weight and strength have returned, and that though this may entail some discomfort at first, his appetite is certain to return when more food is taken. It is essential to be present during the first meals after treatment is begun, and to be prepared to spend a very long time arguing over every mouthful until the meal is at last finished. As resistance almost invariably breaks down under these conditions, the task of supervising subsequent meals can be left to a good nurse, who must at first never leave the patient, as otherwise food is likely to be hidden or thrown away. The patient should from the first day of treatment be given a full diet without restrictions of any kind, and should be induced to eat everything he is given.

With tact, explanation and persuasion this is always possible. The psychological origin of the trouble should not be discussed until the patient has greatly improved; even then such discussion is not always necessary, and it is rare for anything more than simple psychological explanation without any deep analysis to be required. Special diets, organotherapy, including gonadotrophic and pituitary hormones and the use of insulin to stimulate the appetite, and the administration of vitamins are of no use in the treatment of anorexia nervosa.

NAUSEA

Nausea most commonly precedes vomiting and is relieved when the stomach is empty. When associated with headache it is generally a result of migraine. It may occur as an independent symptom in chronic achlorhydric gastritis, chronic cholecystitis and in the earliest stage of carcinoma of the stomach. It is sometimes the most prominent symptom in early tuberculosis and at the commencement of pregnancy. It may occur in nephritis and infections of the urinary tract, and in men it may result from prostatic disease; in these conditions it is generally an indication of the onset of uræmia, of which it may be the first symptom. All these possibilities should be excluded before regarding it as of nervous origin, but there is no doubt that it is occasionally an hysterical symptom and due to the perpetuation by auto-suggestion of nausea which originally resulted from the emotion of disgust, although the actual exciting incident may have been forgotten.

Nausea may be constant or periodic. It may be specially associated with the consumption of fatty food or less frequently of meat, but it is often quite independent of the kind or nature of the food taken. The patient may wake up with severe nausea, which makes it difficult for him to eat any breakfast. He often thinks it is due to some disease of the stomach, and he consequently reduces the amount of food he takes; severe loss of weight may result. Nausea is often increased by emotional disturbances and may be less troublesome when the mind is fully occupied.

GASTRIC FLATULENCE: AEROPHAGY

Flatulence, or the presence of excess of gas, may occur simultaneously in the stomach and the intestine, but in many cases it is confined to the stomach or to some part of the intestines.

Ætiology.—Gastric flatulence may be caused by (*a*) excessive production of gas by fermentation or putrefaction; (*b*) the introduction of excess of air by aerophagy; and (*c*) deficient elimination.

(*a*) Achlorhydria may be associated with the formation of a small quantity of gas by bacterial activity, but this is very rarely sufficient to cause discomfort. In pyloric carcinoma, achlorhydria is associated with severe gastric stasis, and a considerable excess of foul gas may be produced.

(*b*) Aerophagy is the commonest cause of flatulence. It is often associated with functional dyspepsia, but it is equally common in organic diseases,

especially cholecystitis and less frequently gastric and duodenal ulcer, and the pain in angina pectoris frequently causes aerophagy. The patient feels discomfort in the stomach, which he thinks is due to "wind," and which he imagines he can "disperse" by eructation; as there is really no excess of gas present, the attempt proves unsuccessful and results in the swallowing of air. After half a dozen or more attempts have been made without success, air being swallowed on each occasion, the stomach becomes distended with air, which is noisily expelled. The excessive salivation, which often occurs in gastric disorders associated with hyperchlorhydria, and in septic conditions of the mouth and naso-pharynx, also leads to flatulence, as air is swallowed with each mouthful of saliva. The severest cases of aerophagy occur independently of dyspepsia in intensely neurotic women; the symptom is then hysterical. A little saliva with a large quantity of air is swallowed until the stomach is distended, when it is noisily pumped backwards and forwards between the stomach and œsophagus by spasmodic movements of the diaphragm, and is periodically expelled with a loud report.

(*c*) Deficient elimination of gas occurs when absorption is diminished owing to chronic gastritis with much secretion of mucus or to the obstruction of the portal circulation which occurs in cirrhosis of the liver and heart failure; swallowed air and the gases produced by fermentation are insufficiently absorbed and severe flatulence results.

Symptoms.—Gastric flatulence gives rise to a sensation of fullness in the epigastrium, which may extend under the left costal margin. The accumulation of gas in the stomach pushes up the diaphragm; this may cause palpitation and attacks of dyspnœa in individuals who are predisposed by such conditions as asthma and cardiac weakness. Flatulence may also be the immediate cause of an attack of true angina pectoris, though more frequently the angina is the cause of the aerophagy.

In rare cases a valvular mechanism is set up at the cardia, which does not impede swallowing but prevents the passage of gas in the opposite direction. This *aërogastrie bloquée* may result from spasm of the lower end of the œsophagus associated with an œsophageal ulcer, or from a kink caused by the dislocation of the stomach from the pressure of a distended splenic flexure in intestinal carbohydrate flatulence or a distended pelvic colon in megacolon. An enormous quantity of gas may collect in the stomach, the distension of which causes great pain, which is relieved by lying down, when the gas passes on into the duodenum, or instantaneously by the passage of a stomach tube.

Diagnosis.—When a patient complains of "flatulence," it is first necessary to ascertain whether excess of gas is really present. This can be done most readily and accurately by means of X-rays, as it is often difficult to distinguish by percussion whether an accumulation of gas is in the stomach or in the splenic flexure of the colon.

Pseudo-flatulence is generally due to the patient misinterpreting the sensation of fullness which is caused by the increased intragastric pressure produced by sudden distension of the stomach, especially if it is of the short, high form, with excess of food and drink which have been too rapidly consumed. There is no abdominal swelling or increase in gastric resonance, and the patient is unable to bring up any gas, but the condition is often complicated by aerophagy. The eructation of swallowed air may relieve the discom-

fort which prompted the aerophagy; this is probably due to the increased intragastric pressure overcoming the resistance of a pyloric sphincter closed as a result of achalasia or spasm at the same moment as the resistance at the cardia is overcome.

Excess of gas in the splenic flexure in intestinal carbohydrate dyspepsia and in the pelvic colon in megacolon often gives rise to a feeling of fullness in the left hypochondrium, which is mistaken by the patient for gastric flatulence and may lead to aerophagy.

Pseudo-flatulence may also be caused by *hysterical spasm of the diaphragm*. This may occur as an independent condition or as a complication of some organic disorder, such as gastric ulcer or colitis, or after a blow on the abdomen. It is also the cause of the abdominal distension in *pseudocyesis*, in which pregnancy is simulated. The spasm may be continuous and last for weeks or months. More frequently it occurs in attacks; a sensation of great distension is experienced and the abdomen becomes so protuberant that the clothes have to be loosened. The "distension" disappears as suddenly as it comes without eructation or passage of flatus. It often leads to a mistaken diagnosis of intestinal obstruction, and laparotomies have been performed in spite of the fact that the distension disappears under an anæsthetic. The lower ribs are drawn in as a result of the pull of the contracted diaphragm, and firm manipulation of the abdomen causes the abdomen to become flat and the diaphragm to rise. The absence of excess of gas in the stomach and intestines can be recognised with the X-rays, which also show the very low position of the diaphragm and the shallow respiratory movements. The patient should be taught to breathe properly with his diaphragm, but improvement is often very slow.

The gas expelled in aerophagy is odourless; when caused by purtefaction in pyloric obstruction it is offensive, and this is occasionally the first symptom of a growth, though it may also occur in non-malignant obstruction. Aerophagy is probably present if eructation is frequently repeated; the diagnosis is certain if it occurs several times in rapid succession, as fermentation cannot give rise to such a large quantity of gas. Eructation occurring before breakfast in the absence of pyloric obstruction is always due to aerophagy, as there is nothing in the stomach from which gas could be produced. The diagnosis can be confirmed by means of the X-rays, with which it is easy to watch the whole process of aerophagy.

Treatment.—The treatment of flatulence due to excessive fermentation consists in removing the cause. When flatulence is due to aerophagy, it is generally only necessary to explain to the patient the cause of his trouble in order to cure him. He should be told not to eructate, however much he may desire to do so. If he finds it very difficult to restrain himself, he should open his mouth or clench his teeth upon a cork, whenever the desire is very strong, as it is then difficult to swallow air, though any excess of gas in the stomach can be expelled. When aerophagy is secondary to dyspepsia, this requires appropriate treatment. Momentary relief, sufficient to help the patient to forego eructation, can generally be obtained by sipping hot water or chloroform water, or by taking a few drops of a carminative, such as oil of cinnamon or peppermint on a lump of sugar, but the use of spirits for this purpose should be prohibited.

NERVOUS DYSPEPSIA

Ætiology.—Most neurasthenic patients suffer from indigestion, partly as a result of their abnormally irritable nervous system and partly as a result of chronic toxæmia, depressing emotions, mental and physical overwork, and the other factors concerned in the production of neurasthenia, as these tend in themselves to inhibit the motor and secretory functions of the stomach.

Anxiety neuroses are often accompanied by visceral symptoms. The nature of the latter depends upon the patient's past history and physical make-up. If he has suffered from indigestion in the past or if he has an organ inferiority in the form of the hypersthenic or hyposthenic gastric diathesis, nervous dyspepsia is likely to develop.

Symptoms.—The gastric symptoms in nervous dyspepsia are characterised by their extreme irregularity, the patient feeling very ill one day and comparatively well the next without any obvious reason for the change. The most constant complaint is of vague abdominal discomfort, which rarely amounts to actual pain. It is generally worst in the morning and improves towards evening, but in some cases the symptoms increase when the patient becomes more fatigued towards evening. The discomfort is aggravated by meals, a sensation of fullness being felt as soon as a small quantity of food has been eaten, but it may be present to a less extent before breakfast. It has little relation to the amount or the kind of food, differing in this way from the discomfort of organic gastric disorders. It is increased by worry and excitement, while some new interest, whether it be a change of surroundings, a game, a conversation, a new medicine or a new doctor, leads to its temporary disappearance. Nausea sometimes occurs, but vomiting is unusual. Many patients complain of flatulence, which is generally due to aerophagy, but may be nothing more than the result of misinterpreting the sensation of fullness, no excess of gas being present (see p. 574). The appetite is always diminished, though it varies considerably from day to day. As insufficient food is taken, the nervous system becomes more depressed; this reacts again on the digestion, a vicious circle being produced.

Physical and radiological examination of the stomach very rarely shows any abnormality. Evacuation of the gastric contents may be slightly delayed owing to periods of inertia alternating with periods of normal peristalsis. The secretion of gastric juice may be temporarily diminished. If nervous dyspepsia develops in a patient with the hypersthenic gastric diathesis, the symptoms are likely to simulate those of duodenal ulcer. Constipation is almost always present. The abdominal muscles may be tense so that examination is difficult, but there is never any great degree of tenderness, and what is present is diffuse and variable in position rather than localised and constant. In other cases the abdominal muscles are weak, and symptoms resulting from this may be added to those resulting from the neurasthenia or anxiety neurosis.

The gastric symptoms are always associated with other nervous symptoms, such as headache, backache and insomnia, and the anorexia leads to progressive loss of weight and strength. The abdominal discomfort may be accompanied by flushing of the face, palpitation and coldness of the ex-

tremities. The patient is generally depressed and pessimistic; he pays great attention to all his bodily functions, constantly looking at his tongue taking his temperature and examining his stools. His account of his symptoms is full of details, and he often has some theory to account for them, believing himself to be suffering from some mythical disorder such as acidity, a dropped stomach or colon, mucous colitis or intestinal auto-intoxication, and not infrequently he fears he has cancer. He may seek advice for dyspepsia on its own account or because he thinks that it is the cause of his purely nervous symptoms.

Treatment.—The patient's confidence can be gained only after a very thorough examination. He can then be told that he has no organic disease, and that with perseverance he will get well. The general neurasthenic condition first requires attention: for this mental and physical rest, followed by graduated exercise, and sufficient food to overcome the inanition are the chief indications. Congenial surroundings, cheerful companions and appetising food are of great importance, and consequently strict isolation is not required. For the anxiety symptoms psychotherapy, preferably of a simple kind, is essential. The dyspepsia itself generally requires no special treatment, as it disappears with reassurance that there is no organic abdominal disorder and with successful treatment of the underlying nervous condition.

HYSTERICAL GASTRIC SYMPTOMS

When symptoms such as vomiting, anorexia, nausea and abdominal pain have been caused by emotional disturbance or by gastritis, gastric ulcer, appendicitis or other organic cause, they may continue or recur as the result of suggestion after the original cause has disappeared. They are then hysterical symptoms. Hysterical digestive symptoms are always curable by psychotherapy. In severe cases it is essential to remove the patient from his home surroundings. In the majority of cases explanation, persuasion and re-education effect a cure without recourse either to gross suggestion or to elaborate psycho-analysis.

Hysterical Vomiting

Hysterical vomiting occurs during or immediately after meals. It is effortless and generally unaccompanied by nausea, so that a patient may vomit meat and vegetables, and immediately afterwards be ready to eat a sweet which he retains without difficulty. The stomach is generally only partially emptied, so that nutrition is preserved, but in rare cases nothing is retained, and severe emaciation, together with the changes in the urine which follow starvation and have erroneously been ascribed to toxæmia, results. The diet has often no effect, vomiting being as frequent with milk alone as with a full diet.

When the vomiting of early pregnancy, which is probably reflex in origin, occurs after every meal instead of only in the morning, and when it persists after the eighth week, it is often called the *pernicious vomiting of pregnancy*. It has generally been regarded as toxic on account of certain changes in the urine and associated symptoms. I am convinced, however,

that it is always hysterical, as in my experience it can invariably be cured by psychotherapy with great rapidity. The changes in the urine—excess of organic acids and a rise in the ammonia index (the proportion of nitrogen present as ammonia compared with that as urea) are entirely secondary to the starvation and dehydration which result from persistent vomiting. However marked these changes may become—and I have known the ammonia-index rise from the normal 5 to 28—and however severe the so-called toxic symptoms may be, such as a dry, black tongue and a pulse as rapid as 160, they all disappear within 24 or 48 hours with psychotherapy in the form of explanation and persuasion without either suggestion or drug treatment. The condition must of course be distinguished from the vomiting, which begins in the later stages of pregnancy and is only one symptom of some obviously toxic condition, such as eclampsia or acute necrosis of the liver.

Hysterical vomiting was a common sequel of the acute gastritis caused in the War of 1914–1918 by gassing, when some of the irritant gas was dissolved in saliva and swallowed. The vomiting persisted without any other symptoms after the gastritis had disappeared. It was always rapidly cured by simple psychotherapy.

Treatment.—A patient with hysterical vomiting should be kept in bed and isolated. After the exciting cause has been discovered and the reason for the continuation of the vomiting has been explained to him in language suited to his intelligence, he should be made to realise that now that the primary cause is no longer operative, his stomach has simply developed a bad habit, which it must be educated to give up. Full diet should be given from the onset. It is always desirable to be present whilst the patient takes his first meal under the new regime in order to encourage him to suppress his desire to vomit. After one meal has been eaten without vomiting complete recovery is generally very rapid.

HÆMATEMESIS AND MELÆNA

Ætiology.—Hæmatemesis results most frequently from a chronic ulcer of the stomach, duodenum or œsophagus, or of the jejunum after gastro-jejunostomy. It occurs generally in smaller quantities, in cancer of the stomach. The term *gastrostaxis* was at one time applied to the hæmorrhage which was supposed to occur in the absence of any organic lesion; but gastroscopy and examination of fresh specimens removed at operation have proved that very small rapidly healing and often multiple erosions or acute ulcers, which readily escape detection both on external examination during an operation and at autopsy, are present in such cases in association with gastritis. Hæmorrhage may occur in susceptible people from areas of the mucous membrane which become congested and hæmorrhagic on contact with fragments of aspirin. There is no evidence that vicarious menstruation from the stomach ever occurs, although hæmatemesis is rather more common during menstruation than in the intervals. The varicose veins which develop in the œsophagus in cirrhosis of the liver may bleed, and hæmorrhage may also occur from the congested gastric mucous membrane in cirrhosis and heart failure. Bleeding from the stomach is a common symptom of splenic anæmia, even in the early stages when the liver is still comparatively healthy.

It may also occur in the hæmorrhagic diathesis, which is in most cases associated with a reduction in the number of blood platelets and delayed bleeding time (thrombocytopenic purpura); it is then generally preceded and accompanied by purpura and often by hæmorrhage from the nose, kidneys or other organs, but in some cases it may be the sole manifestation of the condition. In rare cases hæmatemesis is caused by bleeding from multiple telangiectases of the gastric mucous membrane in patients with familial telangiectasia; it is then almost invariably associated with epistaxis. Finally, blood from the naso-pharynx, mouth, œsophagus and lungs may be swallowed and vomited.

Diagnosis.—Direct examination of the nose, gums and pharynx excludes the possibility of the blood coming from these sources. Hæmatemesis may be distinguished from hæmoptysis by the fact that in the former the blood is generally dark, partly coagulated and mixed with more or less food, whereas in the latter it is bright red, frothy and uncloted; in the former the symptoms may point to gastric disease, in the latter to disease of the lungs or the heart; melæna is present in most cases and occult blood in all cases after hæmatemesis, and the hæmorrhage is not often repeated, whereas in hæmoptysis the stools contain no blood, and the patient generally continues to expectorate blood-tinged sputum for several days. In chronic ulcer and carcinoma of the stomach a history of other gastric symptoms can almost always be obtained, though in chronic ulcer they may be very mild in character and of short duration. In cirrhosis of the liver, symptoms of alcoholic gastritis are often present, and the liver is generally hard and enlarged. When hæmatemesis occurs without other symptoms, gastritis with an acute ulcer or erosion is generally present, if splenic anæmia can be excluded by the absence of splenomegaly and leucopenia, the hæmorrhagic diathesis by absence of purpura or bleeding from other mucous membranes and the presence of a normal number of blood platelets and normal bleeding time, and familial telangiectasia by absence of epistaxis and telangiectasia of the face. The possibility of an idiosyncrasy to aspirin should always be considered when a patient is in the habit of taking the drug frequently, especially if he swallows tablets whole and apart from meals.

Prognosis.—The mortality among patients with hæmorrhage from an ulcer is about 1·5 per cent. in general practice. As the incidence of hæmorrhage in cases of gastric, duodenal and anastomotic ulcer taken together is about 25 per cent., the mortality from hæmorrhage in all cases of ulcer, whether they have previously bled or not, is about 0·4 per cent. The mortality of cases of ulcer admitted into Guy's Hospital under my care on account of hæmorrhage is 4·8 per cent.; the mortality from hæmorrhage in patients with a history of hæmorrhage from ulcer or admitted for ulcer is under 2·5 per cent., and the mortality from hæmorrhage of all cases of ulcer, including those which have never bled, is about 1 per cent.

Treatment.—The patient should be kept completely at rest without transportation to a nursing home or hospital. He should be kept in the supine position, and should not leave his bed even to micturate or defæcate until there has been no hæmorrhage for 48 hours. In order to keep him completely at rest and to allay anxiety it is generally advisable to inject morphine. Nothing should be given by mouth for 24 or 48 hours; small quantities of dilute citrated milk may then be drunk and the quantity rapidly increased so that within a while the patient is on the ordinary strict ulcer diet (p. 594)

with 5 oz. hourly feeds. The so-called Meulengracht diet has nothing to recommend it for use in England. The improved results following immediate feeding recorded by Meulengracht were due to the prolonged starvation and deprivation of fluids formerly practised in Denmark. In England death is almost always a direct result of hæmorrhage from a large hole in a sclerotic artery and not from starvation or dehydration. Normal saline solution, ½ to ¾ pint, should be given four hourly by rectum until sufficient fluid is taken by mouth. Constipation requires no treatment, as the bowels generally open spontaneously on the third day after one of the saline injections.

If the hæmoglobin falls below 30 Oer cent., the patient should be transfused. Not more than 10 oz. of blood should be given and the transfusion should not be repeated unless the hæmorrhage recurs. Transfusion is required to prevent a patient from dying from anæmia; it is not required for the restoration of the blood to the normal level, as an average gain of 1 or 2 per cent. of hæmoglobin per diem occurs when 30 grains of iron and ammonium citrate, which is always well tolerated, are given three times a day. Clotting is most likely to occur when the circulation is at a low ebb with the blood pressure low and the patient collapsed. A rapid rise in blood pressure may lead to recurrence of hæmorrhage, which would not take place if the rise in hæmoglobin is as gradual as it is with the administration of iron. If the hæmorrhage is gastric and not duodenal in origin and continues to a dangerous extent, a stomach tube attached to Senoran's evacuator should be passed; the stomach is emptied and then washed with successive half-pints of iced water until the latter is no longer tinged with blood, when 60 minims of solution of adrenaline hydrochloride (1 in 1000) may be left in the stomach.

For surgical treatment *vide* p. 596.

ORGANIC DISEASES OF THE STOMACH

ACUTE GASTRITIS

(*a*) Acute Catarrhal Gastritis

Ætiology.—Acute catarrhal gastritis is caused by severe irritation of the mucous membrane of the stomach. A large indigestible meal and excess of alcohol are common causes, especially if the patient is already suffering from chronic gastritis. In many cases the irritant is a toxic product of bacterial activity in food, several individuals being often simultaneously affected. The symptoms of gastric influenza are due to acute gastritis produced by the influenza toxin, and the toxins of scarlet fever, septicæmia and other acute infections and those of uræmia may also be excreted into the stomach and give rise to gastritis. The swallowing of saliva in which irritant gases were dissolved often resulted in the production of acute gastritis during the War of 1914–1918, but the symptoms were generally overshadowed by the more serious pulmonary symptoms; in some cases the occurrence of hæmatemesis indicated the severity of the lesion. Recovery was always rapid, and when vomiting persisted it was always hysterical.

Symptoms.—The symptoms start acutely soon after the entrance of the irritant into the stomach, but they may be postponed for several hours when the attack is due to a toxin produced by bacterial activity within the stomach. A sensation of fullness and discomfort is felt in the epigastrium; heartburn is common, and in severe cases there is acute pain. Tenderness is diffuse and generally only moderate in degree, but in serious cases it may be extreme. The abdomen may be distended. The appetite is completely lost, but thirst is excessive. The tongue is covered with a thick dirty fur, and there is an unpleasant bitter taste in the mouth. The patient constantly eructates, and the gas brought up may be foul-smelling. Vomiting, preceded by nausea, almost always occurs, and gives more or less relief to the discomfort and pain. The food eaten at the previous meal, mixed with mucus but with little or no gastric juice, is first rejected; subsequently mucus with saliva, which is generally secreted in excess, bile and occasionally small quantities of blood are vomited. Severe constipation is present unless the irritant also acts upon the bowels and causes diarrhœa. The vomited matter contains no free hydrochloric acid, but is generally acid in reaction owing to the presence of lactic, butyric and other fatty acids; the saliva and mucus present may, however, give it an alkaline reaction. Microscopically, leucocytes, epithelial cells, and sometimes blood are found.

The patient is pale and prostrated and complains of headache. These symptoms are most marked in infective cases, when the patient may also be drowsy and even delirious. The temperature is generally slightly raised, but it may be high, especially in children, and the pulse is rapid. Leucocytosis is common, even in the absence of pyrexia. The urine is concentrated and may contain a trace of albumin. Herpes labialis is sometimes present. Contrary to what might be expected, a test-meal given 12 to 24 hours after the onset shows that the initial paralysis is followed by increased motor activity and the acidity tends to be high rather than low, though it subsequently falls, as a second test-meal given a week later shows that hypochlorhydria gives place to achlorhydria and an average acidity to hypochlorhydria. Mucus, leucocytes and epithelial cells are present in excess.

Diagnosis.—In severe pyrexial cases the symptoms may simulate the onset of an acute infection, such as typhoid fever, but the rapid improvement soon makes the diagnosis clear. I have seen cases in which the pain, tenderness and rigidity were so severe that considerable doubt was felt at first whether a gastric ulcer might not have perforated.

Prognosis.—Recovery generally takes place within 24 or 48 hours, but in toxic and infective cases the acute symptoms may persist for several days, at the end of which they may suddenly disappear. The condition often passes into chronic gastritis, which may remain completely latent, though the stomach is often abnormally irritable for a considerable time.

Treatment.—The patient should be kept warm in bed with hot applications to the abdomen. If the stomach is not spontaneously emptied, vomiting should be induced by drinking half a pint of warm water, in which 60 grains of sodium bicarbonate has been dissolved; when this fails, the stomach should be washed out.

Chloroform water often relieves the nausea. Castor oil, followed, if necessary, by a saline aperient, should be administered if there is constipa-

tion. No other drugs need be given except in the rare cases in which very severe pain persists after the stomach is empty, when an injection of morphine may be required. Nothing but water, which may be flavoured with tea, should be taken until all the acute symptoms have disappeared; sweetened arrowroot made with water may then be given, and, as the appetite returns and the tongue cleans, dilute citrated milk, farinaceous food, eggs, and lastly, fish, chicken and meat can be added to the diet. A test-meal should be given when the patient is convalescent, as if chronic gastritis, with or without achlorhydria, has developed, appropriate treatment may prevent the onset of various complications at a later date.

(*b*) Acute Suppurative Gastritis

Ætiology.—This very rare disease is due to the invasion by streptococci or less frequently pneumococci, staphylococci or *B. coli*, of the submucous tissue through a carcinomatous ulcer, or still more rarely through a chronic ulcer or the wound left after an operation on the stomach. In exceptional cases the point of invasion cannot be recognised. The condition may also occur in pyæmia, anthrax and smallpox.

Symptoms.—Epigastric pain and tenderness are severe. Vomiting is always present. The vomitus may contain pus owing to the rupture of a localised abscess into the lumen of the stomach. Peritonitis generally supervenes in the course of 2 or 3 days. The general symptoms present are those common to severe infections.

Prognosis.—A local submucous abscess may burst inwards and spontaneous recovery follows, but more commonly it ruptures outwards, producing general peritonitis. Diffuse suppurative gastritis always ends in peritonitis.

Treatment.—In very rare cases a localised abscess has been treated successfully by operation.

(*c*) Acute Phlegmonous Gastritis

Ætiology.—Phlegmonous gastritis results from the ingestion of irritant poisons, such as concentrated acids and alkalis, arsenic and antimony.

Symptoms.—The local symptoms are similar to those of acute suppurative gastritis, except that the vomited matter frequently contains blood and sometimes sloughs. The patient is collapsed and may become comatose, the symptoms depending upon the nature of the poison.

Prognosis.—Death frequently occurs from shock, general peritonitis or the effect of the poison on other parts of the body. If the patient recovers, achylia gastrica is almost always present as a result of atrophy of the mucous membrane, and pyloric obstruction frequently develops. A patient of mine vomited a complete cast of the pyloric half of his stomach a month after swallowing spirits of salts; recovery followed gastro-jejunostomy performed for the obstruction which ensued.

Treatment.—An attempt should be made to dilute and neutralise the poison. When this is impossible the stomach should be washed out. Morphine should be injected to relieve pain and to keep the patient quiet.

CHRONIC GASTRITIS

Ætiology. — Chronic gastritis is a very common condition. Its ætiology and pathogenesis have been discussed in the Introduction (p. 558).

Catarrh of the gastric mucous membrane is a frequent sequel of the congestion caused by diseases of the heart, lungs and liver.

Symptoms.—Chronic gastritis, especially the atrophic form, is often completely latent. When symptoms occur, their nature depends upon whether the condition has developed in an individual with the hypersthenic gastric constitution—acid gastritis, or in one with the hyposthenic gastric constitution—achlorhydric gastritis.

(*a*) *Acid gastritis.*—Acid gastritis rarely gives rise to symptoms unless it is complicated by acute or chronic ulcer (*q.v.*). In the exceptional cases in which symptoms occur in the absence of a chronic ulcer they are indistinguishable from those of duodenal ulcer, and a diagnosis can be made only when repeated X-ray examinations show that there is no constant gastric or duodenal deformity in spite of the presence of typical symptoms, tenderness and rigidity associated with hyperchlorhydria, and sometimes occult blood in the stools. Hæmatemesis may occur from an acute ulcer or erosion, which gives no radiological signs of its presence, but which can be clearly demonstrated by gastroscopy, which generally shows the presence of the hypertrophic form of gastritis. As the hypersthenic stomach is incapable of secreting much mucus, the absence of mucus from the fractions of a test-meal is no evidence against the presence of gastritis.

The treatment is that of ulcer, but the period of bed and strict dieting need not be prolonged more than a week unless occult blood continues to be present in the stools. It is, however, essential that the patient should permanently follow the "post-ulcer regime" (p. 595), as otherwise an ulcer will almost certainly develop sooner or later.

(*b*) *Achlorhydric gastritis.*—In the Introduction it was pointed out that achlorhydria is almost certain to develop if chronic gastritis occurs in a patient with the hyposthenic gastric constitution. The symptoms are mainly due to the achlorhydria and the complications to which it gives rise, so that it is unusual for the condition to be discovered when there is still free acid in any fraction of the test-meal.

The most common gastric symptom is nausea, although it is only present in a small percentage of cases. It occurs especially in the early morning, but may last throughout the day. When severe it leads to anorexia, which may also be present in the absence of nausea. The association is particularly evident in alcoholic gastritis, in which morning nausea with inability to eat any breakfast in spite of a good appetite for lunch and dinner is a characteristic symptom.

Pain never occurs in uncomplicated achlorhydric gastritis, but slight epigastric discomfort, generally described as fullness, pressure or heaviness, is not uncommon. It follows immediately after meals, and may last several hours in the small group of cases in which evacuation is slow. It is often partially relieved by belching, but frequent attempts to eructate may result in aerophagy. In spite of the presence of achlorhydria heartburn and sour

regurgitation, which are relieved by sodium bicarbonate, may occur. Tenderness is slight and ill-defined, and there is no rigidity.

Vomiting occurs if nausea is severe, or if the epigastric discomfort is unusually prolonged. It is often to a large extent voluntary, the patient having discovered that it gives relief. The vomited material generally consists of undigested food mixed with mucus and often with bile, but the morning vomit of alcoholics is an alkaline, mucous fluid, composed of swallowed saliva and secretion from the inflamed pharynx and œsophagus.

Constipation is generally present, but in one group of cases chronic or intermittent attacks of diarrhœa occur, and may persist for many years with little or no gastric symptoms which might suggest its gastrogenous origin (*vide* p. 623).

The tongue is generally clean, but in alcoholic gastritis it is often furred and the patient complains of an unpleasant taste in his mouth. When achlorhydric gastritis is associated with anæmia, whether simple or Addisonian, atrophy of the filiform papillæ is often present, generally accompanied by recurrent attacks of subacute glossitis, in which the patient complains of soreness of the tongue.

The size, tone and rate of evacuation of the stomach are generally normal, but evacuation is unusually rapid and the stomach short and high in some cases of complete achylia. In the achlorhydria following the gastritis of an acute infection it may be slow owing to the rapid exhaustion of peristalsis, the X-rays showing periods of complete inertia alternating with periods of normal activity.

The test-meal gives some indication of the severity of the gastritis. In early cases a little free acid may be present in some of the fractions, but more commonly by the time the patient comes under observation achlorhydria is complete. In most cases mucus is present in the resting juice and in each fraction, and the curve of total acidity remains moderately high above the base line. In advanced cases, in which atrophy of the mucous membrane has occurred and involved the superficial mucus-secreting cells as well as the tubules, mucus is absent and the total acidity is much reduced. So long as mucus is present, treatment is likely to result in recovery of the power of secreting free acid, but this is very rare in the absence of mucus. In the former case, but not in the latter, an injection of histamine when fasting or at the end of the test-meal is generally followed by the secretion of free acid. It is, however, unnecessary to perform this test, as histamine never succeeds in producing free acid when treatment with lavage fails, and treatment is occasionally followed by restoration of secretion in histamine-refractory achlorhydria.

Treatment.—All possible causes of gastritis should be removed as far as possible. The teeth should be put into perfect condition and artificial ones supplied when necessary. Septic tonsils should be enucleated, and nasal infections thoroughly treated. If the tongue is furred it should be frequently scraped, and sufficient dry food should be given to promote an adequate secretion of saliva. The food should be thoroughly chewed and eaten at regular times, the last meal at least two hours before going to bed. The patient should rest for half an hour after meals, and, if he is tired, for half an hour before meals.

Alcohol should be entirely prohibited, and smoking limited to a few

cigarettes with plugs of wool in the mouthpiece after meals. Tea must be weak and freshly brewed, and coffee (unless caffeine-free) only drunk if mixed with at least an equal quantity of milk. Meat should be allowed at only one meal a day and should be very tender. Game and ripe cheese, coarse bread substitutes and oatmeal, skins and pips of fruit, salads, pickles and green vegetables, except as purées, should be prohibited. A purée of spinach is particularly useful, as it contains a histamine-like substance which is a powerful stimulant of gastric secretion, even when taken by mouth. In severe cases, especially if the stools contain occult blood, it is best to start with a diet similar to that required for the treatment of ulcer.

If any mucus is present in the test-meal, the stomach should be washed out every morning with dilute hydrogen peroxide, beginning with 60 minims and increasing gradually to 240 minims to the pint. The nascent oxygen given off dislodges the mucus from the surface of the mucous membrane, and at the same time acts as an antiseptic and perhaps stimulates the secretion of gastric juice. The patient should learn to wash his own stomach out so that the lavage can be continued every day until no mucus is washed away; it can then be given every other day, then twice a week, and finally once a week for some months. The test-meal should be repeated after the mucus has disappeared; the secretion of acid returns in 80 per cent. of cases, often within a fortnight, but occasionally only after 4 to 6 weeks. If the original test-meal showed that no mucus was present, it is rarely worth while trying treatment by lavage, as the atrophy of the gastric mucous membrane is generally too far advanced for the secretion of acid to return.

In old and debilitated patients, for whom lavage seems too strenuous a treatment, a teaspoonful of sodium bicarbonate in a glass of soda water, drunk whilst fasting first thing in the morning, has a similar though less powerful action.

If treatment by lavage does not result in the return of secretion, and in all cases in which mucus is absent from the original test-meal, hydrochloric acid should be given. From 60 to 120 minims in 5 to 10 oz. of water to which sugar and the pulp and juice of an orange have been added, are drunk before breakfast and as a beverage with lunch and dinner; 5 grains of pepsin should be added to the two latter doses.

In hypertrophic gastritis, in which free hydrochloric acid is still secreted, lavage with silver nitrate solution is the most satisfactory treatment. The stomach is washed out every morning with successive quantities of a 0·05 per cent. solution until no more white precipitate of silver chloride is evacuated; when three clear washings have been obtained a final wash should be made with plain water. If the lavage causes no pain the strength of the solution should be increased successively to 0·1, 0·15 and 0·2 per cent.

The bowels should be kept regular by taking honey, fruit jelly, stewed fruit, from which pips and skins have been separated, and green vegetable purées. If necessary, liquid paraffin can be given, but irritating aperients should be avoided.

GASTRIC AND DUODENAL ULCER

Ætiology.—A chronic gastric ulcer was found by Stewart in 2·2 per cent. and a chronic duodenal ulcer in 3·8 per cent. of 4000 consecutive autopsies.

The scars of healed ulcers were found in the stomach in 2·3 per cent. and in the duodenum in 3 per cent. of the series. Chronic ulcers or scars were found in the stomach and duodenum of the same individual in 0·5 per cent. Thus a chronic ulcer, healed or unhealed, was found in 9·5 per cent. of post-mortems, and it may therefore be assumed that about 10 per cent. of all individuals suffer at some time in their lives from a chronic gastric or duodenal ulcer. Duodenal ulcers occur between three and four times as frequently as gastric ulcers in better-class practice, but gastric and duodenal ulcers are about equally common in hospital patients.

Chronic gastric ulcer occurs with equal frequency in males and females, but duodenal ulcer is about four times more common in males than females.

Chronic ulcer is rarely diagnosed in children, but the symptoms date from the age of 14 to 20 in about 12 per cent. of cases recognised later in life. It is rare for an ulcer to develop after the age of 50 in women, but in men the first symptoms not infrequently appear between 50 and 60 and occasionally even later. The average age of onset of gastric ulcer in women is 26 and in men 45 ; that of duodenal ulcer is 38 in both sexes.

Chronic ulcer frequently occurs in several members of a family in one or more generation. The ulcer is generally either gastric or duodenal in all the affected members. In familial cases the symptoms tend to begin at an earlier age than usual, and there is a great tendency for anastomotic ulcers to form after operation. There is also a special tendency in some families for the ulcers to be complicated by hæmorrhage.

Pathogenesis.—The pathogenesis of chronic ulcer has already been discussed in the Introduction, and only certain points require further consideration here. The peculiar type of ulcer found in the stomach and duodenal bulb occurs nowhere else except in the part of the jejunum immediately distal to the anastomosis after gastro-jejunostomy and partial gastrectomy, in the lower end of the œsophagus when relaxation of the cardiac sphincter allows gastric juice ro regurgitate, and also in association with heterotopic gastric mucosa in the lower extremity of the œsophagus and in Meckel's diverticulum. The one common feature of these situations is the presence of acid gastric juice.

Acute and chronic gastritis are frequently associated with localised loss of the superficial tissue, which varies in size from minute erosions only recognisable on microscopical examination to acute ulcers which are more or less easily recognisable with the naked eye. Acute ulcers occur in any part of the stomach, in the duodenal bulb, and in the region of the anastomosis after gastro-jejunostomy or partial gastrectomy. The vast majority of erosions and acute ulcers heal rapidly, but if one occurs in an individual with the hypersthenic gastric diathesis it is likely to become chronic. Probably all chronic ulcers have this origin. The various conditions already described which give rise to gastritis can thus also be regarded as factors in the development of chronic ulcers.

The tendency to develop a chronic duodenal ulcer is increased by excessive smoking ; the nicotine apparently acts through the autonomic nervous system by exaggerating the already excessive motor and secretory activity of the stomach.

One of the oldest theories of the origin of gastric ulcer was that the occlusion of small blood vessels led to local anæmia of the mucous membrane

which allowed digestion by the gastric juice to occur. It seems not unlikely that vasomotor spasm may be one factor, as something of this kind could alone explain the undoubted influence of emotional upsets and to a less extent of sudden change of temperature in the production of relapses of gastric and especially of duodenal ulcer.

Acute Gastric and Duodenal Ulcer

Symptoms.—An acute ulcer gives rise to no symptoms unless it causes hæmorrhage, which is often profuse but very rarely fatal, or, in very exceptional cases, perforation. Hæmorrhage or perforation occurring without any previous indigestion is thus usually due to an acute ulcer. The gastritis, of which it is a complication, is often completely latent, but it may give rise to any of the symptoms described on p. 584.

Acute duodenal ulcer is the most common cause of *melæna neonatorum*. Less frequently it causes hæmatemesis, and it may also give rise to vomiting and marasmus without obvious hæmorrhage during the first four months of life.

Prognosis.—Acute ulcers can develop into chronic ulcers, but the majority heal rapidly, leaving no trace of their presence. There is a great tendency to relapse, but the patient is able to take a full diet without discomfort between the attacks.

Treatment.—For the treatment of the hæmorrhage, see Hæmatemesis. All possible causes of gastric irritation should be dealt with, the after-treatment being that of chronic ulcer. The patient should be kept in bed on a strict ulcer diet until no occult blood has been present in three consecutive stools. The diet can then be rapidly increased.

Chronic Gastric Ulcer

Symptoms.—The onset is generally insidious, the symptoms first appearing after big or indigestible meals. The pain, which is often burning in character and may be very severe, is situated in the middle or slightly to the left of the epigastrium and may radiate upwards and to the back; it is much increased by indigestible food and generally disappears with a milk diet. In ulcers situated near the cardia it begins almost immediately after meals, and in prepyloric ulcers two or three hours after, intermediate intervals indicating an ulcer on the lesser curvature. The pain generally disappears spontaneously after about an hour. It is completely relieved by vomiting and by alkalis, but as a rule only partially by food. Some relief may follow lying down and the application of warmth to the epigastrium.

A small area of tenderness, the position of which is constant for each case, may be present in the epigastrium. It is more severe than in any other gastric disease; it is most marked in the presence of spontaneous pain. It is associated with rigidity of the left rectus.

With increasing pain vomiting appears; it occurs at the height of the pain, a small quantity of acid fluid with a little well-digested food being brought up. When the pain is severe, vomiting is often induced by the patient and may eventually develop into a voluntary act.

Occult blood is almost always found in the stools and vomited material, but disappears slowly when the patient is dieted. In about 25 per cent. of cases obvious hæmatemesis occurs: when the blood is abundant it is bright in colour and the stools are tarry; when less abundant it is coffee-coloured and mixed with food, and is recognisable in the stools only by chemical and spectroscopic examination. Melæna may also occur without hæmatemesis, but much less frequently than in duodenal ulcer.

The appetite is good at first and the tongue is clean, but fear of pain may lead to diminished intake of food with consequent loss of weight and weakness; in some cases, however, the relief given by food encourages the patient to eat heartily. Constipation is commonly present.

In uncomplicated cases there may be some delay in evacuation owing to reflex achalasia of the pyloric sphincter; in rare cases of lesser curvature ulcer I have seen 12 and even 24 hours' gastric stasis, probably the result of obstruction by the associated gastritis. A spasmodic narrowing is sometimes observed with the X-rays in the centre of the stomach when the ulcer is situated on the lesser curvature (*vide* p. 601). Conclusive evidence as to its position is almost always obtainable by the discovery of a "niche" formed by the crater of a chronic ulcer, which is filled with the opaque salt and is the site of the maximum tenderness.

A test-meal gives no constant result, but hyperchlorhydria is much more common than in normal individuals. In very chronic cases hypochlorhydria and even achlorhydria may be present, but these are caused by the associated chronic gastritis, as a second test-meal given after the ulcer has healed shows a considerable increase in acidity and often hyperchlorhydria, the treatment having led to disappearance of the gastritis.

Diagnosis.—A presumptive diagnosis of gastric ulcer may generally be made from the symptoms if hæmatemesis has occurred, but in its absence it is impossible to be certain without the aid of the X-rays. If the latter do not reveal the presence of a niche, a chronic ulcer can generally be excluded, but gastroscopy occasionally reveals a small chronic ulcer which has escaped recognition with the X-rays. The diagnosis is confirmed by the presence of occult blood in the stools. For the diagnosis from other conditions causing hæmatemesis, *vide* p. 580.

In cancer free hydrochloric acid is absent in 60 per cent. of cases; a chronic ulcer may give rise to a palpable tender tumour, but much less frequently than cancer, in which anorexia and wasting are also likely to be present. In chronic gastritis discomfort rather than pain is present; it generally begins directly after meals, and there is no localised tenderness. For the diagnosis of œsophageal and duodenal from gastric ulcer, *vide* pp. 554 and 591. The gastric symptoms associated with cholecystitis and recurrent subacute appendicitis may simulate ulcer, but the relation of the pain to the nature and time of meals is less regular, and less relief is given by alkalis; tenderness is present over the gall-bladder in addition to the epigastrium. It should be remembered that cholecystitis and appendicitis may be associated with gastric ulcer. With good technique it ought always to be possible to settle the diagnosis by means of the X-rays.

Complications.—Perforation of an anterior ulcer leads to general peritonitis (*vide* p. 753). It is rare for a gastric ulcer to be situated sufficiently near the pylorus to cause obstruction on healing, but the swelling and œdema

round a prepyloric ulcer together with reflex interference with the normal relaxation of the sphincter often result in temporary pyloric obstruction which disappears when the ulcer heals as a result of treatment. Recurrent cicatrisation over a period of many years of a large and very chronic ulcer in the body of the stomach in women may cause hour-glass constriction. Very chronic gastric ulcers, especially in the prepyloric region, occasionally become carcinomatous (p. 596), but such ulcers may form definite tumours without being malignant. The earlier onset, increased severity and absence of remission of pain should suggest the possibility of malignant degeneration.

Chronic Duodenal Ulcer

Symptoms.—The earliest symptom of duodenal ulcer is generally a sense of discomfort or fullness three hours after the largest meals. This is gradually replaced by pain, which occurs between two and four hours after every meal, the interval being longer the larger the meal. It frequently wakes the patient in the early part of the night, particularly if the last meal was finished less than three hours before going to sleep. It is generally situated in the middle line rather nearer the umbilicus than the ensiform cartilage; it may radiate to the right or be situated on the right side only; in rare cases it is on the left. The pain is often associated with a feeling of hunger and is relieved by taking food; it is therefore commonly known as "hunger pain." It is also relieved by alkalis and when the stomach is emptied by vomiting, which is, however, rare in uncomplicated cases, though regurgitation of mouthfuls of scalding, very acid, fluid may occur when the pain is at its height.

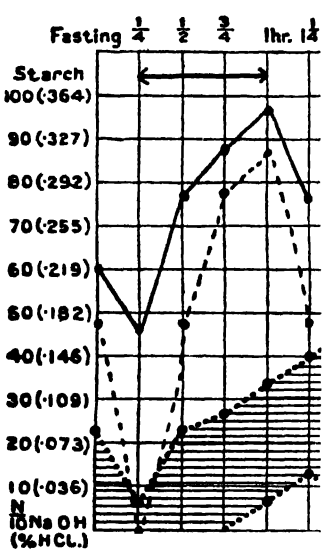


Fig. 16.—Fractional test-meal in case of duodenal ulcer, showing hyperchlorhydria and rapid evacuation. Continuous line, total acidity; dotted line, free HCl; shaded area, limits of free HCl in 80 per cent. of 100 healthy students.

Constipation is almost always present. The appetite remains good, and the patient does not lose weight or strength.

Periods of hunger pain lasting some weeks or months alternate with periods of more or less complete freedom from symptoms. The attacks are more common in cold weather than in hot, but the autumn and early spring are generally more trying than winter. Attacks are liable to be brought on suddenly by worry, exposure to cold, an acute naso-pharyngeal or bronchial infection, an indigestible meal, and excessive smoking or drinking.

In the large majority of cases occult blood is found in the stools. Severe hæmorrhage occurs in about 25 per cent. of cases: it always results in melæna and may also give rise to hæmatemesis.

In early cases the X-rays show that the stomach is often of the short high type and empties itself with unusual rapidity. In more chronic cases reflex achalasia of the pyloric sphincter may lead to delayed evacuation and consequent increase in size of the stomach, the greater curvature of which then reaches below the umbilicus. Irregularity in the outline of the duodenal bulb, due partly to the deformity caused by the ulcer itself and partly to secondary spasm, is always found, and affords conclusive evidence that an ulcer has been present, but unless it is tender or a definite niche is seen, the deformity may be produced by the scar of a healed ulcer. The niche formed by an ulcer on the lesser curvature of the duodenal bulb can be recognised in the silhouette of the bulb; one on the anterior or posterior wall can only be recognised when a radiograph is taken whilst the bulb is being compressed. A test-meal generally shows hyperchlorhydria with a climbing curve and hypersecretion (Fig. 16); if a lower curve is obtained, this is generally due to associated gastritis, and is replaced by a high curve if the meal is repeated when treatment has resulted in healing of the ulcer and disappearance of the gastritis.

Diagnosis.—When the symptoms have been present for a short time only, an actual ulcer is not as a rule present, but a pre-ulcerative duodenitis, which may be associated with a rapidly emptying duodenal bulb but no constant X-ray deformity and occult blood in the stools; it is likely to result in ulcer if not adequately treated. Excessive smoking, over-fatigue and anxiety may give rise to almost identical symptoms in individuals with the hypersthenic gastric diathesis, but the X-rays show no abnormality and occult blood is absent from the stools.

The diagnosis from gastric ulcer depends upon the later onset of pain, the greater relief on taking food, the rarity of vomiting, the greater frequency of a climbing hyperchlorhydric curve obtained with a fractional test-meal, the frequent situation of pain and tenderness to the right of the middle line, the more frequent periods of complete freedom from symptoms, and the results of X-ray examination, which occasionally, however, reveals the presence of an ulcer in the stomach as well as in the duodenum. Hæmatemesis without melæna is much more common in gastric than in duodenal ulcer, and melæna only is more common in duodenal ulcer. The symptoms may closely resemble those of cholecystitis, but in the latter condition the pain is much less regular in its time relations, the tenderness is over the gall-bladder, and evidence of gall-bladder disease is obtained by cholecystography and duodenal intubation. In rare cases cancer and syphilis of the stomach may produce similar symptoms, but the presence of achlorhydria and the X-ray examination should prevent a mistake in diagnosis.

Complications.—The inflammatory swelling round a large ulcer may lead to obstruction, the first symptom of which is generally vomiting. In very chronic cases cicatricial obstruction may develop.

Perforation may occur and lead to general peritonitis, or, much less commonly, to a localised abscess. Sub-diaphragmatic abscesses, due to duodenal ulcer, are always to the right of the suspensory ligament; unlike those secondary to appendicitis, they may contain gas. Duodenal ulcers differ from gastric ulcers in showing no tendency to become malignant, probably owing to the absence of the powerful peristaltic waves which rub hard particles of food against an ulcer in the stomach.

Treatment of Chronic Gastric and Duodenal Ulcer[1]

The patient should be kept warm in bed throughout the treatment, but he should get up every day to have a bath and to open his bowels, the difficulties with which are greatly reduced if a bed-pan can be avoided. No smoking should be permitted during the period of strict treatment.

The object of dietetic and drug treatment is to reduce the secretion of gastric juice as much as possible, and to keep the hydrochloric acid in the stomach completely neutralised. The evidence is conclusive that free hydrochloric acid delays the healing of an ulcer, whatever additional factors may have contributed towards its production in the first instance. At the same time as much food as possible is required to maintain the patient's nutrition, especially when he has lost much weight, as is often the case with gastric, though rarely with duodenal ulcer. Finally, the food should be as unirritating in its mechanical and chemical characteristics as possible.

Five ounces of milk, which can be flavoured with tea or cocoa, are given every other hour from 8 a.m. to 10 p.m., an equal quantity of custard, junket or other milky food, or white vegetable purée being given at the odd hours. To each milk feed 10 grains of sodium citrate are added. It is a valuable alkali, and by combining with the lime in the milk it prevents the formation of clots by the rennin of the gastric juice. An additional feed should be given each time the patient wakes during the night. Thin bread and butter, rusks and one or two coddled eggs can be safely added to the diet; they should be thoroughly chewed, and the fluid feeds should be slowly sipped. Apple or other fruit jelly may be used to flavour some of the feeds, and an ounce of strained orange juice should be given three times a day. Immediately before three of the feeds half an ounce of olive oil is taken, and an ounce of cream is added to three of the other feeds. The oil inhibits the secretion of gastric juice; at the same time it supplies a digestible and unirritating food of very high nutritive value in a concentrated form. Immediately before two other feeds $\frac{1}{150}$ gr. of atropine sulphate is given in 60 minims of water, and double the dose at night. The dose is increased by 10 minims every day till the maximum the patient can take without unpleasant dryness of the mouth or paralysis of accommodation. This varies in different individuals from gr. $\frac{1}{150}$ and $\frac{1}{75}$ at night to $\frac{1}{50}$ and $\frac{1}{25}$ respectively.

Thirty grains of magnesium trisilicate should be given half-way between meals and 60 grains last thing at night. It absorbs and neutralises acid so efficiently that on this regime very little free acid appears in the stomach except in the night. It does not, however, affect the reaction of the body fluids, and in contrast with all the usual alkalis it can, therefore, be given in unlimited doses without fear of causing alkalosis. Sodium bicarbonate and magnesia have the further disadvantage of stimulating the secretion of more acid after they have neutralised what is present in the stomach at the moment.

If the ulcer is in the neighbourhood of the pylorus and is giving rise to any obstruction, continuous hypersecretion of gastric juice will occur throughout the night. It is then impossible for the ulcer to heal, and in the past it has been supposed that such cases require operation. But the obstruction is generally due entirely or in great part to surrounding œdema and inflammatory swelling and pyloric achalasia or spasm, and in such cases, if the ulcer

[1] For the treatment of hæmorrhage *vide* p. 580.

can be caused to heal, any scarring produced is insufficient to give rise to obstruction. No feed should be taken after 6 p.m., and at 10 p.m., immediately before the last alkaline powder is given, the stomach is completely emptied by Senoran's evacuator; if not more than 4 ounces of fluid are present on two consecutive nights this can be discontinued. A double dose of the atropine is then given in order to inhibit the further secretion of gastric juice. In most cases the continued nocturnal secretion is rapidly controlled by this treatment.

Constipation can generally be prevented by the use of magnesia or liquid paraffin, but if the bowels are not opened on two consecutive days an enema should be given.

The strict treatment should be continued until, for at least 2 weeks, the patient has had no spontaneous pain and no trace of tenderness or rigidity, no occult blood has been found in the stools, and the X-rays no longer show the presence of an ulcer crater. A gastric ulcer should not be regarded as cured until gastroscopy shows that healing is complete; the crater may be filled with granulation tissue so that no niche is seen with the X-rays a fortnight or more before it is replaced by mucous membrane. In no case should the strict treatment last for less than 4 weeks, and for large and chronic ulcers 8 or 12 weeks may be required. The pain generally disappears within 48 hours; the other signs of activity disappear considerably later, the exact time depending upon the size and age of the ulcer and its proximity to the pylorus.

The diet can now be rapidly increased until at the end of a fortnight everything is taken with the exceptions I shall presently enumerate. It is not difficult to cause an ulcer to heal by suitable treatment in bed, but the predisposing causes are still present, and the exciting causes may still be operative unless special precautions are taken to prevent a recurrence. It is advisable to give instructions in writing for the patient to follow (*vide infra*).

From the beginning of treatment the swallowing of infective material should be kept in check as far as possible by careful dental hygiene, and as soon as the patient is convalescent thorough treatment of the teeth should be undertaken, and the patient should subsequently have his teeth put into good order at least twice a year. Any infective foci in the throat and nose should also be treated.

The patient should eat slowly and masticate thoroughly. It is a good plan to give him solid food during the last days he remains under strict observation, so that he may get into the habit of eating slowly, for when the habit is once acquired it is easy to continue in the same way. It should be impressed upon busy men that when they have no time to sit down to a proper meal it is better to drink some milk or eat some plain chocolate than to bolt some less digestible solid food. Tough meat, new bread and other articles of diet which cannot easily be chewed to a fluid consistence should be prohibited. The patient should avoid the pips and skins of fruit, whether raw, cooked or in jam, cake or puddings, and pickles, salads and all uncooked vegetables, such as celery; green vegetables are best given as purées with butter, but spinach, which is a very powerful stimulant of gastric secretion, should be permanently avoided. No strong tea or coffee, no aerated drinks, and no alcohol should be allowed, except a little diluted whisky or light wine with meals for those who feel the need of it. Condiments, vinegar, and unripe and acid fruit, high game,

sausages and curry should be prohibited. The patient should be allowed to smoke only in strict moderation. He should remain on this regime until he has been free from symptoms for two years, and should follow it in a modified form for the rest of his life.

The bowels should be kept regular; this can be done most conveniently by means of light oxide of magnesia, which should be given after each meal, as it helps to neutralise the free acid in the gastric contents. The most convenient way to take it is in a fluid preparation, containing 5 grains of magnesia to 60 minims, from 30 to 240 minims being required as a dose. If the magnesia is insufficient to control the constipation, a tablespoonful of liquid paraffin may be given after one or more meals.

The patient should continue to take a tablespoonful of olive oil half an hour before meals. He should for a time take a teaspoonful of magnesium trisilicate after meals and subsequently have some always available so as to be able to take just enough to keep himself perfectly comfortable at the slightest suspicion of heartburn or gastric discomfort. He should be warned of the danger of recurrence, and should be told to go to bed on a milk diet at the first indication of a return of symptoms. If he does this, treatment for a few days is often sufficient to ward off an attack. If, on the other hand, he waits until the symptoms become fully developed, a prolonged stay in bed will be required. The strict ulcer treatment and the post-ulcer regime can be summarised as follows.

Strict Ulcer Treatment

The patient should remain in bed on the strict treatment without alteration until healing is complete

Every other hour from 8 a.m. to 10 p.m. 5 oz. of milk. This can be warm or cold and may be flavoured with tea.

Every other hour from 9 a.m. to 9 p.m., a 5-oz feed which may be made of any of the following:

(*a*) Arrowroot, farola, Benger, junket, custard. These can be made more appetising by the addition of a little red currant, apple or other fruit jelly, and the junket may be flavoured with chocolate.

(*b*) At least two should consist of a thick soup or semi-solid purée of potato, artichoke, cauliflower or parsnip.

During the night the patient should have citrated milk by his bedside, so that whenever he wakes he can take a feed.

A rusk with butter should be eaten with three feeds. A "coddled egg" and some thin bread and butter may be taken once or twice a day by patients who can be relied upon to chew them thoroughly.

Small quantities of water may be drunk between feeds. An ounce of strained orange juice should be taken with three of the drinks.

One oz. of cream should be added to the 11 a.m., 1 p.m. and 5 p.m. feeds, and ½ oz. of olive oil should be taken before the 9 a.m., 2 p.m. and 7 p.m. feeds.

Ten grs. of sodium citrate in a teaspoonful of water should be added to each milk feed.

Sixty minims of atropine mixture (atropine sulphate, gr. $\frac{1}{150}$, in min. 60 water) before the 8 a.m. and 3 p.m. feeds, and 120 minims before the 10 p.m. feed. The dose should be increased by 10 minims every day until an unpleasant degree of dryness of the mouth or paralysis of accommodation occurs; the dose should then be reduced to that of the previous day.

Thirty grains of magnesium trisilicate half-way between feeds and 60 grains last thing at night.

Wash the mouth out after each feed.

No smoking during the strict treatment.

The patient should be weighed once a week. If he is too thin and has not gained weight, as often happens with gastric ulcers, the feeds should be increased to 6 or 7 oz. If he is too fat and has not lost weight, as sometimes happens with duodenal ulcers, the feeds should be reduced to 4 or 3 oz.

Post-Ulcer Regime

To be followed permanently

Avoid alcohol except, if desired later on, a small quantity of light wine or diluted whisky at meals. Avoid effervescing drinks and coffee.

Avoid all pips and skins of fruit (raw, cooked or in jam, and raisins and lemon-peel in puddings and cake), nuts and all unripe fruit. An orange may be sucked but not eaten. Currants, raisins and figs are particularly undesirable.

Avoid all raw vegetables, whether taken alone (celery, tomatoes, cucumber, water-cress) or in pickles and salad; green vegetables must be passed through a sieve and mixed with butter in the form of a purée. Avoid spinach. Porridge is only allowed if made with the finest oatmeal.

Avoid vinegar, lemon juice, sour fruit; pepper, mustard, curry, chutney, excess of salt; new bread; cooked cheese; fried fish; tough meat; pork; high game; clear and thick meat soup. During the first six months after recovery from an ulcer it is best to avoid meat altogether.

Take plenty of butter and cream, and a tablespoonful of olive oil before each meal.

Eat slowly and chew very thoroughly. An adequate time should be allowed for meals; rest for at least a quarter of an hour before and after meals. Meals must be punctual.

Do not smoke excessively; cigarettes should have an absorbent plug in their mouth-piece. No smoking at all if any indigestion.

A meal or feed (milk, plain biscuit or chocolate) should be taken at intervals of not more than 2 hours from waking to retiring, and again if awake during the night.

A teaspoonful or two tablets of magnesium trisilicate should be taken an hour after meals and also whenever the slightest indigestion or heartburn is felt. If the curve of acidity is very high, the atropine mixture should be taken before meals.

The bowels should be kept regular by means of magnesia and liquid paraffin, but no other aperients should be taken.

Have your teeth attended to regularly every six months.

Take no drugs in tablet form. Avoid aspirin in any form.

Special care should be taken to avoid chills. If you get a cold, sore throat, influenza or other infection, remain in bed on a very light diet until you have completely recovered.

If you have the slightest return of symptoms, go to bed on a strict diet. Consult your doctor and do not wait for the symptoms to get serious.

Surgical Treatment

An operation should be advised under the following circumstances.

1. At the earliest moment after a perforation.
2. For pyloric obstruction without active ulceration.
3. For pyloric obstruction with active ulceration, if it is still present after three weeks of rest, dieting and evacuation every night.
4. For a gastric ulcer causing organic hour-glass contraction sufficiently severe to produce 3-hour stasis in the proximal segment. This is very rare.
5. When the symptoms recur after one or more courses of thorough medical treatment followed by adequate after-treatment; the number of such courses which may be tried depends upon such circumstances as the social position, occupation and place of residence of the patient. Thus the better the social position of the patient, the less strenuous his occupation and the less important occasional absences from business, and the warmer and more equable the climate, the less urgent is the necessity for operation. In my experience recurrence after medical treatment is very unusual in the absence of pyloric obstruction if the ulcer has once completely healed, the teeth are in good condition and the after-treatment is conscientiously carried out. The results of surgery are least satisfactory when evacuation is rapid and in young people and are best when the stomach empties slowly and after the age of 50, especially in women.
6. As it is rare for death to occur from hæmorrhage, an operation is hardly ever indicated. It is required only when severe hæmorrhage recurs more than once whilst the patient is under the strictest treatment, especially in patients past middle age with sclerotic blood vessels and a long history of ulcer. An attempt should then be made to excise the ulcer or, if this is impossible, to ligature the bleeding point; failing this also, a series of sutures should be tied round the ulcer so as to cut off as much as possible of its blood supply. Gastro-jejunostomy alone is quite useless unless pyloric obstruction is present. The patient should be given a continuous transfusion to bring the hæmoglobin up to 80 per cent. immediately before the operation.
7. When for any reason, such as the persistence of pain or of occult blood in the stools whilst under strict treatment, it appears possible that a growth of the stomach is present, the abdomen should be explored, and unless a growth can be excluded with certainty, partial gastrectomy should be performed.
8. As malignant degeneration occurs about ten times more frequently in the comparatively rare prepyloric than in the common lesser curvature ulcers, and as it is often impossible with the X-rays to distinguish a simple ulcer from an early malignant ulcer in the prepyloric region, partial gastrectomy should be performed in all cases of prepyloric ulcer which do not rapidly respond to medical treatment, but not a gastro-jejunostomy, as it is im-

possible to exclude early malignant changes even by inspection and palpation during the operation.

Partial gastrectomy is the only satisfactory operation for a gastric ulcer, wherever it is situated. Gastro-jejunostomy is the best operation for duodenal ulcer producing obstruction. Partial gastrectomy has recently become popular as treatment for duodenal ulcer. But it leads to achlorhydria in only 50 per cent. of cases in contrast with almost 100 per cent. when performed for gastric ulcer, and in my experience it is no more uncommon for an anastomotic ulcer to develop in the remaining 50 per cent., in which hyperchlorhydria persists, than after gastro-jejunostomy. As the mortality of the operation is considerably higher than for the latter, and as further surgery is almost out of the question when an anastomotic ulcer develops after partial gastrectomy, I am convinced that the operation should not be performed for duodenal ulcer.

After an operation for gastric or duodenal ulcer the patient should follow exactly the same after-treatment as after medical treatment, or various ill-results, the most serious of which is the production of a gastro-jejunal or jejunal ulcer, may ensue.

Post-Operative Gastro-Jejunitis and Acute and Chronic Gastro-Jejunal and Jejunal Ulcer; Gastro-Colic Fistula

Ætiology.—The incidence of gastro-jejunal ulcer and jejunal ulcer after gastric operations depends upon the acidity of the gastric contents following the operation. It is consequently much more common after gastro-jejunostomy performed for duodenal ulcer, occurring in at least 10 per cent. of cases, than when performed for gastric ulcer, and it never follows operations for carcinoma. It may occur after partial gastrectomy, especially when performed for duodenal ulcer or gastro-jejunal ulcer, as hyperchlorhydria persists in about 50 per cent. of cases. It is especially likely to occur if septic foci are present in the mouth or naso-pharynx and if the patient does not follow a strict dietetic regime. In 20 per cent. of cases the anastomotic ulcer develops immediately after the operation and in the majority within 2 years, but I have known one develop after 21 years of freedom from symptoms.

The condition begins with inflammation of the anastomotic area, the neighbouring gastric mucous membrane, and the first inch of the distal limb of jejunum. Acute ulcers, which may cause severe hæmorrhage or perforate, follow; these may heal spontaneously or develop into chronic ulcers. Gastro-jejunal and jejunal ulcers are of equal frequency.

Symptoms.—The indigestion which follows gastro-jejunostomy is due in a large proportion of cases to an anastomotic ulcer. The commonest symptom is pain, which comes on soon after meals in contrast with its comparatively late onset before the operation, and it is generally situated to the left of the umbilicus instead of at a higher level and in the middle line or to the right. Hæmatemesis, which is often the only symptom, occurs in about 50 per cent. of cases, and occult blood is always present in the stools. Perforation may also occur without warning. In about 5 per cent. of cases the ulcer becomes adherent to the colon, and a gastro-colic, gastro-jejuno-colic or jejuno-colic fistula develops. This may at first cause little or no change in the symptoms, but sooner or later diarrhœa, which is occasionally

fatty, and vomiting of fæculent material or eructation of foul gas occur. In rare cases the proximal part of the colon becomes obstructed and severe pain and distension from accumulated fæces results.

A "niche," corresponding with an ulcer crater, can generally be recognised with the X-rays when a chronic ulcer is present, but in the frequent cases in which recurrent acute ulcers develop nothing abnormal can be seen. Gastroscopy has demonstrated the frequency of acute inflammation with or without erosions in the mucous membrane on the gastric side of the anastomosis in cases in which nothing abnormal is revealed with the X-rays, especially when hæmorrhage is the only symptom. Direct pressure over the stoma or the jejunum just beyond it often gives rise to pain. Free acid is invariably found after a fractional test-meal if care is taken not to allow the tube to pass through the stoma; in the majority of cases there is hyperchlorhydria. An opaque meal can sometimes be seen to pass direct into the colon if a fistula has developed; in other cases the fistula can be recognised only after an opaque enema, when some of the barium is seen to pass direct from the colon into the stomach.

Treatment.—Prolonged treatment of exactly the same kind as that described for gastric and duodenal ulcer generally results in healing. The hypertrophic gastritis, which often occurs around the stoma in the absence of a chronic ulcer and which is a common cause of recurrent hæmorrhage, responds to lavage with silver nitrate, as described on page 586. When medical treatment fails or when the symptoms recur in spite of following a careful regime after healing, the whole of the anastomotic area should be excised and the parts restored to their original anatomy unless pyloric or duodenal obstruction is present, in which case a partial gastrectomy must be performed. It should be remembered that no sign of the ulcer may be visible on external examination, and that it is useless merely to divide any adhesions which may be found, as they are never responsible for the symptoms.

TUBERCULOSIS OF THE STOMACH

Tuberculosis of the stomach is very rare. In miliary tuberculosis the mucous membrane may be involved, but no symptoms are produced. In advanced pulmonary tuberculosis a tuberculous ulcer may form, generally near the pylorus. The symptoms are indistinguishable from the dyspepsia common in such cases, unless hæmatemesis occurs; this may, however, be due to the presence of a simple ulcer. I have seen one case of chronic gastric ulcer and one of carcinoma, in which microscopical examination of the specimen removed at operation showed that secondary tuberculous infection had taken place. Both were associated with achlorhydria and had no distinctive symptoms, and the primary infection which was presumably present in the lungs was completely latent.

SYPHILIS OF THE STOMACH

Ætiology.—Syphilis of the stomach is apparently not uncommon in America and some Continental countries, but it is certainly very rare in

England. It occurs in males twice as frequently as in females. Its incidence is greatest between the ages of 30 and 40, and it may develop any time between 4 and 40 years after infection.

Pathology.—Characteristic gummatous infiltration of the walls of the stomach, especially the pyloric end, has been found in specimens excised at operation and much less frequently at autopsy. In at least two post-mortem specimens spirochætes were discovered.

Symptoms.—Epigastric pain generally occurs immediately after meals; less frequently it is delayed as in ulcer. Fluids and small meals give some relief. Vomiting is common, but nausea, anorexia and anæmia are rare. The symptoms become steadily worse with increasing loss of weight and strength. Hæmorrhage is very rare, and occult blood is only occasionally found in the stools. Achlorhydria is present in 85 per cent. of cases and hypochlorhydria in most of the remainder. The lesion is most frequently prepyloric, but pyloric incompetence owing to rigidity of the outlet of the stomach is as common as pyloric obstruction, and less frequently an hour-glass contraction is present. A tumour is only occasionally palpable. In 25 per cent. of cases other clinical signs of syphilis are found.

The X-rays generally reveal a local or diffuse involvement of the walls, which lead to stiffening, diminished mobility and abnormal peristalsis. The stomach is generally small. Less frequently there is a filling defect and very rarely a niche.

Diagnosis.—The possibility of syphilis should always be considered when symptoms suggestive of cancer are present; even if there is no history or other evidence of syphilis the Wassermann reaction should be tested. The diagnosis would be confirmed by the rapid improvement with anti-syphilitic treatment in spite of the failure of other measures. In one case typical symptoms of duodenal ulcer were present, but no improvement had followed prolonged treatment of the usual kind. Achlorhydria was then discovered to be present instead of the hyperchlorhydria of duodenal ulcer, and there was no duodenal deformity; the Wassermann reaction was positive, and rapid recovery with restoration of gastric secretion followed anti-syphilitic treatment.

Treatment.—The usual treatment for syphilis should be given; it is generally very successful. In late cases a short-circuiting operation may be required for pyloric obstruction caused by cicatricial contraction if anti-syphilitic treatment has failed to give relief.

CARCINOMA OF THE STOMACH

Ætiology and Pathogenesis.—Carcinoma of the stomach is commonest between the ages of 45 and 65; but, when allowance is made for the number of people living at each age, it is found that there is a steady rise in the incidence throughout adult life. This is due to the fact that the exciting causes act very slowly and require a considerable fraction of the normal span of life before they become effective.

Carcinoma never develops in a normal stomach. Clinical and pathological evidence shows that it occasionally develops from chronic gastric ulcer; this happens much more frequently in the relatively rare prepyloric ulcer than in the common lesser curvature ulcer. In about 6 per cent. of

chronic ulcers excised by operation, which appear innocent to the naked eye, small areas are found in the margin which show microscopical evidence of malignant degeneration, and in about 16 per cent. of cases of obvious carcinoma there is pathological or clinical evidence that the disease followed a simple chronic ulcer (Stewart). Cases of *ulcer-cancer* generally give a history of ulcer and have free hydrochloric acid in the gastric contents. I believe that the remaining cases of carcinoma of the stomach, most of which are associated with achlorhydria or extreme hypochlorhydria, are a sequel of chronic gastritis, which was either latent or caused comparatively trivial symptoms (*gastritis-cancer*). Numerous cases have been observed in which carcinoma developed in a patient who was known to have achlorhydric gastritis, associated with digestive symptoms, pernicious anæmia or subacute combined degeneration of the cord, months or years before the first symptom of carcinoma appeared. The achlorhydria is not a result of the carcinoma, but of the primary gastritis which is always found involving the part of the mucous membrane not attacked by the growth.

For the development of cancer two intrinsic factors, the individual constitutional susceptibility to cancer and a constitutional organ inferiority (the hypersthenic and hyposthenic gastric diatheses in the case of the stomach) are essential, but until an extrinsic factor in the form of chronic irritation is present the organ will escape disease. The first factor—the constitutional susceptibility to cancer—is constant, as the total incidence of cancer is approximately the same in both sexes, all social classes and all countries. But the incidence of carcinoma of the stomach differs greatly in the two sexes and in different classes and nations. It is more common in men than women, because so many women susceptible to cancer develop it in the breast or uterus, but the incidence in the stomach compared with the remaining organs is the same in men and women. Clinical and post-mortem statistics show that the stomach accounts for only 30 per cent. of deaths from cancer of the alimentary canal in England compared with 65 per cent. in Holland and Sweden, and cancer of the stomach occurs in England with double the frequency in the poor compared with the well-to-do, although the relative frequency of cancer in other organs is approximately the same in all countries and in all classes. These differences are almost certainly due to the third factor (extrinsic irritation) and not the second (organ inferiority).

Carcinoma involves the pylorus in 66 per cent. of cases. The fundus, especially in the neighbourhood of the cardia, and the lesser curvature are next most frequently involved.

Symptoms.—When an individual above the age of 40, who has hitherto had a good digestion, suddenly begins to suffer from gastric symptoms, the possibility of cancer should always be considered. The most common symptom is epigastric discomfort or pain immediately or soon after meals. After a time the pain, which is generally dull and distressing, but not very acute, becomes continuous, but it is still aggravated by meals. In a small proportion of cases the pain begins 2 or 3 hours after meals and is relieved by food, thus simulating duodenal ulcer, but there are never spontaneous remissions of symptoms, and in these cases achlorhydria is always present. At an early stage the appetite diminishes, the patient having a special repugnance for meat. This may be the first symptom in achlorhydric cases, but in ulcer-cancer the appetite is often maintained for a time. The anorexia may be

associated with nausea, which can also occur independently, occasionally as the earliest symptom. In about one-fifth of the cases there is a long history of symptoms suggestive of gastric ulcer, the pain having recently become more severe and continuous instead of intermittent.

Though anæmia is often present, the blood picture may remain normal even in very extensive and inoperable growths with much occult blood in the stools. The anæmia is partly due to constant oozing from the ulcerated growth, but this has comparatively little effect unless actual hæmatemesis or melæna occurs; anæmia of this kind can be overcome by treatment with iron and, in severe cases, repeated transfusions. It is often of the simple achlorhydric type, which responds rapidly to treatment with large doses of iron, and occasionally it is Addisonian and responds to treatment with liver in spite of the presence of a growth. Flatulence is commonly present, the gas brought up being at first odourless, but subsequently foul. Vomiting is generally present sooner or later. In cancer of the cardiac end of the stomach dysphagia with regurgitation of food immediately after swallowing occurs, the symptoms being indistinguishable from those of a growth of the lower end of the œsophagus. Vomiting is commonly preceded by pain and nausea, both of which it temporarily relieves, but less completely than in gastric ulcer. The vomited matter contains blood more often than in gastric ulcer: it often has the appearance of "coffee grounds." Hæmatemesis is rare, but in exceptional cases may be the earliest symptom. In a very large proportion of cases blood constantly oozes from the surface of the growth, so that one or more of the specimens obtained with a fractional test-meal may be obviously blood-stained, and all are likely to contain occult blood. The oozing is unaffected by diet, so that occult blood is present in every stool examined, however carefully the patient is dieted. The growth sooner or later involves the pylorus in two-thirds of all cases; the special symptoms then present are described in the article on pyloric obstruction.

The patient rapidly loses strength and weight, the emaciation being more than can be accounted for by the vomiting and diminished intake of food. In the late stages the disappearance of subcutaneous fat, loss of elasticity of the skin, œdema of the abdominal wall, back and ankles, and anæmia give the patient a characteristic cachectic appearance.

In the earlier stages nothing abnormal is found on abdominal palpation; but sooner or later a hard, moderately tender tumour is generally felt. It is often most easily palpable when the stomach is empty, but occasionally only becomes obvious after meals. When the fundus or body is involved the tumour is felt descending from under the left costal margin. In carcinoma of the lesser curvature and pylorus the tumour lies across the upper part of the epigastrium.

The X-rays often show an irregular filling defect in the outline of the stomach, which coincides with the tumour if one is palpable, and often involves the greater curvature. The normal progress of the peristaltic waves is interrupted, sometimes before any obvious deformity is present. The first radiological sign may be irregularity in the arrangement of the folds of mucous membrane seen in a radiograph taken after swallowing one or two mouthfuls of a suspension of barium sulphate. In carcinoma of the fundus, the arc formed by the gas under the diaphragm is irregular in shape and reduced in size, and the growth itself may be faintly visible through the gas bubble.

If there is the slightest reason to suspect cancer a fractional test-meal should be given. The resting-juice often contains pus cells in excess of the leucocytes present in a specimen of spittle obtained at the same time, and even if the specimen is not obviously blood-stained, red corpuscles are generally found on microscopical examination. In 60 per cent. of cases complete achlorhydria is present, and in at least another 20 per cent. there is hypochlorhydria; in most cases secondary to ulcer free acid is present, sometimes actually in excess. If pyloric obstruction and achlorhydria are present, but not otherwise, the resting-juice generally contains lactic acid. It is, however, absent if the stomach is washed out thoroughly the previous evening. It is thus a product of the decomposition of stagnating food and is not a secretion of the growth. Moreover, the lactic acid is the inactive variety, and therefore of fermentative and not animal origin. Consequently lactic acid, though most often found in pyloric carcinoma, may also be present in other conditions, such as migraine, if achlorhydria and gastric stasis are present together.

Secondary deposits frequently occur in the liver and in 5 per cent. of cases in both ovaries, and the symptoms they give rise to may be the most prominent clinical manifestation. Direct spread to the peritoneum and omentum is common, and irregular abdominal masses are often palpable; ascites may occur as a result of the malignant peritonitis. A small gland just beneath the insertion of the left sterno-mastoid muscle is generally attacked before any other cervical glands, and less frequently deposits occur in the inguinal glands. The growth may spread along the urachus to involve the umbilicus, where a hard nodular mass can be felt. A rectal examination should always be made, as a deposit is not infrequently present in the recto-vesical or recto-vaginal pouch at a comparatively early stage.

Perforation may occur, general peritonitis being usually prevented by the presence of old adhesions, so that a local abscess forms; less frequently the colon becomes involved and a gastro-colic fistula results, the patient then rapidly dying from emaciation due to constant fæcal vomiting and severe diarrhœa.

Other terminal complications are suppurative gastritis, pylephlebitis, suppurative parotitis, thrombo-phlebitis migrans, septic pneumonia, empyema and infective endocarditis.

Diagnosis.—Apart from the history and the discovery of a tumour, the X-ray examination is the most important means of distinguishing a growth from other gastric disorders. Occult blood is present in the stools for prolonged periods in many cases of ulcer, but achlorhydria is very rare; and in the few cases of very chronic lesser curvature ulcers in which there is no free acid, it generally reappears if the meal is repeated after washing out the stomach. Moreover, the characteristic X-ray appearance of an ulcer crater is quite different from the appearance produced by a growth. In gastric ulcer the pain begins only at an interval after meals, and if present when food is taken it is temporarily relieved, whereas in cancer the pain generally begins directly after meals and is rarely relieved by food. In the group of cases in which duodenal ulcer is simulated, the absence of periods of freedom from symptoms, the presence of achlorhydria and the X-ray appearance should prevent a mistake in diagnosis. Pernicious anæmia may closely simulate a growth of the stomach; the presence of occult blood in the stools

is distinctive of the latter and rarely occurs in the former; the megalocytosis, high colour index, and positive indirect but negative direct van den Bergh's test of pernicious anæmia are in striking contrast with the absence of megalocytes, normal or low colour index and negative van den Bergh's test of cancer, however severe the anæmia is. It should, however, be remembered that an extensive growth may be present even with a hæmoglobin percentage of 100, and that in rare cases pernicious anæmia may be associated with carcinoma of the stomach.

Prognosis.—The average duration of life after the appearance of the first symptoms is a year. Temporary improvement and considerable gain in weight may occur as a result of rest and careful dieting. Death is most frequently due to exhaustion; in other cases it results from one of the complications already mentioned.

Treatment.—Medical treatment is only palliative. In ulcer-cancer with free acid present, the post-ulcer regime (p. 595) with alkalis may keep the patient quite comfortable. In gastritis-cancer with achlorhydria a gastritis diet should be given; occasional lavage may give much relief, and an acid mixture may improve the appetite. Analgesic drugs, especially aspirin, are generally sufficient to control the pain, and it is only rarely necessary to give morphine, but when nothing else gives relief there should be no hesitation in giving very large doses.

An operation should be performed in all cases in which there is no evidence of secondary deposits or involvement of glands beyond those in the immediate neighbourhood of the stomach, unless it is found impossible to improve the patient's condition sufficiently to hold out any hope of success. If anæmia is present it should be treated before operation with large doses of iron, and, if necessary, repeated transfusions until the hæmoglobin percentage is 80. When the pylorus is obstructed, the stomach should be washed out every morning and evening for a week before operation and large quantities of saline solution given by rectum. With proper preparation and bold and skilful surgery many apparently inoperable tumours can be completely removed. If secondary deposits make a radical operation impossible in a case of pyloric carcinoma, much relief follows gastro-jejunostomy. Small nodules in the liver are not a contra-indication of partial gastrectomy, as they may grow very slowly so that the patient remains quite comfortable for many months after the operation.

HOUR-GLASS STOMACH

A gastric ulcer situated on the lesser curvature may give rise to spasm of the corresponding segment of circular muscle fibres, which leads to a depression or "incisura" on the greater curvature, like a finger pointing at the "niche" on the lesser curvature. The degree of spasm varies with the activity of the ulcer, but a slight spasm may persist after healing is complete. It never gives rise to sufficient obstruction to cause stasis or increased peristalsis in the proximal segment. It may disappear on vigorous massage or after strongly contracting the abdominal muscles and sometimes, but not always, after the administration of atropine. A less persistent spasm may occur as a reflex result of duodenal ulcer, disease of the gall-bladder and appendicitis.

Cicatrisation of a very chronic gastric ulcer may produce an hour-glass constriction. This hardly ever occurs in men, the large majority of cases being in women with such a high threshold of sensibility to pain that, though they may have had an ulcer for 20 or 30 years, they have never suffered from indigestion of sufficient severity to raise a suspicion of the presence of organic disease. The frequency of hour-glass stomach has steadily diminished during the last 25 years and the condition is now rare, probably owing to earlier diagnosis and better medical treatment. In 50 per cent. of cases found *post mortem* the ulcer has healed completely and is replaced by a scar. The comparatively rapid healing of a lesser curvature ulcer by medical treatment, however large the ulcer may be, never results in an hour-glass stomach, a period of many years with alternating periods of activity and spontaneous healing being essential for its development. The obstruction caused by an hour-glass contraction with a still active ulcer is always exaggerated by the presence of spasm, so that the narrowing found at operation is often much less than would be suspected from the radiograph.

One of the two hour-glass stomachs I have seen in men was caused by a band passing from an ulcer on the lesser curvature to the omentum; the constriction disappeared when this was divided. Hour-glass constrictions caused by cancer and syphilis are extremely rare.

Symptoms.—In organic hour-glass stomach a history of comparatively slight indigestion occurring intermittently for many years, possibly with one or more hæmorrhages, can almost always be obtained. The symptoms are similar to those of pyloric obstruction due to ulcer, with the exception that the amount vomited is generally less, and greater relief is obtained on lying down. There is no visible peristalsis unless the proximal segment is unusually large. The X-rays are the only reliable method of diagnosis; the constriction can be seen whether the patient is standing or lying down, and in the former position the neck passes from a point above and to the right of the lowest part of the proximal segment. If an active ulcer is present, the niche produced by the crater is seen on the lesser curvature.

Treatment.—If no niche is present and the upper sac of the stomach is empty within 4 hours, the patient often keeps perfectly well by following the "post-ulcer regime" (p. 595). If the ulcer is still active, surgery is indicated. When the constriction is sufficiently narrow to produce definite stasis in the proximal sac, a gastro-gastrostomy should be performed. If this is impossible for technical reasons, or if there is little or no stasis in the proximal sac, a partial gastrectomy should be performed. As an hour-glass constriction is occasionally associated with pyloric obstruction, the condition of the pylorus should always be investigated in case a gastro-jejunostomy is required in addition to a gastro-gastrostomy.

PYLORIC OBSTRUCTION

Ætiology.—Pyloric obstruction may be organic and incurable or functional and curable. Organic obstruction of the pylorus or duodenal bulb is caused by the contraction of fibrous tissue formed during cicatrisation of an ulcer in its neighbourhood, 85 per cent. being duodenal and 15 per cent. prepyloric. Two-thirds of all cases of carcinoma of the stomach involve the pylorus.

Pyloric obstruction occasionally results from chronic gastritis: this may be due to (1) a generalised sclerosis of the mucosa, submucosa and muscular coats. (2) simple muscular hypertrophy; and (3) swelling of the mucosa alone. Syphilis is a rare cause of pyloric obstruction. In infants, obstruction may result from hypertrophy of the pyloric sphincter (p. 606).

External pressure very rarely causes pyloric obstruction, and simple adhesions between the pylorus and the neighbouring viscera do not as a rule interfere with the passage of food into the duodenum. In exceptional cases, however, cholecystitis may lead to such strong and extensive adhesions with the pylorus that a certain amount of obstruction results. Gastroptosis never causes pyloric obstruction (*vide* Visceroptosis, p. 746).

The œdema and congestion round an active duodenal or prepyloric ulcer may cause severe obstruction, which disappears when the ulcer heals as a result of treatment. In such cases the obstruction is exaggerated by the presence of achalasia or spasm of the sphincter, which may also occur with an ulcer on the lesser curvature and with cholecystitis.

Symptoms.—In the early stages attacks of severe pain may occur at varying intervals after meals owing to the violent peristalsis of the stomach in its attempt to overcome the obstruction. Later, nothing more than an unpleasant sense of fullness is experienced, especially after meals, but if frequent vomiting or treatment by lavage prevents the stomach from becoming much distended, attacks of pain are likely to persist. With an ordinary diet vomiting occurs regularly every day, but this characteristic symptom is less marked if the patient takes food which leaves little or no solid residue. The vomiting generally occurs at first in the afternoon or evening; but in the later stages, when dilatation has supervened, large quantities are vomited several times a day and often during the night. Articles of food may be brought up which have been eaten many hours or even days before. The odour is sour in non-malignant and rancid in malignant cases. Excessive fermentation and putrefaction may give rise to very offensive eructation, and in rare cases this is the first symptom noticed by the patient, especially, but not exclusively, in malignant obstruction. Wasting is progressive, and the tissues become abnormally dry and inelastic. The patient has generally little appetite, but complains of great thirst. The urine is scanty, and obstinate constipation occurs.

Pyloric obstruction occasionally gives rise to tetany and to symptoms simulating uræmia, but although there is a considerable rise in the blood urea the condition is caused by chlorine deficiency and alkalosis and not renal insufficiency.

In addition to the symptoms already enumerated, others depending upon the cause of the obstruction, such as ulcer or carcinoma, are of course also present.

Pyloric obstruction leads to distension of the stomach. The signs of this, together with the distinctions between the malignant and non-malignant cases, are considered in the section on the examination of the stomach.

Treatment.—The treatment of organic pyloric obstruction is surgical. It is useless to waste time in well-marked cases with lavage or other medical treatment, as the improvement which follows operation is immediate and progressive. The immediate mortality of the operation can, however, be greatly reduced by preliminary medical treatment for a few days. The stomach is completely emptied every night by Senoran's evacuator. Small

quantities of custard, junket and similar soft easily digestible foods, but no fluids, are given during the day, saline solution being given by rectum. By this means the tone of the stomach rapidly improves, and the danger of severe intoxication due to alkalosis is overcome.

When the obstruction is only partial and an active ulcer is present, the effect of medical treatment of the ulcer should be tried, as the obstruction is largely due to the surrounding inflammation, which disappears when the ulcer heals, and when healing is rapid the scar generally gives rise to no obstruction.

ARTHUR F. HURST.

CONGENITAL HYPERTROPHY OF THE PYLORUS

Synonym.—Hypertrophic Pyloric Stenosis.

Definition.—This is a disease of early life, formerly believed to be a rarity, but now recognised as of not uncommon occurrence. It consists essentially in a great thickening of the pylorus, leading to gastric stasis, with all the symptoms that result from such a condition.

Ætiology.—The pathogeny of the disease is still obscure. The theory that it is simply a congenital malformation is not in harmony with the clinical facts, and the most generally accepted view is that it results from an over-action of the pyloric sphincter, the consequence of a lack of co-ordination between the gastric and pyloric mechanisms. There is some reason to suppose that the Anglo-Saxon and Teutonic races are more affected by the disease than the Latin, but it is exceptional to get a history of other cases having occurred in the family. Boys are affected at least four times as often as girls, and in a remarkably high proportion the patient is the first child of the family.

Pathology.—The most striking change is an immense thickening of the pylorus, due to overgrowth of its circular muscle-fibres. The stomach is dilated, its muscular coat somewhat hypertrophied, and the mucous membrane in a state of catarrh. The other post-mortem appearances are those usually met with in inanition.

Symptoms.—The child has usually been born at full time, after a natural labour, and in the majority of cases has been breast fed. For a week or two or longer all goes well, and then vomiting sets in. The vomiting is "projectile" in character, the stomach contents being violently shot out. The vomit is usually larger in quantity than the last meal, and is often mixed with mucus; the presence of any blood in it is very rare. Meanwhile the child steadily loses weight, but does not look really ill, and maintains his strength and activity. The bowels are obstinately constipated, and the motions small and dark.

The most characteristic sign of the disease is the presence of *visible gastric peristalsis*. On inspection of the abdomen, waves of contraction can be seen sweeping across its upper part from left to right. Sometimes three such waves can be seen at once, each being about the size of a golf ball. The waves may not be seen unless the child has recently been fed, and if they are sluggish in appearing a little gentle stimulation below the left costal margin will often succeed in eliciting them. In most cases the overgrown

pylorus can be felt as a tumour by palpating deeply in the right hypochondrium. Sometimes, however, it is so tucked up under the liver that it cannot be felt.

Complications and Sequelæ.—The complication most to be dreaded is the supervention of an infective diarrhœa, which in these cases is apt to prove fatal. Some degree of biochemical disturbance is also apt to develop in severe cases. There are no sequelæ of the disease; if recovery takes place, it is complete and permanent, and indeed, many of the patients ultimately attain a degree of health and development beyond the average. The hypertrophy of the pylorus disappears.

Course.—The course of the disease varies greatly in different cases, and depends also to a large extent upon the treatment adopted, but unless operation is resorted to, it is always prolonged and recovery gradual. Even when the vomiting ceases, the weight may for long fail to rise, and the child may remain in a state of inanition, during which intercurrent disease may easily supervene.

Diagnosis.—This should not be difficult, provided the existence of the disease is remembered. The vomiting is distinguished from that of indigestion by its projectile character, and the coexistence of constipation is characteristic. The great diagnostic, however, is the presence of the visible peristalsis, and in the absence of this it is unwise to conclude that the disease is present. Many experts maintain that the pyloric tumour is palpable in the majority of cases. Mild cases of pyloric spasm may simulate true stenosis, but in these the symptoms are less severe, and definite waves of peristalsis are absent, The patient is often a girl. Stenosis of the duodenum from congenital malformation may simulate pyloric stenosis, but the symptoms in the duodenal cases date *from birth*, and bile is present in the vomited matter. An X-ray examination often helps in the diagnosis.

Prognosis.—It is very difficult to estimate the chances of recovery or the relative merits of different forms of treatment statistically. Much depends upon the severity of the particular case, but in general it may be stated that no case is so severe that recovery is impossible. Cases treated in private do much better than those seen in hospital.

Treatment.—There are two methods of treatment—medical and surgical. Medical treatment consists in washing out the stomach once or twice daily with normal saline, and carefully regulating the feeding. If breast milk is not available, a half-cream dried milk with the addition of dextrimaltose is the best substitute, and should be given in quantities of one or two ounces every 2 or 3 hours, depending upon the degree of vomiting. Atropine (3 to 9 drops of a 1 in 1000 solution of the sulphate, half an hour before each feed) is sometimes used with alleged benefit, and recently atropine methyl nitrate (eumydrin) (0·5 mgrm. given seven times daily half an hour before each feed) has been recommended as less toxic than atropine. If under this treatment the vomiting ceases, and the weight begins to rise, good and well. If not, or if the symptoms have set in early and with great severity, operation should be had recourse to, Rammstedt's plan of splitting the pylorus longitudinally being the procedure to be preferred.

ROBERT HUTCHISON.
ALAN MONCRIEFF.

ACUTE DILATATION OF THE STOMACH

Ætiology.—After operations, especially for acute abdominal conditions, and much less frequently in the course of acute infections, especially pneumonia, the stomach suddenly becomes greatly dilated owing to a complete loss of tone. The dilatation, which is often much aggravated by severe aerophagy, leads to complete obstruction of the duodenum by the mesentery at the point where the latter crosses it, and the dilatation then becomes extreme.

Symptoms.—The abdomen is very distended, large quantities of dark but not fæcal fluid are vomited, and the patient rapidly becomes very collapsed. "Black vomiting" after operations is almost always due to acute dilatation of the stomach, and not to the intestinal paralysis with which it is often associated.

Treatment.—The stomach should be kept empty by aspirating through a Ryle tube kept continuously in position, however ill the patient may be. Nothing should be given by the mouth, but saline solution should be injected continuously into a vein by the drip method. If recovery does not occur in two or three days, a jejunostomy should be performed, the patient being fed through the stoma till the stomach contracts to its normal size.

CHRONIC DUODENAL ILEUS

Ætiology and Pathogenesis.—Just before the duodenum turns upwards to end in the duodeno-jejunal flexure, it is crossed by the root of the mesentery. When the mesenteric vessels arise at a lower level than usual or the horizontal portion of the duodenum is situated unusually high, the slight anatomical variation from the average normal leads to some narrowing of the lumen of the duodenum where it is crossed. If the abdominal muscles are lax and the small intestines drop into the pelvis, they may be partially incarcerated there and the obstruction becomes more marked. In rare cases obstruction at the same point is caused by localised simple or tuberculous chronic peritonitis. The proximal part of the duodenum becomes dilated, and the violent peristalsis, which can be seen with the X-rays to give rise to backward and forward movements of its contents in its effort to pass the obstruction, results eventually in hypertrophy of its muscular coat.

Symptoms.—The condition generally gives rise to no symptoms and is discovered accidentally during a routine X-ray examination, but it may cause right-sided discomfort, which sometimes simulates duodenal ulcer or gall-bladder disease. Paroxysmal attacks of bilious vomiting may be the only symptom, especially in neurotic women. In rare cases it is the cause of cyclical vomiting in children, which persists into adult life; in one such case the consequent malnutrition led to dwarfism. The duodenal stasis may be a factor in the development of duodenal ulcer and of cholecystitis, when chronic ileus is present in an individual who is already predisposed to these conditions. An anterior duodenal ulcer associated with ileus is specially liable to perforate.

Treatment.—In most cases postural treatment gives complete relief. The patient should for a few weeks adopt a position for a quarter of an hour

every day in which the X-rays have shown that the obstruction is overcome. Lying on the right side or face downwards may be sufficient. In more severe cases the patient leans over the end of a couch with his head downwards, so that his trunk is perpendicular to the ground; this allows the incarcerated small intestine to drop out of the pelvis, and complete and permanent recovery may follow.

In my experience the results of duodeno-jejunostomy have been satisfactory only when the obstruction is sufficient to cause considerable duodenal stasis. In neurotic women with paroxysmal vomiting the symptoms almost invariably recur after a short interval of freedom.

When a duodenal ulcer is associated with duodenal ileus the danger of perforation calls for operation: gastro-jejunostomy is often successful, but it is sometimes followed by persistent vomiting, so that a duodeno-jejunostomy should probably be performed at the same time.

ARTHUR F. HURST.

DISEASES OF THE INTESTINES

INTRODUCTION

I. THE FUNCTIONAL DIVISIONS OF THE INTESTINES

i. *The small intestines.*—In the duodenum the food is mixed with the pancreatic juice, which is essential for the digestion of protein and fat, and with bile, which promotes the absorption of the products of fat digestion. In its passage through the small intestines the chyme is mixed with the succus entericus, which contains enterokinase, which activates the pancreatic ferments, and invertase, maltase and lactase. The chyme passes rapidly through the jejunum and greater part of the ileum, in the last 12 inches of which it remains for a considerable time. The terminal ileum indeed forms an "ileal stomach," in which the greater part of the digestion of protein, fat and carbohydrate takes place and the products of digestion are absorbed.

ii. *The proximal colon.*—Observations on patients with cæcal fistulæ show that about 350 g. of fluid chyme, containing 90 per cent. of water with very small quantities of sugar, fat, coagulable protein and of the soluble products of their digestion pass through the ileo-cæcal sphincter in a day. As the average weight of fæces is 135 g. and they contain only 75 per cent. of water with no sugar, coagulable protein or soluble products of digestion, it is clear that much water and all the soluble constituents of the chyme which reach the cæcum must be absorbed in the colon. This absorption takes place in the cæcum, ascending colon and proximal half of the transverse colon, which may therefore be regarded as the "colonic stomach."

iii. *The distal colon.*—The pelvic colon acts as a storehouse for fæces, to which they are conveyed through the transverse colon, the descending colon and the iliac colon when digestion in the colonic stomach is complete. Here they remain until the time for defæcation arrives.

iv. *The rectum.*—The rectum has the important function of maintaining

the regular evacuation of fæces. It is empty except immediately before defæcation, and the distension of its walls when fæces enter it is the normal stimulus to the defæcation reflex. The same stimulus produces the sensation which prompts the individual to perform the voluntary acts which help in the efficient performance of the reflex.

II. THE INTESTINAL MOVEMENTS

The movements of the intestines have two main objects: (1) mixing the food with the digestive juices and bringing them into contact with the mucous membrane which absorbs the products of digestion and water; and (2) propulsion of its contents from the duodenum to the rectum, and of the indigestible residue of the food from the rectum.

i. *The small intestines.*—In the small intestines peristalsis and segmentation take place simultaneously, the former with the object of propelling the chyme into the "ileal stomach," and the latter with the object of mixing the food with the digestive juices and exposing it to as large an area of mucous membrane as possible. In the jejunum and greater part of the ileum peristalsis is the predominating motor activity, but when the ileal stomach is reached it ceases almost completely and segmentation becomes extremely active. After a varying interval peristalsis becomes active again, and as the ileo-cæcal sphincter relaxes with the arrival of each peristaltic wave, the ileal stomach empties its contents into the cæcum.

ii. *The colon.*—When the colon is examined after an opaque meal it appears to be completely immobile. In spite of this, both segmentation and peristalsis occur under normal conditions, but their character differs considerably from the corresponding movements in the small intestine. Peristalsis occurs only in the form of "mass movements" about three times a day: a single very powerful peristaltic wave travels slowly along a considerable part or even the whole length of the colon, pushing in front of it most of the contents. Deep segmentation movements, which are too slow to be visible with the naked eye, can be recognised by comparing radiographs taken at three-minute intervals and often in those taken at intervals of a single minute. Segmentation is the result of the ceaseless activity of the muscularis mucosæ, the normal "haustration" of the colon seen with the X-rays being produced by projecting folds of mucous membrane. As a result of the continuous segmentation in the colonic stomach much of the water and all of the soluble constituents of the food and the products of their digestion which have escaped the small intestine are absorbed.

The chyme leaves the ileal stomach very slowly except during and immediately after meals, when as a result of a gastro-ileo-cæcal reflex frequent peristaltic waves pass down the terminal ileum to the ileo-cæcal sphincter, which opens widely as each wave reaches it. The chief stimulus to mass peristalsis of the colon is a gastro-colic reflex. On comparing these events it becomes clear that the ileal stomach passes its contents into the cæcum when it is necessary that it should be empty for the reception of the food coming down from the stomach after a meal, and that the colonic stomach similarly evacuates itself to leave room for the reception of the contents of the ileal stomach.

III. DEFÆCATION

During defæcation the contents of the pelvic colon, together with any fæces which may be present in the descending and iliac colon, pass into the rectum; the distension of the rectum causes it to contract as a whole just like the bladder and at the same time causes reflex relaxation of the sphincter ani, so that the contents of the rectum are evacuated. Simultaneously the contents of the cæcum and ascending colon pass into the transverse colon, whilst the contents of the latter pass into the pelvic colon.

Normal defæcation depends upon a conditioned reflex. The infant is taught at an early age to empty his bowels directly he is placed on a chamber. The act quickly becomes a purely reflex one, and it continues to be so when he grows older and the chamber is replaced by the seat in the w.c. Breakfast by itself gives rise to a simple gastro-colic reflex; sitting down on the familiar seat in the w.c. is, however, the starting-point of the more elaborate conditioned reflex, which produces the most efficient gastro-colic reflex of the day, in which the whole colon from the cæcum to the rectum takes part. In the healthy adult defæcation remains to a great extent a conditioned reflex. It is enough to sit down in the accustomed place, perhaps with a pipe and a newspaper, for the reflex to begin, often without the "call to defæcate"—the perineal sensation produced by the entry of fæces into the rectum, and without the voluntary stimulus produced by the increased intra-abdominal pressure caused by descent of the diaphragm and contraction of the abdominal muscles, though these, together with the final contraction of the levator ani muscles, are always brought into action to help in the complete expulsion of the fæces.

Failure to open the bowels on the first day of a holiday is not due, as is popularly supposed, to the "hard water" of the locality, deficient exercise in a train or on board ship, but to the unfamiliar w.c. and perhaps the unusual hour of getting up—or the absence of getting-up, such small changes being enough to upset for the moment the delicately adjusted conditioned reflex.

EXAMINATION OF THE INTESTINES

SIZE, SHAPE AND POSITION OF THE COLON

The cæcum and iliac colon are the only parts of the bowel which are always palpable under normal conditions. In very thin individuals and in patients with very lax abdominal muscles the whole colon except the splenic flexure and the pelvic colon can often be felt. Apart from these conditions the colon may become palpable when in a state of spasm or when filled with fæces, and tumours involving it can often be recognised by abdominal examination. In all intestinal cases a rectal examination must be made; by this means not only the rectum but also part of the pelvic colon can be palpated. For a thorough investigation of the size, shape and position of the whole colon in the erect as well as the horizontal postures an X-ray examination

after a barium meal is essential. The pelvic colon, and less frequently the descending and iliac colon, cannot always be seen satisfactorily, as they may be full only in the early morning, and defæcation empties them completely before it is convenient to make an X-ray examination. In such cases a barium enema renders all parts of the colon easily visible; the artificial distension produces a considerable amount of distortion, the error due to which can be overcome by making an additional examination after most of the fluid has been allowed to escape.

MOTOR FUNCTIONS

(*a*) PALPATION.—In every case of intestinal disorder an abdominal and rectal examination should be made. No medicine or enema should be given during the preceding 24 hours, but before this the colon should be emptied by whatever means the patient is in the habit of using. The quantity of fæces present in each part of the colon varies greatly according to the time at which meals are taken and defæcation occurs. With a normal individual whose bowels are satisfactorily opened after breakfast the whole of the colon is empty during the greater part of the morning, though a thin layer of soft fæces may cover the wall of the cæcum and perhaps the ascending colon and so render them partially opaque to the X-rays if a barium meal was taken 24 hours earlier, and a small quantity of semi-solid fæces may be present in the distal part of the transverse colon. Between 3 and 4 hours after breakfast the cæcum begins to fill; the filling becomes much more rapid after lunch, so that in a short time the ascending colon also becomes filled. During the rest of the day palpation shows the cæcum and ascending colon, and often the proximal part of the transverse colon, to be filled with soft fæces; as a rule this can be recognised much more easily in the part of the colon in the right iliac fossa, owing to the solid background it affords than in the more distal part. The resonant note which is generally obtained on percussion over the right half of the colon in the morning is replaced by a dull note in the afternoon.

In the early morning the rectum is empty, but the pelvic colon can be felt through the anterior rectal wall to be filled with solid scybala, which sometimes extend upwards into the iliac and the descending colon. On getting up, but often only after breakfast, the pelvic colon empties some of its contents into the rectum, giving rise to the "call to defæcate"; from this moment until defæcation has occurred is the only time in the day in which the rectum of a normal individual is filled with fæces. At all other times it is completely empty, and a proctoscope shows that there is not even a trace of fæces adherent to the mucous membrane. In defæcation the whole of the colon beyond the splenic flexure empties itself. Consequently the descending iliac and pelvic colon are empty during the whole morning, except that fæces may be conveyed during defæcation from the transverse colon into the lower part of the pelvic colon, and more may arrive from the proximal colon with the mass peristalsis occurring after lunch. Apart from this, the pelvic colon is generally empty or almost empty until after tea or more commonly after dinner, when another wave of mass peristalsis fills it with the contents of the colon from the neighbourhood of the hepatic flexure and the proximal half of the transverse colon.

The details of the movements vary greatly in different individuals, but the average conditions just described show how greatly the fullness of the different parts of the colon varies with the time of day, and how unjustifiable, for example, it is to diagnose cæcal and ascending colon stasis because these parts of the colon are full of fæces when examined in the afternoon.

If the rectum is full of fæces and the patient has no desire to defæcate, dyschezia can be diagnosed. If the fæces are soft it is clear that there can have been no delay in the passage to the rectum, such as is likely to have occurred if it contains hard and dry scybala. When the rectum is empty but the pelvic colon can be felt through the anterior rectal wall to contain scybala, the form of dyschezia which is due to inability of the pelvic colon to empty its contents into the rectum is present, but this can be diagnosed with certainty only if the patient has made an effort to open his bowels after breakfast and the examination is made before lunch. In severe cases hard scybala may also be felt in the iliac and perhaps the descending colon.

A full cæcum and ascending colon are of significance only if the examination is made within three hours of breakfast; even then primary right-sided stasis can be diagnosed only if the rectum and pelvic colon are empty.

(*b*) The Charcoal Method.—By giving two or three charcoal lozenges with some food 8 hours after defæcation and observing after what interval black fæces are passed, the total time taken in their passage through the alimentary canal can be ascertained. If, for example, a patient's bowels have been opened at 8 a.m., charcoal should be given at 4 p.m. the same day. If some of the charcoal is not passed at latest the second morning after being taken, the patient must be regarded as constipated. The method has, however, the great disadvantage of giving no indication as to the part of the bowel in which stasis occurs.

(*c*) X-ray Examination.—i. *Opaque meal.*—The only reliable means of determining whether a patient is suffering from chronic intestinal stasis, and of ascertaining exactly what parts of the alimentary canal are at fault, is a series of examinations with the X-rays. Examination with the fluorescent screen gives more information than is obtainable from radiographs. If the bowels have not been spontaneously opened the morning before the opaque meal is to be taken, an enema should be given in the evening. It is very important to discontinue the use of all aperients for at least 48 hours before the first examination, as the intestinal functions might otherwise be observed whilst still under their influence instead of under natural conditions. No aperients and no enemata should be used till the examination is finished, but the patient should make an attempt each morning to open his bowels naturally. If the attempt is successful, the stools should be examined to ascertain whether any of the barium has been evacuated. The patient should follow his usual occupations and take his ordinary diet. An examination should be made in the morning and evening of each day until all or most of the barium has been passed in the fæces or has reached the rectum.

ii. *Opaque enema.*—Although an opaque meal is the best means of obtaining information of the motor functions of the colon, an opaque enema generally gives earlier and more exact information concerning the possible presence of a stricture, especially in the iliac and pelvic colon, which often cannot be satisfactorily examined by the former method. A suspension is

made by adding 8 oz. of barium sulphate and 4 oz. of kaolin to a pint and a half of water. The patient lies on his back, and the fluid is run in from a container at a pressure of between 2 and 3 feet through a valveless Higginson's syringe connected with a rubber tube introduced just within the rectum, the syringe being used, when necessary, to help the passage of the opaque mixture with light pressure. It often reaches the cæcum in 2 minutes and almost invariably within 5 minutes. When the examination is complete, part can be run out through the tube, the rest being evacuated in the ordinary manner; a further inspection with the X-rays is then made. Additional information, especially as to the presence of polypi, can often be obtained by injecting air into the colon after the greater part of the opaque enema has been evacuated.

An organic stricture of the colon generally obstructs the passage of the fluid, the shadow ending at the seat of the obstruction, which can be overcome only incompletely or not at all by waiting an additional 10 minutes, by increasing and decreasing the pressure of injection, by massage and by changes in posture. The flow of the enema is often prevented in cases of growth long before there is any clinical evidence of obstruction; the bowels may still act normally or diarrhœa may be present, and an opaque meal may pass through the whole colon without delay. This is probably due to the occurrence of a spasmodic contraction of the bowel, which occurs at the seat of obstruction as soon as the enema reaches and distends the part immediately below it.

An opaque meal or, more frequently, an opaque enema may show the presence of a filling defect in the colon caused by a growth. The latter also shows the exact length and position of fibrous strictures, and it is generally the most satisfactory way in which the presence of diverticula can be determined.

EXAMINATION OF FÆCES

The consistence, smell, colour and reaction of the stools when no aperient is being taken should be noted, abnormal acidity indicating excessive fermentation and abnormal alkalinity excessive putrefaction. The presence of mucus with solid stools is not in itself a sign of disease, but if it is mixed with blood or pus or present with fæces which are unformed though no aperient has been taken, some organic disease is certainly present. The presence of mucus with hard scybala or with soft stools obtained after the use of an aperient is due to the normal reaction of the colon to a mechanical and chemical irritant respectively, mucus being secreted in order to protect the mucous membrane. Blood by itself may come from hæmorrhoids or a rectal polyp; if associated with mucus or pus or both, inflammation or cancer of the anal canal, rectum or colon must be present. The larger the fragments of mucus and the brighter the colour of the blood the lower is their source. The presence of pus always indicates disease of the pelvic colon or rectum.

Pale, bulky stools generally indicate the presence of excess of fat. It is important to ascertain whether this is chiefly in the form of neutral fat, as in pancreatic insufficiency, or in the form of fatty acids and soaps, as in

deficient absorption caused by jaundice, sprue, cœliac disease and obstruction of the lacteals with normal pancreatic digestion. This can generally be decided by microscopical examination, but in doubtful cases an accurate chemical analysis should be undertaken.

Microscopic examination may reveal the presence of blood corpuscles, pus, amœbæ or their cysts, and the ova of intestinal worms, in addition to fragments of animal and vegetable food which have escaped digestion.

A bacteriological examination of the stools should always be made in cases of diarrhœa, with or without colitis. The presence of a relative excess of enterococci or *B. coli communis*, the normal inhabitants of the colon, or of strains of streptococci or *B. coli* which are not normally present, or of parenteric, enteric, dysentery and tubercle bacilli may be discovered. If a sigmoidoscopic examination is made, a swab should be taken for bacteriological examination from the mucous membrane; if any mucus or pus is seen, this should also be taken for examination. In doubtful cases the agglutinating power of the patient's blood for abnormal bacteria isolated from the stools should be tested.

Occult Blood

When blood is swallowed or is derived from an ulcer or growth in the œsophagus or stomach or an ulcer in the duodenum it is evacuated in the stools partly as acid hæmatin and partly as hæmatoporphyrin. Both also appear in the stools when the blood originates in the colon unless diarrhœa is present, when the blood does not remain in the bowel long enough for the former to be converted into the latter. The chemical tests for "occult blood"—traces of blood insufficient to produce any change in the appearance of the fæces—depend upon the conversion of a substance with little or no colour, such as guaiac or benzidine, into a coloured substance when oxidised by hydrogen peroxide in the presence of a carrier, such as hæmatin. The guaiac reaction is preferable to the benzidine, as, unlike the latter, it does not give a colour-reaction when iron salts are given by mouth; it can, therefore, be used in patients with ulcer who are receiving iron on account of post-hæmorrhagic anæmia. Hæmatoporphyrin, which contains no iron, gives neither reaction. A spectroscopic examination of the stools should also be made, as even considerable quantities of hæmatoporphyrin, which is occasionally present in the absence of acid hæmatin, would otherwise escape recognition. Moreover, a positive spectroscopic finding is valuable confirmation of a positive chemical reaction, as, although it is much less sensitive, there is less chance of error.

Before the stools are examined the patient is given a hæmoglobin-free diet. Chlorophyll should also be excluded, as it gives a feebly positive guaiac reaction, and its many-banded spectrum may cause confusion in the spectroscopic examination. A charcoal biscuit is given with the first meal on the restricted diet, and the first and subsequent stools passed when the fæces are no longer blackened by the charcoal are examined. For the guaiac test a small amount of fæces is macerated with glacial acetic acid into a thin paste. An equal quantity of ether is then added to extract the pigment and the ethereal extract is poured off, some being kept for the spectroscopic examination. Two or 3 drops of tincture of guaiac are added to the re-

mainder; a small quantity of ozonic alcohol is then poured in, and a change of colour is looked for at the junction of the two fluids. A "positive" reaction is one in which a deep blue colour rapidly appears; a "feeble positive" reaction is one in which the colour is faint purple, bluish or greenish. If 1 c.c. of blood enters the stomach or intestines, the next day's stool will give a faintly positive reaction.

A positive guaiac reaction signifies the presence of occult blood. A negative guaiac reaction proves its absence, except occasionally at the end of a period of hæmorrhage, when the spectroscopic test may alone be positive, as the traces of blood still present may then be completely converted into hæmatoporphyrin, which gives a characteristic spectrum, but does not give the chemical reaction.

By the spectroscopic test of the stools one can recognise (1) the acid hæmatin, which also gives a positive guaiac and benzidine test, and (2) the other hæmoglobin derivatives, *i.e.* porphyrins, which do not give a positive colour-reaction. The spectrum of acid hæmatin is so faint that it can be seen only in fairly concentrated solutions: the typical band of acid hæmatin (λ 620) is found only when considerable quantities of blood are present in the stools.

Small amounts of chlorophyll are easily discovered by the characteristic band in red on λ 662, *i.e.* left of λ 650, whereas the band of alkaline porphyrin lies right of λ 650 on λ 630. Moreover, on addition of HCl the bands of alkaline porphyrin immediately change to the acid spectrum (a narrow band in red (λ 605-600) and a broad band in yellow (λ 590-550)), whereas the chlorophyll spectrum remains unaltered.

In the absence of hæmorrhoids and rectal polypi (which may be quite latent) and of bleeding from the mouth, throat and nose, the presence of occult blood in the stools is strong evidence that an ulcer or growth is present in the œsophagus, stomach or intestines. It is occasionally found in gastritis, with gall-stones, diverticulitis and localised adhesions involving the alimentary tract.

PROCTOSCOPIC AND SIGMOIDOSCOPIC EXAMINATION

Wherever there is any possibility of organic disease of the pelvic colon or rectum a proctoscope and, if necessary, a sigmoidoscope should be passed after a preliminary digital examination. No special preparation is required, but the patient should endeavour to get his bowels emptied as completely as possible without the aid of aperients or enemata shortly before the examination. The instrument should be passed without an anæsthetic in the knee-elbow position.

The passage of a proctoscope requires little experience, whereas a sigmoidoscope should be used only by experts. As the rectum is involved from the onset and is the last part to recover in ulcerative colitis, proctoscopy gives all the information required, and it has the advantage of allowing examination from a shorter distance. Moreover, the pelvi-rectal flexure, which is the commonest situation of cancer, is within its range. But when nothing abnormal is found with a proctoscope in suspected cases of malignant disease, it is essential to pass a sigmoidoscope.

FUNCTIONAL DISORDERS OF THE INTESTINES

CONSTIPATION

Definition.—Constipation may be defined as a condition in which no residue of the food taken during one day is excreted within the next 48 hours.

Ætiology and Pathology.—Constipation may be due to (1) the passage through the colon being delayed, whilst defæcation is normal—colonic constipation; (2) the evacuation from the pelvic colon and rectum being inadequately performed, whilst the passage through the colon is normal—dyschezia; and (3) insufficient formation of fæces.

1. Colonic Constipation.—Delay in the passage of fæces through the intestines is due to their motor activity being deficient, or to the force required to carry the fæces to the pelvic colon being excessive. The motor activity of the colon may be deficient owing to deficient reflex activity, inhibition, or uncontrolled and irregular action. There is no evidence that it is ever due to actual weakness of the muscular coat. The reflexes which maintain intestinal activity may be deficient owing to lack of mechanical and chemical stimulants in the food, or to some endocrine deficiency as in hypothyroidism. The inhibitory sympathetic nerves may be stimulated centrally by depressing emotions, and reflexly in painful diseases and injuries of any part of the body, but particularly of the abdominal and pelvic viscera.

Constipation may result from painful spasm, induced reflexly by the presence of an irritant in the colon of a patient with an abnormally excitable nervous system (*spastic constipation*). The irritant which gives rise to the exaggerated reflexes is in most cases hard fæces, which may have been retained as a result of constipation caused by insufficient and unsuitable food and of dyschezia. Spasm may result from irritation by organic acids in intestinal carbohydrate dyspepsia, in which constipation may alternate with diarrhœa. Spastic constipation is a constant symptom of diverticulitis. The reflex may also be excited by disease in other parts of the abdomen, especially the gall-bladder and appendix. Similar spasmodic contractions of the intestines occur as a result of excessive smoking and in lead poisoning.

The work to be done by the intestinal musculature is excessive when the fæces are abnormally hard and dry owing to insufficient consumption of water or its excessive loss in the urine or sweat, and when there is a diminution in the intestinal lumen owing to organic stricture.

2. Dyschezia.—Dyschezia may be due to inefficiency of the defæcation reflex, to abnormally hard and bulky fæces requiring excessive force for their evacuation, or an obstacle to efficient defæcation, such as spasm or congenital or acquired strictures of the anal canal. Dyschezia due to inefficient defæcation is the most common cause of severe constipation. It often originates in neglect to respond to the call to defæcate owing to laziness, insanitary condition of the w.c. or false modesty. The conditioned reflex upon which defæcation normally depends is gradually lost. The rectum dilates so that an increasing quantity of fæces is needed to produce the adequate internal pressure required to give the sensation of fullness which is the natural call to defæcation. Finally the sensation is lost com-

pletely. But the patient is still capable of emptying his rectum if he tries. He has, however, by now often convinced himself that he cannot get his bowels to open unless he takes enemata or such enormous doses of aperients that the fluid fæces practically act as enemata. He suggests to himself that his rectum is powerless to act by itself; the dyschezia is then in part hysterical.

Dyschezia may be due to various other causes, such as weakness of the voluntary muscles of defæcation, the assumption of an unsuitable position during defæcation, and voluntary inhibition from fear of pain in diseases of the anal canal. But whatever the primary cause, the final result is the same. The conditioned defæcation reflex is lost, and the incomplete evacuation of the rectum results in the accumulation of fæces and consequent dilatation of the rectum.

Careful training is required from earliest infancy in order to develop the defæcation reflex. Neglect of this, together perhaps in some cases with a congenital deficiency of the muscle-sense of the rectum, is the cause of the dyschezia of infants, in whom the slight additional distension produced by the introduction of a finger or a piece of soap into the rectum results in an adequate stimulus.

The rectal muscle-sense is abolished or defective in diseases of the spinal cord in which the defæcation centre itself or the fibres connecting it with the brain are involved.

3. The third great class of constipation is due to the quantity of fæces formed being insufficient to produce an adequate stimulus in the pelvic colon and rectum, and to a less extent in the rest of the colon. The insufficient bulk of fæces is due to an inadequate quantity of food residue reaching the colon as a result of anorexia or of œsophageal or pyloric obstruction, or to unusually complete digestion and absorption of food, the result of a "greedy bowel."

Symptoms.—Many people regard themselves as ill if they do not have one action of the bowels a day; but this is really nothing more than a question of convenience, being found to suit the habits and diet of the majority of civilised people. Perfect health may be maintained by individuals who defæcate regularly two or three times a day, and by others who obtain an evacuation once in two, three or more days. The latter, so long as defæcation, when it does occur, is complete, can no more be regarded as diseased than those otherwise normal people, whose hearts beat only forty or fifty times a minute. The majority, however, although they may suffer no inconvenience for a considerable time, finally develop symptoms due to fæcal accumulation, gradually increasing quantities of fæces being retained. For practical purposes, therefore, an individual may be considered constipated if his bowels are not opened at least once in every 48 hours. A less frequently recognised variety of constipation is that in which insufficient fæces are excreted, although the bowels may be opened every day—a condition analogous to retention of urine with overflow.

It is important to distinguish the symptoms of constipation from those of the conditions which may give rise to it. There is no doubt that anxiety neuroses and hypochondriasis, epilepsy, asthma, nephritis, diabetes, painful pelvic disorders and many other diseases may be greatly aggravated by constipation. Apart from these conditions, headache, fatigue, anorexia and pigmentation of the skin may result directly from intestinal intoxication

and, with the exception of pigmentation, from the reflex effects of constipation. Toxic symptoms never develop unless stasis occurs in the cæcum and ascending colon, in which the fæces are still soft, and then only if it is associated with impairment of the functional efficiency of the liver, which normally destroys intestinal toxins or renders them innocuous, or of the kidneys, which normally excrete any toxins which have escaped the liver. Reflex symptoms, on the other hand, occur chiefly in dyschezia as a result of the pressure produced by hard fæces. The latter differ from the former by their almost instantaneous disappearance on defæcation.

Fæcal retention is a common cause of intestinal flatulence and colic. In rare cases a fæcal tumour may form, generally in the pelvic colon, and give rise to obstruction. A fæcal accumulation in the rectum may cause hæmorrhoids, pruritus ani, catarrhal proctitis and neuralgic pains in the perineum, back and down the legs. Hard fæces make defæcation painful, and their passage may give rise to anal ulcers.

Diagnosis.—It is comparatively rare for a patient to consult a doctor on account of constipation without having already attempted to cure himself

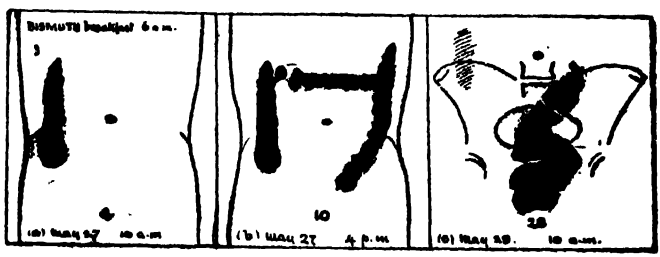


FIG. 17.—Dyschezia in a girl of 17, whose bowels had not been opened for 5 weeks when admitted to Guy's Hospital. (First case of constipation examined with X-rays: May 1907.)

with aperients. But no accurate diagnosis can be made until it has been ascertained whether he is actually constipated at all. The symptoms generally ascribed to auto-intoxication caused by intestinal stasis are often really produced by purgatives, which lead to the excessive production of toxins by hastening the half-digested contents of the small intestine into the cæcum, where fermentation and putrefaction are consequently increased. Purgatives also cause the contents of the transverse, descending and pelvic colon to be fluid instead of solid, so that absorption of toxins continues throughout the whole length of the bowel instead of in the cæcum and ascending colon alone. In spite of his probable protests the patient is instructed to see what happens if no drugs are taken for three days, an effort being made to open the bowels each morning. In most cases he loses his abdominal pain and his so-called toxic symptoms. The bowels are often opened daily, in which case a diagnosis of hysterical pseudo-constipation can be made—hysterical because the patient had suggested to himself, as a result of faulty education combined with the reading of pernicious advertisements, that he was constipated and required aperients to keep himself well, whereas a little psychotherapy, in the form of explanation of the physiology of his bowels and the origin of his symptoms and persuasion to try to open his bowels each morning

without artificial help, results in a cure. In some cases, however, the patient does not succeed in opening his bowels, although he may feel more comfortable than when he was taking drugs. A second abdominal and rectal examination should then be made. If no sign of organic disease is present and the rectum is found to be filled with fæces, dyschezia can be diagnosed. In spite of this the patient has no desire to open his bowels; a normal individual would feel an urgent call to defæcation under such conditions, but the rectum has dilated as a result of being constantly full of fæces and the call to defæcation is no longer felt.

In severe cases it is advisable to investigate the motor activity of the intestines with the X-rays, a barium meal being given after the patient has discontinued taking aperients. Ileal stasis should be diagnosed only if no trace of barium has reached the cæcum 6 hours after the opaque meal, or if a considerable quantity of barium-containing chyme is still in the end of the ileum 6 hours after evacuation of the stomach is complete. If most of the barium is still in the cæcum and ascending colon at the end of 24 hours, stasis is present, even if a little has passed to the more distal parts of the colon; but a faint shadow of the cæcum is often visible in normal individuals even 3 days after the meal. If the splenic flexure is reached in 24 hours, and the greater part of the barium is in the transverse colon at the end of 48 hours, there must be stasis in this part of the bowel. In dyschezia most or all of the barium has accumulated in the rectum in 24 hours (Fig. 17). In pelvic colon dyschezia a similar accumulation occurs in the pelvic colon, but the rectum remains empty.

Treatment.—Under no circumstances should the patient fail to make an effort to open his bowels after breakfast, even if he feels no desire to do so, and a call to defæcation felt at any other hour in the day should be obeyed at once. Sufficient time should be spent over the act of defæcation, and it is often advisable to pay two visits to the closet at short intervals, perhaps before and after breakfast. In order to prevent the temptation to hurry over defæcation, the closet should be clean, devoid of smell and properly warmed in winter. In dyschezia with weak abdominal muscles a footstool, 9 inches lower than the seat, should be provided. In many cases of dyschezia no treatment is required beyond explaining to the patient the nature and cause of his condition, and persuading him to give up aperients and to make an effort to empty his rectum, which he must realise is quite capable of doing its work. By perseverance it is generally possible to re-develop the lost conditioned reflex upon which normal defæcation depends.

It is most important to see that sufficient food is taken, as constipation is often as much due to its insufficient quantity as to its unsuitable quality. The diet should contain an increased proportion of vegetable foods, especially those which contain much cellulose and organic acids. Fresh or dried fruit should be taken three times a day, and green vegetables or salad should be eaten at lunch and dinner. Stewed prunes taken at breakfast, the number being regulated according to the degree of constipation, are especially valuable. Porridge and cream and wholemeal brown bread are also useful. Sufficient fluid should be drunk; a glass of cold water taken on rising in the morning often helps the bowels to act after breakfast.

The majority of cases of constipation can be cured without drugs if proper treatment is instituted at a sufficiently early stage. In dyschezia purgatives

act only when fluid stools are produced, colic and toxic symptoms often resulting and a considerable quantity of fluid and nutritive material being wasted. In the treatment of diseases which are aggravated by co-existing constipation, purgatives should be regularly given. They are also useful for making the stools soft when straining at stool is accompanied by danger, as in patients with weak hearts or high blood pressure. In colonic constipation, when non-medical treatment proves insufficient, purgatives must also be used, but an effort should be made to dispense with them at the earliest possible moment. The stool produced by an aperient should be normal in size and consistence; the dose should be so regulated that one stool is passed every day and the desire to defæcate is felt immediately after breakfast. It should cause no pain or discomfort, and should not irritate the intestinal mucous membrane sufficiently to lead to the appearance of mucus in the stools. An infusion of senna pods in cold water is particularly useful, as senna acts on the colon alone, and the dose can be regulated from day to day by the patient; an attempt should be made at intervals to reduce the number of pods by one at a time, until finally none may be required.

In constipation caused by a greedy bowel the bulk of the fæces must be increased by the administration of liquid paraffin or of an unirritating vegetable mucilage, such as isogel or coreine, which pass through the intestines without undergoing decomposition or absorption. These preparations are valuable when the fæces are hard and dry; they are therefore useful in other varieties of constipation besides that due to a greedy colon, as fæces always become hard and dry as a result of their abnormal retention in the bowel. In dyschezia the soft stools which result from their use are expelled with less difficulty than ordinary fæces. From 60 minims to 1 fluid ounce of paraffin or double the dose of a plain 50 per cent. paraffin emulsion should be taken immediately after one, two or three meals every day. Sixty grains of isogel or coreine, which absorbs water to form a bulky gelatinous mass which becomes intimately mixed with the fæces, is taken with one or more meals in addition to or as a substitute for paraffin.

The majority of cases of moderately severe constipation are more or less cumulative, excess of fæces being always present in the large intestines. It is therefore necessary that the colon should be completely evacuated before other methods of treatment are adopted. This can best be done by washing the colon out with a pint and a half or two pints of warm water run into it from a douche-can or funnel at low pressure through a soft catheter inserted just beyond the anal canal. The regular use of enemata, Plombières douches and of continuous intestinal lavage with many pints of fluid are very harmful both from a physical and psychological point of view.

It is essential in treating dyschezia to keep the rectum and pelvic colon empty, so that they may in time regain their normal tone and contractile power. This can be accomplished by the use of a 1-ounce enema consisting of equal parts of glycerin and water every morning, if a prolonged attempt to defæcate naturally has proved unsuccessful The strength of the enemata should be gradually reduced by replacing a drachm of the glycerin by water every other day until only water is used. As a rule the normal defæcation reflex and with it the tone and contractile power of the rectum slowly return.

When dyschezia is due to inability of the pelvic colon to empty its contents

into the rectum, six ounces of paraffin should be injected on going to bed and retained during the night; the bowels are then generally opened without difficulty in the morning. If, however, they fail to act, a plain water enema should be given.

When the sphincter ani is in a condition of spasm as a result of inflamed hæmorrhoids or an anal ulcer, or when the anal canal is congenitally too narrow or a stricture has followed an operation for hæmorrhoids, complete relief can be obtained by dilating the passage by means of diathermy applied locally through a conical electrode.

Regular exercise in the open air is a valuable means of preventing constipation, especially in individuals who follow a sedentary occupation. When any of the voluntary muscles of defæcation are weak, considerable benefit can be gained by the performance of remedial exercises every morning and evening. Special attention should be devoted to the levator ani muscles, especially in women in whom the pelvic floor has been injured during parturition, and in cases in which there is any tendency to prolapse on straining at stool (see p. 750). Stasis in the proximal part of the colon may be benefited by massage applied directly to the affected part. Its efficacy is greatly increased if the first treatment is given during an X-ray examination, as the masseur can then see the exact position of the colon and can find what manipulations have most effect upon it.

DIARRHŒA

Definition.—Diarrhœa is a condition in which unformed stools are passed. Defæcation generally occurs several times in the day, but mere frequency of defæcation is not diarrhœa, for this may even be associated with constipation. The bulk of fæces excreted in 24 hours is generally excessive, but this again may occur without diarrhœa, as excessive fæces are occasionally formed when the passage through the alimentary canal is not abnormally rapid. The one essential factor in diarrhœa is the abnormally rapid passage of the food residue through the alimentary canal.

Ætiology.—1. Excessive Stimulation of Motor Activity.—The most common cause of diarrhœa is the presence in the food of excess of the mechanical and chemical stimulants of intestinal activity. Thus over-indulgence in green vegetables, salads and especially unripe fruit is a familiar cause. Chemical irritants may also be swallowed in decomposing food, as in some cases of fish and meat poisoning, but food may also cause diarrhœa by giving rise to a bacterial infection of the intestine. Diarrhœa very frequently results from the habit of taking aperients, either in excess of what is required for the correction of chronic constipation, or even when the bowels left to themselves would act quite normally. Thus many of the symptoms often ascribed to constipation are really due to the diarrhœa caused by purgatives, as it results in the absorption of excess of poisons from the too fluid fæces.

Chronic diarrhœa is a common sequel of the acute diarrhœa following infection with a pathogenic organism which gains access to the intestines in contaminated food or water, and it may follow acute general infections such as influenza. In both cases the subsequent diarrhœa may be gastrogen-

ous (*vide infra*) and associated with achlorhydria resulting from gastritis caused by the infection, and not the direct result of bowel infection. In some cases the infection is derived from a septic focus in the mouth, nose or pharynx, and in rare cases recurrent subacute appendicitis is the source of a chronic infection of the colon. Some infective bacteria, such as those of the parenteric group, act chiefly on carbohydrates and may lead to excessive fermentation. Others, such as streptococci and various anaerobes, act on proteins and lead to putrefactive diarrhœa. Severe intestinal carbohydrate dyspepsia (p. 644) may give rise to chronic diarrhœa or alternating constipation and diarrhœa, and deficient digestion of proteins, resulting from either gastric or pancreatic insufficiency, may lead to a non-infective putrefactive diarrhœa. Deficient digestion of fat and deficient absorption of fatty acids and soaps give rise to fatty or soap diarrhœa respectively (*vide*, p. 626).

Diarrhœa is often gastric in origin. This *gastrogenous diarrhœa* may occur when the gastric juice is deficient or absent. An abnormal number of organisms reaches the intestines in these circumstances, as the partial protection afforded by the bactericidal action of the hydrochloric acid in the stomach is lost. As in addition to the digestion of meat in the stomach the connective tissue of meat and the cellulose of vegetables are normally softened by the hydrochloric acid of the gastric juice, undigested lumps of meat and fragments of vegetable leave the stomach and pass through the small intestine to the colon, where they are liable to undergo bacterial decomposition. The irritation of the mucous membrane of the intestines by the insufficiently divided fragments of food and by the products of bacterial decomposition leads to diarrhœa, which may become aggravated by secondary enteritis or entero-colitis if the irritation is sufficiently intense or prolonged. Similar gastrogenous diarrhœa may occur after the performance of a gastro-jejunostomy or partial gastrectomy, the food leaving the stomach with such rapidity that the intestines are overwhelmed with undigested and irritating food.

Lastly, chemical stimulants to intestinal activity may be produced in the body and excreted into the colon; this is the cause of diarrhœa in uræmia, hyperthyroidism and septicæmia.

2. Over-excitability of the Neuro-muscular Mechanism which controls the Intestinal Movements.—(*a*) *Post-prandial diarrhœa.*—Under normal conditions the entry of food into the empty stomach gives rise to a gastro-colic reflex, which is the chief stimulus to the movements of the colon. In most individuals this is followed by defæcation only after breakfast, as the pelvic colon is then full, and the sudden passage of fæces from it into the rectum gives rise to the call to defæcation. Sometimes the gastro-colic reflex is abnormally active. This may manifest itself after breakfast; a formed stool is passed first, but in the course of the next half-hour or hour one or more loose stools are passed in addition. In severer cases the bowels are also opened after dinner and less frequently after lunch, the stools again being often soft or fluid.

(*b*) *Nervous diarrhœa.*—It is not uncommon for a fright to result in the immediate passage of a semi-fluid stool. In some patients, who are often not otherwise neurotic, attacks of diarrhœa occur whenever they are in any place where it would be awkward for them to relieve themselves. When this has once happened, it is likely to recur under similar circumstances,

largely owing to fear that it will do so. Post-prandial and nervous diarrhœa are often associated together, a patient suffering from the former being particularly likely to feel an urgent desire to defæcate if he is at a dinner-party or in a railway carriage without a lavatory.

Diarrhœa, whatever its cause may be, tends to be worse after meals, especially breakfast, and it is occasionally also influenced by nervousness; it is important, therefore, to exclude some other primary cause before diagnosing a case as one of pure post-prandial or pure nervous diarrhœa.

(*c*) *Irritable bowel.*—When the mucous membrane of any part of the intestines is inflamed or ulcerated, mechanical and chemical stimulants are likely to produce an excessive reflex response, so that the diarrhœa which is probably already present is aggravated. Apart from this many people, who have lived in the tropics and have suffered there from dysentery or from diarrhœa due to some less defined cause, continue to be liable to diarrhœa for many years after their return to a temperate climate.

3. Organic Intestinal Disease.—(*a*) *Enteritis.*—The profuse, watery diarrhœa of acute food poisoning and acute infections such as abdominal influenza and septicæmia is a result of acute enteritis, which is generally accompanied by acute gastritis, especially if vomiting is present, but the colon is often spared. The irritating products of the excessive bacterial activity resulting from the stasis in organic obstruction of the small intestine give rise to enteritis; consequently diarrhœa and not constipation is almost always present in chronic small intestine obstruction. In all these conditions the chyme from the stomach passes so rapidly through the small intestine that they are quite fluid and very bulky when they reach the cæcum; they consequently act as an enema and are almost immediately evacuated, even if the colon remains quite healthy.

(*b*) *Colitis.*—Diarrhœa is a constant symptom of acute inflammation of the colon, except in the rare cases in which it is confined to the proximal part. Thus it is always present in ulcerative colitis and bacillary dysentery, in which the disease begins and remains longest in the pelvic colon and rectum, but it may be absent in mild cases of amœbic dysentery in which the cæcum alone is involved. Diarrhœa may occur in carcinoma of the colon, especially the distal part, before the lumen has been narrowed sufficiently to lead to fæcal retention. The diarrhœa in these conditions is due to irritation of the bowel by the products of bacterial decomposition of the albuminous exudate of the diseased parts, and in colitis also to deficient absorption of fluid by the inflamed mucous membrane.

Symptoms.—The chief and sometimes the only symptom of diarrhœa is the abnormally frequent passage of abnormal stools. In small intestine diarrhœa discomfort and colicky pain are often felt round the umbilicus. In severe cases of diarrhœa, whatever its origin, discomfort or even pain is felt over the whole of the lower part of the abdomen for a short time before the bowels are opened. It may be followed by a sensation of soreness, but the abdomen is neither tender nor rigid, and warm applications generally relieve it. Occasionally severe colic occurs, which may be temporarily relieved each time the bowels are opened or flatus is passed. The passage of a large and watery stool is often followed by a feeling of exhaustion and faintness, which may be accompanied by sweating and coldness of the extremities and occasionally even by syncope.

In severe cases of acute diarrhœa and in persistent cases of chronic diarrhœa the nutrition suffers and the patient loses weight; sometimes an extreme degree of emaciation results. When the diarrhœa is associated with abnormal bacterial activity in the intestines, especially if this is of the putrefactive type, symptoms of intestinal toxæmia may develop.

Diagnosis.—When a patient complains of diarrhœa, it is first necessary to ascertain whether the passage of fæces through the intestines is really taking place with abnormal rapidity. Many people think that frequent defæcation, particularly if the stools are in part fluid, is sufficient evidence that diarrhœa is present, whereas this is by no means necessarily the case. The stools of every patient supposed to be suffering from diarrhœa should be examined; if they are of a uniform semi-solid or fluid consistence, true diarrhœa is probably present, whereas numerous stools, if they are small and solid, and fluid stools containing small solid fragments suggest a diagnosis of pseudo-diarrhœa. In a doubtful case, 2 or 3 charcoal lozenges should be given with some food immediately after the bowels have been opened in the morning; each stool is now examined and the time which elapses before black fæces are passed is noted. If charcoal is seen in the stools within 12 hours, true diarrhœa is present; if in less than 4 hours, the small intestine must be involved as well as the colon. If no charcoal appears within 48 hours, constipation and not diarrhœa is present. A series of X-ray examinations after a barium meal affords a more accurate method of determining the rate of passage through the alimentary canal, and it has the advantage of showing in what part of the bowel the rate is excessive. In small intestine diarrhœa the head of the opaque meal may reach the cæcum within an hour or two; when the colon alone is involved, it arrives after the usual interval of 3 or 4 hours.

The most common cause of pseudo-diarrhœa is dyschezia; although the rectum is never properly emptied, the patient feels a constant desire to open his bowels, and as a result of his efforts a very small quantity of hard fæces may be passed. The constant presence of fæces in the rectum calls forth the secretion of clear mucus. In slight cases there may be nothing more than a thin layer of mucus over the hard lumps of fæces; in severer cases a larger quantity of fluid mucus, which is often stained brown, is passed either alone or with hard particles of fæces. In all such cases the discovery of solid fæces in the rectum immediately after the bowels have been opened should remove any further doubt as to the diagnosis. A growth of the rectum or pelvic colon, and less frequently a growth in other parts of the colon, though rarely on the proximal side of the splenic flexure, may lead to pseudo-diarrhœa, fæces being retained above the growth, whilst the serous and often blood-stained exudation from its surface, mixed with mucus produced by the irritant action of the exudation on the mucous membrane below it, are passed at more or less frequent intervals, so that the patient regards himself as suffering from diarrhœa. The character of the stools should at once make it obvious that endoscopic and radiological examinations are required, even if nothing abnormal is felt on abdominal or rectal examination.

When it is known that genuine diarrhœa is present, it is next necessary to determine whether it is due to a functional or an organic cause. The history is often a great help. Post-prandial or nervous diarrhœa of long

duration is generally gastrogenous. An acute onset suggests that the cause is some toxic or infective agent, whereas a more gradual onset of chronic diarrhœa in a middle-aged individual, who has hitherto been regular or constipated, suggests the possibility of a growth. A careful abdominal and rectal examination should be made in every case; the former may reveal the presence of a tumour or an abnormally dilated or contracted condition of the colon; by means of the latter the existence of ulcerative colitis may sometimes be recognised, as well as the presence of a growth in the rectum or pelvic colon. In doubtful cases an endoscopic examination should also be made before deciding that the diarrhœa is functional in origin, as the mucous membrane of the accessible part of the colon is almost always involved when diarrhœa is due to some form of colitis.

The examination of the stools is of the greatest importance, as it gives valuable indications for treatment as well as helping in diagnosis. In small intestine diarrhœa the stools are watery, whereas in colonic diarrhœa they are unformed but not fluid. The presence of mucus indicates active inflammation, and blood with or without pus simple or malignant ulceration. Thus the watery diarrhœa caused by enteritis can be distinguished from that caused by excessive irritability or irritation of the small intestine by the presence of flakes of mucus floating in the fluid fæces. In acute enteritis the mucus is often blood-stained and microscopical examination shows the presence of red corpuscles, degenerated epithelial cells and pus cells; as the inflammation subsides the mucus becomes cell-free and finally disappears. Similarly the unformed, but not watery fæces of an irritable or irritated colon can be distinguished from the fæces of colitis by the presence of mucus, pus and blood in the latter.

The presence of excess of starch, meat fibres or fat indicates a small intestine diarrhœa. Excess of undigested starch is found on microscopical examination in fermentative diarrhœa, and of striated muscle fibres in putrefactive diarrhœa. The fæces are often frothy and have an acid smell and reaction when fermentation is excessive; they are alkaline and have a putrefactive odour when excessive putrefaction is present.

The stools passed when fat is insufficiently digested or absorbed are easily recognised by their pale colour and increased bulk. If the excess is in the form of neutral fat, the stools are oily (*fatty diarrhœa*), and pancreatic insufficiency can be diagnosed; striated meat fibres are also likely to be present. This condition is, however, rare in the absence of jaundice caused by obstruction of the common bile duct. More frequently most of the fat is present as fatty acid and soaps (*soap diarrhœa*), showing that pancreatic digestion is normal, but that absorption is deficient. This may result from absence of bile salts in obstructive jaundice, from the functional disorder of the small intestines which is the cause of *cœliac disease* in children, and *sprue* and *non-tropical sprue* in adults. Soap diarrhœa is also caused by obstruction of the lacteals by tuberculous, simple inflammatory or secondary malignant disease of the mesenteric glands. In the case of the latter the stools becomes perfectly normal on a fat-free diet, the digestion of meat and vegetable food being unaffected. In soap diarrhœa almost all the calcium in the food combines with fatty acid to form calcium soap in these conditions; the blood calcium is consequently diminished, and tetany may result. In children growth is greatly impaired, and deformities result from the softness

of the long bones. The inability of the intestines to absorb fat may be associated with deficient absorption of sugar, iron (causing microcytic anæmia), hæmopoietin (causing pernicious anæmia), neuropoietin (causing subacute combined degeneration of the cord), and vitamins A, B, D, E and K.

A bacteriological examination should always be made in the hope that the nature of any infection which is present may be discovered.

Prognosis.—If thorough treatment is instituted from the onset, the prognosis of diarrhœa is good, unless it is due to some serious organic disease. If, however, it is neglected, strict treatment must be continued for a prolonged period in order to be successful. This is particularly the case when the diarrhœa is infective in origin.

The tendency to post-prandial and nervous diarrhœa often remains throughout life, though considerable improvement and even a cure can result from treatment. Unlike other forms of diarrhœa, they rarely affect the general health, and are chiefly troublesome on account of the inconvenience they cause.

Treatment.—*Acute diarrhœa.*—The patient should be kept warm and at rest in bed until the attack has completely subsided. If it is due to food poisoning and he is seen within 12 hours of the onset, he should be given from ½ to 1 ounce of castor oil to clear the irritant material out of the small as well as the large intestine, unless the diarrhœa is so severe that it appears probable that this has already occurred. No food should be given for 24 hours or even longer in severe cases, but the patient may drink as much water as he likes. Sweetened arrowroot made with water should then be given, but nothing else until the diarrhœa has ceased. Milk, junket, bread and butter, and milk puddings are next allowed, after which a gradual return should be made to an ordinary diet, the speed with which this is done depending on the severity of the case. The only drugs which are of real use in acute diarrhœa are kaolin and opium and its alkaloids. A tablespoonful of kaolin should be given three times a day. If the diarrhœa shows no signs of abating after 24 hours, codeine should be given, the dose being regulated according to the severity of the diarrhœa and the general condition of the patient, but sufficient must be given to stop the diarrhœa in 48 hours. If the diarrhœa is accompanied by vomiting, a test-meal should be given about a month later, even in the absence of all symptoms, as the accompanying acute gastritis may have led to achlorhydria, which is likely to give rise to chronic diarrhœa or other trouble later unless the underlying chronic gastritis is overcome.

Chronic diarrhœa.—In all cases of chronic diarrhœa recovery occurs most rapidly if the patient remains in bed during the first few days of treatment. In many instances the diarrhœa, which may have been present for months, disappears in a few days, and the patient may even become constipated. Unless, however, other treatment is instituted, the diarrhœa is very likely to return as soon as he gets up again. As the improvement which results from staying in bed is due in part to the rest and in part to warmth, it is important for the patient to avoid over-exertion and to keep his abdomen warm by means of a woollen binder for a considerable period after the symptoms have disappeared. Exposure to cold should be avoided as much as possible, and if the patient feels chilled at any time he should have a hot bath and go to bed at once; by these means he is likely to prevent a recurrence. Patients who have recently suffered from chronic diarrhœa should never go

to the tropics, and they should even avoid visiting the southern parts of Europe, as a slight intestinal attack from bad food is likely to have much more serious results with them than in an individual who has not before suffered from any intestinal disorder.

The successful treatment of chronic diarrhœa depends upon the recognition of its cause. The treatment of diarrhœa which is secondary to organic disease of the intestines, such as colitis and cancer, is considered elsewhere.

1. Excessive Stimulation of the Intestinal Movements.—Whatever the actual cause of the diarrhœa, it is important to avoid anything which could produce mechanical irritation of the colon. The food should be thoroughly chewed, and anything, such as new bread, cheese and tough meat, which is difficult to break up completely, should not be eaten. The patient must avoid all raw vegetables in salads and pickles, and cooked green vegetables are allowed only as purées. The pips and skins of fruit, whether raw, cooked or in jam, and currants, raisins and lemon peel in puddings and cakes must be avoided.

For the treatment of *fermentative diarrhœa*, *vide* Intestinal Carbohydrate Dyspepsia (p. 645). A lacto-vegetarian diet is most suitable for *putrefactive diarrhœa*; no meat should be allowed until the diarrhœa has ceased for 4 weeks, and high game and over-ripe cheese should be permanently avoided.

Fatty and *soap diarrhœa* stops at once on a fat-free diet. In severe cases, in which obstruction of the lacteals is present, it may be necessary for the patient to continue with this diet for the rest of his life.

Gastrogenous diarrhœa rapidly improves on the diet already described as suitable for putrefactive diarrhœa, but a relapse is certain to follow a return to an ordinary diet unless the achlorhydric gastritis is properly treated (*vide* p. 586). When the diarrhœa is infective in origin, a teaspoonful of a fresh liquid culture of *B. acidophilus* should be given fasting each morning.

2. Nervous and Post-prandial Diarrhœa.—Nervous diarrhœa is often completely uninfluenced by diet, but drugs, which diminish the activity of the gastro-colic reflex either peripherally or centrally, are very effective. A mixture containing 5 grains of potassium bromide and 5 minims of tincture of belladonna taken immediately before meals is all that is required in mild cases; in severer cases a small dose of codeine should be added. The exact dose of each drug must be varied to suit each patient, as different individuals react very differently to these drugs, especially to belladonna. When the diarrhœa has been completely controlled, the quantity of each drug should be gradually reduced; then the doses before lunch and dinner, and finally that before breakfast, can be discontinued. In some cases it is advisable to allow the patient to have a pill containing belladonna and codeine always with him, so that he can take one before going to a dinner-party or on any other occasion when he fears that he will have diarrhœa. He soon learns to trust so thoroughly in his pill that it probably acts more by suggestion than in any other way, and the dose can accordingly be progressively reduced until it is infinitesimal.

As in many cases of diarrhœa due to other causes the bowels act most frequently after meals, the treatment just described is often of use in conjunction with that required for the primary condition.

Arthur F. Hurst.

EPIDEMIC DIARRHŒA IN CHILDREN

Synonyms.—Summer Diarrhœa; Infective or Infectious Diarrhœa; Acute Gastro-Intestinal Infection; Acute Ileo-Colitis; Cholera Infantum.

The form of diarrhœa here spoken of used to be one of the chief scourges of infant life, but is certainly much less common now than formerly. It prevails epidemically in institutions, although sporadic cases may be met with at any time, and in hot seasons may become widespread, especially in large towns. It chiefly affects children below the age of 5, but is most fatal in the first year. Boys are more susceptible than girls.

Ætiology.—It is generally agreed that the disease is caused by infection with micro-organisms; but in spite of much research the bacteriology is by no means clear. It would appear that all cases are not due to the same organisms, and various members of the coli-typhoid-dysentery group have been blamed at different times. Recently particular attention has been paid to the Sonne strain of dysentery bacillus.

Next in importance as an ætiological factor must be put the influence of unhygienic surroundings, such as dirt, overcrowding, a contaminated milk supply, and want of cleanliness in feeding utensils. The infection is probably often conveyed by dust, and flies may act as carriers.

Any digestive derangement in the child may predispose to infection, and bottle-fed infants are specially liable. The disease appears to be to some degree contagious, and if introduced into a ward is apt to spread to unaffected infants. The influence of age and sex have already been referred to.

Pathology.—The changes found after death may be surprisingly slight, considering the severity of the disease, and vary materially in different cases and epidemics. As a rule the mucous membrane of the stomach and intestines is in a condition of "mucous catarrh." There may also be areas of congestion, with here and there small petechial hæmorrhages. The lymphoid tissue of the alimentary canal is often swollen, and in severe and protracted cases the solitary follicles in the colon and lower ileum may exhibit superficial ulceration.

Other organs, such as the liver and kidneys, show fatty or parenchymatous degeneration, whilst the lungs are often congested and œdematous, with, in protracted cases, patches of broncho-pneumonia in the lower lobes.

Symptoms.—The clinical picture is often very complicated, and if it is to be understood it is essential to realise that the disease is a general infection and not merely a disorder of the alimentary canal. The supervention of dehydration, acidosis or nephritis, with their own clinical manifestations, tend still further to perplex the observer and make it impossible for him to decide to what extent the symptoms are due to the primary infection or to these secondary developments.

The disease may start insidiously, with a gradually increasing diarrhœa; or the onset may be abrupt, with a rapid rise of temperature and early prostration. The diarrhœa is not necessarily a pronounced feature, and the worst cases are often those with fewest stools. The character of the motions varies; but in the early stage they are usually green, slimy and ill-digested, becoming dark and watery later. In the choleraic cases they are of the profuse "rice-water" type. When the colon is affected, visible mucus and blood may be

passed with much straining. The discharges are usually attended by colicky pain and the passage of flatus. Vomiting is generally present at the onset, but varies greatly in amount. The temperature is always elevated at some period of the disease, but the height, duration and course of the pyrexia are very inconstant. Hyperpyrexia may supervene towards the close in fatal cases. Prostration and circulatory failure are early features, and are shown by depression of the fontanelle, pallor, pinched features, an inelastic skin due to dehydration and coldness of the extremities. Where "intoxication" is a factor, consciousness becomes impaired, and the infant passes into a state of stupor, with intervals of restlessness, which may result in complete coma, sometimes terminating in convulsions. If acidosis is present, the respiration may show the characters of "air-hunger."

The urine is scanty, highly acid and contains a little albumin and a few hyaline casts. Acetone bodies may be present.

Course.—The course of the disease varies greatly. In the severest cases, especially those of the choleraic type, death may ensue within a few hours of the first onset of symptoms. In the milder forms the acute symptoms last for 2 or 3 days, and then gradually the prostration passes off and the stools assume a normal character. Only too often, however, the improvement is but partial, and the child lapses into a marasmic condition, with continued looseness of the bowels, from which recovery may only take place gradually. In all cases relapses, brought on either by re-infection, by meteorological conditions, or by injudicious feeding, are extremely common and apt to prove fatal.

In children above the age of 2 the disease usually assumes a milder form —prostration is not so severe and the range of temperature lower. Vomiting, also, is a less prominent symptom than in infants. Complete recovery is more frequent, and relapses and the continuance of the disease in a chronic form are rare.

In the special type of the disease commonly spoken of as "cholera infantum" the invasion is always abrupt, with a rise of temperature, followed by profuse vomiting and purging. Death usually ensues in a few hours, and is commonly attended by hyperpyrexia.

Diagnosis.—The diagnosis has to be made from simple non-infective diarrhœa, and for the increasingly common forms of diarrhœa secondary to respiratory tract and middle-ear infections. At first the differentiation may be impossible, but continued high temperature, early prostration and failure of rapid improvement on stopping food point to an infective origin. Careful physical examination will exclude secondary types. Epidemic prevalence is in favour of the primary variety. The nervous symptoms may simulate those of meningitis, but in case of doubt a lumbar puncture will determine the diagnosis. Very acute cases in which the colon is much involved, may resemble intussusception, but in the latter the onset is more dramatically sudden, the vomiting, collapse and passage of blood greater, and fever less, whilst in epidemic diarrhœa abdominal rigidity and tumour are absent.

Prognosis.—It is impossible to give any estimate of the fatality of diarrhœa, as it depends greatly on the type of the disease, and on the age, general condition and surroundings of the child, besides varying greatly in different epidemics. The younger the infant, and the poorer its general

nutrition, the worse is the outlook. The existence of rickets also greatly aggravates the danger. The frequency of the stools is of less importance in estimating the chance of recovery in any given case than the amount of prostration and the degree of inelasticity in the skin. Cases with prolonged high temperature and those of the choleraic type usually do badly. Persistence of vomiting also is a bad sign.

Treatment.—Unfortunately there is no specific treatment, and the principles to be aimed at are: (1) to stop the infection; (2) to eliminate and neutralise toxins; (3) to combat collapse; (4) to arrest the vomiting and purging.

1. In attempting to stop further infection, general hygienic measures are of great importance. Whenever it is possible, the child should be removed from a town, and isolated in a large, airy and well-ventilated room. Napkins should be removed and disinfected as soon as they are soiled, and the greatest cleanliness should be observed in regard to the feeding utensils and the nurse's hands. The collection of these cases in institutions should be avoided as far as possible.

If the case comes under observation early, an initial purge of castor oil or, if there is much vomiting, of calomel should be given to clear away decomposed matter from the bowel. Milk, which is the vehicle of infection, should at once be stopped, and for the first day or two the diet should be limited to half-strength normal saline, barley-water, weak tea, rice-water, 5 per cent. glucose, or weak broths, all of which may be given freely.

2. In order to favour the elimination of toxins, the action of the skin and kidneys should be promoted as much as possible. To this end, if the skin is very inelastic, tepid packs are useful, and these may be continued, if necessary, for several hours on end. If the urine is scanty, fluids should be given freely.

In the early stages of the disease no attempt should be made to arrest the diarrhœa entirely, as the retention of poisons would then be favoured. In addition to the initial purge, irrigation of the colon is a valuable aid in removing toxic material. Normal saline administered at a temperature of 100° F. through a rectal tube or large-sized red rubber catheter is the best solution to employ.

3. Collapse has to be obviated by saline infusion and the use of stimulants. Four ounces of normal saline may be injected under the skin of the flank every 6 hours, or saline and dextrose may be given intraperitoneally or into a vein. A continuous drip of normal saline is often life-saving.

Of stimulants, one of the best is alcohol. Ten to 15 drops of brandy may be given in a little water every 3 or 4 hours, or oftener; it should not be added to the feeds. Camphor is useful, and niketham ide (coramine) and adrenaline are also of value. If the collapse is extreme, recourse may be had to the mustard bath.

4. The arrest of the vomiting and especially of the diarrhœa is really a secondary object of treatment. For the vomiting, lavage of the stomach with normal saline is the best treatment, particularly in the early stages, and a poultice may be applied to the epigastrium. Drugs are of little help, but small repeated doses of calomel (*e.g.* $\frac{1}{6}$ grain every hour for six doses) are sometimes useful. Chlorbutol in 1-grain doses may also be used cautiously.

As has already been pointed out, no active steps should be taken to arrest the diarrhœa at the onset. If it continues, however, and seems to be contributing to the exhaustion, one may try to reduce the frequency of the stools. In the early stages, small repeated doses of castor oil are useful for this purpose, and later, when the tongue is clean, bismuth, chalk, catechu and other astringents, as in the case of simple diarrhœa, may be used. A powder composed of 5 grains of bismuth carbonate, with $\frac{1}{8}$th grain each of Dover's powder and calomel, is also a frequent prescription at this stage. Opium should not, however, be given at the outset, and it is best withheld so long as prostration is marked and the temperature high. When prescribed, it may be given in the form of the tincture in the proportion of 1 minim for every year of the child's age. It is specially indicated when the motions are frequent and attended by colic and tenesmus. In cases of the choleraic type, with much vomiting and profuse purging, morphine may be given hypodermically with great advantage. The dose for a child of 1 year is $\frac{1}{30}$th grain, with which $\frac{1}{600}$th grain of atropine may be combined. This may be repeated in an hour if the symptoms have not abated.

"Intestinal antiseptics" are of little help, and may easily be injurious. The best are salicylate of bismuth, salol and resorcinol. If the stools are very watery, nitrate of silver is the most powerful astringent.

After the acuter symptoms have passed off one must return very gradually to ordinary diet. Milk should be given at first malted or fully peptonised and freely diluted with lime water, or condensed or low fat dried milk, or one of the patent foods may be used in place of it. A feed may be given every 4 hours, and water between if the child is thirsty. Any return of the vomiting or diarrhœa must be the signal for again giving up milk in any form. During convalescence change of air and mild iron tonics are of service in restoring the child to complete health. Relapses, which are frequent, must be guarded against with the greatest care.

ROBERT HUTCHISON.
ALAN MONCRIEFF.

HILL DIARRHŒA

Definition.—A peculiar form of gastro-intestinal derangement occurring in Europeans living at high altitudes in India, Ceylon and elsewhere during the hot season, characterised by dyspeptic symptoms, abdominal flatulence and the passage of pale-coloured or white, frothy, fluid stools early in the morning.

Ætiology.—The condition occurs in the Himalayan hill stations of India during the rainy season, and the highlands of Ceylon, Europe and South America, at elevations of 6000 feet or over. Europeans of both sexes and all ages are liable, and in some years the condition has affected a large portion of the hill population, as in the Simla epidemic of 1880. The cause has been variously attributed to the mica content of the drinking water, to its bacterial contamination, with resulting infection of the bowel, as well as to a physiological breakdown of the gastro-intestine under conditions of low barometric pressure and high humidity: the latter view is possibly correct.

Pathology.—Little is known either of the clinical pathology or morbid

anatomy of the disease, the nature of which will remain obscure until it has been investigated along biochemical lines, such as has recently been done in sprue.

Symptoms.—The symptoms are flatulence and abdominal distension associated with morning diarrhœa. Defæcation is urgent and generally first occurs about 5 a.m.; subsequently the bowels may be opened four or five times before noon, after which the patient is comfortable. The stools are copious, fluid, pale-coloured or white, frothy, and generally not objectionable in odour. Often the condition is transient, but if it persists considerable loss of weight may ensue. The stools are said to contain an excess of fatty acids, soaps, undigested food remnants and yeasts, while stercobilin as such is either decreased or absent. These findings are similar to those encountered in tropical sprue, and in view of the marked abdominal distension, intestinal flatulence and gaseous nature of the stools, it would appear that, as in tropical sprue, the intestinal breakdown is characterised by defective absorption of certain food elements—especially fat and glucose.

Prognosis.—This is generally quite good; the only danger is that the condition may develop into sprue, and Rogers states that 20 per cent. of his Calcutta cases commenced with hill diarrhœa.

Treatment.—Until more is known regarding the biochemical nature of the gastro-intestinal breakdown, treatment must remain empirical. An initial dose of oleum ricini (min. 240) and tinct. opii. (min. 15), rest, warm clothing and milk diet are generally advised, but probably a high protein, low fat, low carbohydrate diet, such as sprulac, would prove more valuable. Dilute hydrochloric acid in 60 minim doses after food may be tried, and pepsin has also been advocated. Crombie used to give 60 minims of liq. hydrarg. perchlor. 15 minutes after food. Should these measures not suffice the patient must return to the plains.

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CŒLIAC DISEASE

Synonyms.—This disease was first described by Gee in 1888 under the title of "The Cœliac Affection." Cheadle redescribed it in 1903 as "Acholia," and Herter in 1908 as "Intestinal Infantilism." It is sometimes spoken of in America as "Chronic Intestinal Indigestion," but in this country the term "Cœliac Disease" is now generally applied to it.

Definition.—A wasting disease of childhood characterised by the passage of large, pale, offensive stools which contain an excess of split fat, and leading to emaciation and arrest of growth; various complications due to avitaminosis may be superadded.

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rickets and the blood chemistry is also similar. The essential pathogeny of the disease appears to be a failure in fat and carbohydrate absorption of obscure causation. The ordinary changes of enteritis are not found.

Symptoms.—The disease begins insidiously between the ninth month and the end of the second year. The child loses appetite, fails to thrive, and has slight diarrhœa. Soon the characteristic stools appear. They are large, but not necessarily frequent, pale, extremely offensive and sometimes frothy and fermenting. On chemical examination they contain from 40 to 60 per cent. of split fat instead of the normal 25 per cent., but the amount of unsplit fat present is not altered. Meanwhile the emaciation progresses, the face being least affected by it and the buttocks most. The abdomen, by contrast, is prominent, doughy and distended. Along with these physical signs there is a change in mentality. The child is often remarkably precocious, but is irritable, hysterical and "difficult," especially during the exacerbations. There is frequently a profound anorexia, and muscular weakness may be extreme.

Complications.—Various deficiency symptoms are apt to appear as the result of avitaminosis induced either by impaired fat absorption or by the character of the diet which treatment demands. Rickets may show itself either early, or, after the age of 7, in the "late" form, with genu valgum as its main sign. Symptoms such as œdema and absence of reflexes may suggest beriberi and have been attributed to deficiency of vitamin B. Scurvy is not uncommon, and attacks of tetany may occur in association with a low blood calcium.

Diagnosis.—At the outset the disease may be impossible to recognise, but when the characteristic stools appear diagnosis is easy. Arrest of growth is of great diagnostic value. The distended abdomen may suggest tuberculosis, especially if distended, atonic bowel with fluid fæces mimics the signs of ascites. Cœliac disease presents many points of resemblance to sprue, but the latter is rare in childhood, and in cœliac disease the blood shows a secondary anæmia and not the megalocytic type characteristic of sprue.

Course and Prognosis.—The disease runs a prolonged course with many ups and downs and is peculiarly prone to relapse. It may last into adult life (cases of "non-tropical sprue" may be examples of unrecovered cœliac disease) but usually tends to recovery before puberty. The mortality may be put down at about 10 per cent., and death, when it occurs, is usually due to intercurrent disease. During the active phases of the disease growth is arrested, and even after recovery the patient may be permanently stunted (intestinal infantilism).

Treatment.—Apart from general hygienic measures treatment is essentially dietetic. A diet high in protein, low in fat, and with no carbohydrate (at the outset at least) is the ideal to aim at. It may consist at first of a dried "protein" milk with the addition of underdone scraped meat, white of egg, broth, jellies, etc. Later, small quantities of fat in the form of bacon and butter are added with carbohydrate mainly in dextrinised form (Mellin's Food, grape-nuts, rusks, crisp toast, etc.). Over-ripe bananas often have a beneficial effect. Care must be taken to supply the necessary vitamins in order to ward off complications. Vitamins A and D may be given as radiostoleum; B, as yeast extract; C, as ascorbic acid, 25 mgm. daily. A small

dose of castor oil should be administered when abdominal distension is troublesome; otherwise there is no indication for drugs.

ROBERT HUTCHISON.
ALAN MONCRIEFF.

IDIOPATHIC STEATORRHŒA

Synonyms.—Adult Cœliac Disease; Non-tropical Sprue; Gee-Herter Disease; Herter-Heubner Disease; Gee-Thaysen Disease.

Definition.—This is the adult form of cœliac disease (see above). With certain very rare exceptions it arises in childhood, though some cases remain unrecognised until adolescence or adult life is reached. The main features are: Fatty stools, with or without diarrhœa, and sometimes with dilatation of the colon; tetany; osteomalacia; anæmia of various types; skin lesions; and frequently infantilism.

Ætiology.—This is unknown. Patients affected have not lived abroad, and the disease cannot be classed with sprue, though resembling it in many respects. The affection is neither familial nor congenital. It is slightly more common in females than in males. The disease has been described in the Scandinavian countries, Germany, Switzerland, France, Great Britain and America.

Pathology.—The underlying disturbance is interference with the total function of the small intestine, and this may be referred to as chronic jejuno-ileal insufficiency. Attempts to demonstrate an anatomical lesion have failed even with the microscope. The symptoms develop in spite of an adequate diet, and the patient starves in the midst of plenty. Deficient absorption of various components of the diet explains many of the signs and symptoms. The fat, although split, cannot be digested and produces steatorrhœa. On a low fat diet, the percentage of total fat in the stools forms on the average more than 25 per cent. of the total weight of the dried fæces; on a normal diet this figure reaches 40 to 60 per cent. The fats are mainly split fats, the figure for neutral fat not exceeding 3 per cent.

Sometimes there is carbohydrate dyspepsia, with production of gas which distends the bowel. This arises from the bacterial hydrolysis of starch following the failure of amylolytic digestion by succus entericus. Sugar is poorly absorbed, and the blood sugar curve after glucose is much flatter than normal. Similarly, proteins are ill absorbed and the blood urea is often below normal. Poor absorption of salts is seen in the low figure for serum calcium, usually 8 mg. per 100 c.c., and the low or normal plasma phosphorus. The height of the plasma phosphatase coincides approximately with the degree of active change in the bones. Calcium balance estimations reveal high figures for fæcal output, and very low figures for urinary output.

Defective absorption of iron is followed by hypochromic anæmia; and megalocytic anæmia may appear, presumably because of failure to utilise the anti-pernicious anæmia factor. Occasionally xerophthalmia and toad-skin appear, proclaiming vitamin-A deficiency. Sore tongue, cheilosis, anosmia and pellagra-like skin result from shortage of the vitamin-B complex. Osteomalacia occurs from deficiency of vitamin D. A tendency to sudden hæmorrhages indicates vitamin-K deficiency. It is associated with

a prolongation of the coagulation time and a reduction in the blood prothrombin concentration.

Symptoms.—The presenting symptom is either diarrhœa, pain in the bones with deformity, or tetany. The stools are bulky and pale, though not always conspicuously frequent. The wasting and distended abdomen so constantly found in children with cœliac disease is not a noticeable feature, even though severe diarrhœa be present. The skin shows a dirty putty-coloured pallor, and the hair is fine, mud-coloured and liable to turn grey at an early age. In 50 per cent. of cases a skin eruption is present on the limbs, and to a lesser extent on the trunk. The lesions are moist red abraded areas with scaly brown pigmented borders, resembling pellagra. In 60 per cent. of cases the fingers are clubbed. By means of the slit-lamp small flaky opacities are to be seen in the various layers of the lens. They never progress sufficiently to interfere with vision.

All cases show some degree of skeletal deformity, including genu valgum, bending and bowing of the bones, distortion of the pelvis, beading of the ribs and spontaneous fracture. In 60 per cent. of cases there is dwarfism, but this is not necessarily associated with mental or sexual infantilism. The male genitalia are poorly developed, and the voice high pitched. In women the onset of menstruation is delayed. The disease is usually accompanied by sterility, but should pregnancy occur there is often an acute exacerbation of symptoms. Pelvic deformity may interfere with the normal course of labour. Tetany occurs in almost all cases. Seventy per cent. of patients describe recurrent attacks of tinglings in the fingers and hands, followed by carpo-pedal spasms. These interfere with writing, piano-playing, and even with walking. In 30 per cent. of patients tetany is latent only, its presence being detected on eliciting the Trousseau or the Chvostek signs.

The blood picture is either normal or shows (i) hypochromic anæmia, (ii) hyperchromic megalocytic anæmia, or (iii) erythroblastic anæmia. This polymorphic character of the blood changes is frequently found when anæmia is associated with gastro-intestinal lesions. Achlorhydria is uncommon, occurring in less than 20 per cent. of all cases and in only one-third of those with hyperchromic megalocytic anæmia. This anæmia is therefore not Addisonian pernicious anæmia, a fact confirmed by the observation that it yields to treatment by vitamin-B concentrates. Hæmorrhagic phenomena are rare, even in cases treated for a long time by means of a low-fat diet. They include hæmatemesis, melæna, epistaxis, menorrhagia, hæmaturia, hæmarthroses, subcutaneous hæmatomata and intractable bleeding from wounds. Scurvy is very rarely seen.

In long-standing cases opaque enema examination shows dilatation of the colon, and sometimes this assumes the proportions of megacolon. In all cases radiographs of the skeleton reveal osteoporosis, and if the epiphyses have not united the translucent cup-like metaphyses of rickets are present. Many cases show fine transverse lines of increased density of bone immediately to the diaphyseal side of the metaphyses of the long bones. Distortion of the limbs, spine and pelvis are common.

Diagnosis.—A denial of residence in a country where sprue is endemic is enough to rule out that disease. Chronic jejuno-ileal insufficiency has been observed in gastro-jejuno-colic fistula. Here the history of previous gastro-enterostomy simplifies the diagnosis. Rarely the syndrome of steatorrhœa,

tetany and megalocytic anæmia is produced by diseases which cause obstruction of the lacteals. These include tuberculosis, lymphogranuloma and lymphosarcoma affecting the mesenteric lymph nodes.

Prognosis.—The results of treatment are disappointing in the adolescent and adult cases compared to what is seen in children. Some respond satisfactorily and remain well under treatment. In the majority all that is accomplished is the alleviation of one or more symptoms and the temporary onset of the downward progress. It is none the less gratifying to see the great improvement in the anæmia of many of the cases, and the recovery from the pain and disability of osteomalacia in others. Often there is a great change for the better in the mental outlook of the dwarfed, crippled, anæmic patient as he is gradually relieved of his disabilities. Unfortunately one group of symptoms and signs may clear up completely, and yet the patient may die in inanition. Thus extensive, moist, red excoriated skin lesions may heal under treatment with marmite, yet relapses of diarrhœa and tetany may result in the death of the patient, the skin remaining normal.

Treatment.—This presents great difficulties. While nothing can be done to remedy the primary defect much care can be given to mitigate as far as possible its consequences. The steatorrhœa must be controlled by a low-fat diet. No patient with this disease can be given the amount of fat found in the average diet without risking the occurrence of diarrhœa. The diet should be high in calcium content. The best way to secure a low-fat high-calcium intake is to use skimmed milk and preparations of calcium caseinate, such as casec or laitproto. The items of such a diet include meat, chicken, bread, a scraping of butter, oatmeal, potato, rice, tea, sugar, skimmed milk, cheese, jam, cabbage, apple, banana and tomato. These items can be arranged as follows: carbohydrate 325 gm., protein 90 gm., fat 30 gm. and calcium 2 gm. Sometimes gas formation from carbohydrate fermentation is a prominent symptom, and then the intake of starch should be strictly controlled, and the administration of diastase may be useful.

When tetany occurs, calcium lactate should be given fasting in doses of 5 gm. three times a day. In emergency 20 c.c. of a 5 per cent. solution of calcium chloride or gluconate may be injected into a vein, and if administered very slowly no ill effects are produced. Vitamin D should be given in every case in which there are clinical or radiographic signs of rickets, osteomalacia or osteoporosis. General ultra-violet irradiation is also of value. These measures may relieve bone pain, though any relapse of diarrhœa is liable to interfere with this good effect. Cod-liver oil, or any other form of vitamin D in an oily medium, is contra-indicated in view of the defective fat absorption. Vitamin D should be given in a solid medium—calciferol tablets two or more daily.

Treatment of the anæmia must depend upon examination of the blood. When it is hypochromic or erythroblastic, large doses of iron should be prescribed until the hæmoglobin figure reaches normal. This usually occurs with 30 gr. of Blaud's pill or 6 gr. of ferrous chloride three times a day. When hyperchromic megalocytic anæmia is present, injections of an active liver extract should be repeated until the red cell count remains at 5 millions. The initial dose may be 1 to 4 c.c. daily, and the maintenance dose is often 1 c.c. per week. Marmite by mouth may be used instead of liver extract, as much as 12 gm. daily usually being required. Whatever the form of the

anæmia, it is essential to remember the importance of adequate dosage. For one week in each month a prophylactic dose of vitamin K or its derivative should be given by mouth. A suitable dose is 30 mg. of methyl-naphthoquinone. If hypoprothrombinæmia has already led to hæmorrhage the vitamin or its synthetic analogue should be administered by injection, double the above doses being used.

Orthopædic treatment includes splinting or even osteotomy to correct deformities, such as genu valgum. A cork sole may be necessary, and kyphosis may demand the use of a spinal jacket. The pelvic deformity may necessitate Cæsarean section.

DONALD HUNTER.

SPRUE

Synonyms.—Cochin-China Diarrhœa; Psilosis; Ceylon Sore Mouth, etc.

Definition.—Sprue is a disease of unknown ætiology involving the gastro-intestinal tract, characterised by defects in gastric secretion and inability to absorb adequately fat, glucose, calcium and sometimes vitamins as well. Typically there is an apyrexial, morning diarrhœa with bulky, pale, gaseous, fatty stools, sore tongue, megalocytic, anæmia, asthenia and wasting.

Ætiology.—The disease is mainly confined to the tropics and subtropics, being especially common in parts of India (Bombay), China and Cochin-China, also in Ceylon, Java, the Federated Malay States and Porto Rico in the West Indies. Adult Europeans and people of mixed European blood living in endemic areas are prone to the disease. Except in Porto Rico, the native population is rarely affected. Both sexes are susceptible, but it rarely affects people under 20 years of age. A hot, damp climate, especially on the seaboard, favours its development, while certain bungalows enjoy an unsavoury reputation in this regard. Various theories have been suggested to explain its ætiology. The first infective agent was thought to be *Strongyloides intestinalis*. Later, Ashford and others held it to be a moniliasis of the digestive tract due to *Monilia psilosis*, but the fungoid theory is now being generally abandoned. Scott suggested that there was a metabolic disturbance, resulting in a decreased ionic calcium due to parathyroid involvement. Elders regards sprue as a primary deficiency disease due to lack of vitamins A and B and amino acids, while Castle and his colleagues attribute it to dietary deficiency, *i.e.* an extrinsic factor contained in meat, eggs and whole germ. The difficulty in accepting such a view is the epidemiological fact that sprue often affects the best-fed people in the community, and that, in places other than Porto Rico, people living on a diet deficient in animal protein develop tropical macrocytic anæmia. Finally, the conception of sprue as a primary physiological breakdown, due to climatic and other factors, does not explain its patchy geographical distribution, nor its onset many years after people have left the tropics. Deranged intestinal absorption is the fundamental basis of the sprue syndrome, and until more is known concerning the chemical factors controlling, or involved in, the absorption of such food elements as glucose, fat and calcium, the problem of sprue is likely to remain unsolved. If sprue be a primary deficiency

disease, the deficiency factor must be some unknown vitamin which controls or plays some important rôle in the processes involved in intestinal absorption.

Pathology.—*Morbid anatomy.*—At autopsy the essential lesions consist of an absence of fat, muscular wasting, a small heart, general atrophy of the viscera consequent on malnutrition, a megaloblastic hyperplasia of the red marrow of variable intensity, and atrophic changes in the tongue.

Clinical pathology.—The anæmia, which is by no means invariably present in the early stages, is megalocytic in type, resembling that seen in pernicious anæmia. The Price-Jones curve is also similar. The colour index is usually 1·0 or higher. The blood picture shows numerous megalocytes associated with anisocytosis and poikilocytosis, and in the severer cases polychromasia, basophilic stippling and occasional normoblasts may be observed; megaloblasts are rare. Hypochlorhydria or achlorhydria is common, but 75 per cent. of cases respond to histamine by an increase in HCl secretion. Evidence is accumulating that the megalocytic anæmia has a gastrogenous origin due to defective production of Castle's factor. The total fæcal fat is definitely increased (30 to 70 per cent.), but splitting is adequate. The glucose tolerance test frequently shows a flat type of curve, or one presenting a retarded rise due to malabsorption, while the blood calcium is decreased for the same reason. The blood bilirubin is rarely increased to the extent seen in pernicious anæmia. Malabsorption of fat accounts for the excessively fatty stool, while fermentation of glucose within the lumen of the bowel, consequent on defective absorption, underlies its acid and gaseous characteristics. The pallor of the stool is due to the transformation of stercobilin into colourless leucobilin.

Symptoms.—The incubation period is unknown, but patients have occasionally developed sprue within a few months of arriving in an endemic area. Hill diarrhœa sometimes passes into sprue. Often the onset is insidious with (1) loss of energy, dyspepsia and flatulence; (2) rapid loss of weight; (3) sore tongue or buccal aphthæ; (4) diarrhœa or looseness of the bowels, especially in the early morning. It may be months before the bulky, pale, acid, frothy stools reveal the true nature of the malady. Apyrexia is the rule, and frequently the temperature is subnormal. Once seen, the fully developed picture of sprue makes an indelible impression. Such a patient is asthenic, emaciated, mentally taciturn and often severely anæmic; the skin is parched, wrinkled and often pigmented over the forehead and malar eminences, while the nails are ridged and brittle; the tongue, which is invariably clean, may be patchily inflamed, ulcerated and atrophic, while the thin abdominal parietes scantily protect the attenuated coils of gas-distended bowel visible beneath. Physical examination also often reveals a decrease in the area of the liver dullness: this is partly attributable to atrophy and partly to intestinal distension. Hæmic murmurs may be heard over the heart, which is small, while both systolic and diastolic blood pressure is invariably lowered. On questioning such a patient he often complains of sore tongue and aphthous ulcers made worse by spiced and hot foods, of characteristic early morning stools, and of abdominal distension and intestinal flatulence generally most marked towards evening and often related to the carbohydrate intake. Œdema of the feet, cramps and tetany, associated with Chvostek's and Trousseau's signs, may occasionally be observed.

Paræsthesias are often complained of, and tendon reflexes, especially the knee-jerks, may be absent.

Complications.—Pyrexia should always arouse suspicion of some intercurrent infection or complication, the commonest of which is a *B. coli* infection of the urinary tract. Often this infection is unassociated with fever, and in every case of sprue the urine should be examined for pus cells and cultured for bacteria. Unlike pernicious anæmia, subacute combined degeneration of the cord is not encountered. Neuritic features are not uncommon, tetany with hypocalcæmia occurs in about 2 per cent. of cases, and occasionally purpuric skin eruptions are seen. Anal fissure and hæmorrhoids may develop, while venous thrombosis, eczema and pneumonia are occasionally encountered. Ulcers in the small intestine have been noted in a few cases, and perforation of the bowel has been recorded.

Course.—Sprue is a very chronic disease, showing spontaneous remission and exacerbations, with a tendency to natural cure if the patient leaves the tropics. The causes of death in inadequately treated cases are malnutrition, anæmia and intercurrent disease.

Diagnosis.—The well-established case presents little difficulty, but in the initial stages and in atypical cases considerable clinical experience may be required to make a diagnosis. The differential diagnosis includes pellagra, pernicious anæmia, tropical macrocytic anæmia, gastric carcinoma, gastro-colic fistula, tuberculous adenitis and lymph adenoma involving the mesenteric glands, Addison's disease, chronic pancreatitis and carcinoma of the pancreas. Biochemical and radiological investigations may be essential for their differentiation.

Prognosis.—This largely depends on the co-operation of the patient and the institution of modern treatment which has greatly increased the expectancy of life. In the absence of intercurrent infection, patients recover, provided they are correctly treated, and it is permissible to let them return to the tropics if they are under 55 years of age, otherwise healthy and have been free from symptoms on a normal diet for 6 months without treatment.

Treatment.—The essentials of treatment are: (1) The institution of alimentary rest by appropriate dietary; (2) the treatment of megalocytic anæmia if present; (3) the reinforcement of demonstrable deficiencies by such means as hydrochloric acid, calcium salts, etc. Both in the primary attack and during relapses these asthenic, poorly nourished patients must be put to bed for 5 to 8 weeks under conditions that ensure mental as well as physical rest, while in Europe warmth and the avoidance of chill are essential. (1) *Dietary.*—Many different diets have been advocated, the best known being Manson's milk treatment. The feeds were given in small quantities 2-hourly, commencing with 3½ and increasing gradually up to 7 pints daily. Van den Burg advocated large quantities of pulpy fruit free from acidity, coarse seeds and fibres; ripe bananas, bael fruit, papaya and strawberries are popular, the latter being particularly favoured in Europe. The red meat diet of Cantlie commenced with 2-ounce feeds of lean, minced, underdone steak, which were gradually increased until 1½ to 2 lb. were taken daily. As a result of observations on the defective absorption of fat and carbohydrate in this disease, Fairley introduced graded high protein, low fat, low carbohydrate diets, the ratios of the three fundamental foodstuffs being as

1·0 : 0·3 : 1·3 and the energy values varying from 600 to 3000 calories. Red meat is the main source of protein advocated, but more recently a defatted dried milk (sprulac), with similar food ratios has become available. A convalescent high protein diet with fruit and vegetables is generally permitted in the fifth or sixth week, and subsequently the amount of fat and carbohydrate is gradually increased. (2) *Anæmia.*—The anæmia of sprue is megalocytic in type and almost invariably responds to adequate dosage of liver extract *per os*, provided appropriate dietetic measures are simultaneously instituted to control the diarrhœa. Maximal reticulocytosis occurs about the ninth day and the blood regenerates at a rate comparable to pernicious anæmia. For the first month dried extract, equivalent to 1½ lb. of fresh liver daily, should be given ; generally in the second month the dosage can be reduced to the equivalent of 1 lb. daily, and in the third month to ½ lb. In chronic cases, which have repeatedly relapsed, a maintenance dose of ½ lb. liver daily may be advisable for 3 to 6 months after the blood has been restored to normal. Very rarely are refractory cases encountered in which reticulocytosis is submaximal and blood regeneration inadequate. Here oral treatment can be reinforced by parenteral liver injections, hepastab (4 c.c. daily), pernæmon forte (4 c.c. daily), campolon (6 c.c. daily), for a period of 2 to 3 weeks. In such cases intercurrent infection should be sought for. Unfortunately marmite, even in a dosage of 240 grains daily, is not a satisfactory substitute for liver, since diarrhœa may be increased and the reticulocyte response is generally submaximal and associated with little or no improvement in the anæmia ; exceptionally cases respond dramatically with maximal reticulocytosis and rapid blood regeneration. Blood transfusion is rarely necessary nowadays, its only indication being to tide a dangerously anæmic patient temporarily over the latent interval before a response to liver extract is obtainable. The anæmia in sprue is generally orthochromic or hyperchromic, but in those rare cases where hypochromia is present, or in which there is an undue lag in the production of hæmoglobin following liver extract therapy, intercurrent infection or intestinal ulceration should be suspected. Full doses of iron should, of course, be prescribed. (3) *Treatment of Demonstrable Deficiencies.*—Where acid secretion is defective, acid. hydrochlor. dil. in doses of 60 minims in diluted orange juice should be administered thrice daily after food. Tetany, with hypocalcæmia, calls for the administration of calcium lactate (grains 30 thrice daily) ; even more important is a diet low in fat, since calcium cannot be satisfactorily absorbed when there is an excess of fat in the stools. Vitamin D in the form of calciferol or ultraviolet radiation may also be prescribed as an accessory measure, but is rarely necessary.

B. coli infections of the urinary tract respond satisfactorily to sulphonamide therapy. Proseptasine, in a dosage of 1·0 g. (2 tablets) every eight hours from 7 to 10 days, is well tolerated and generally eradicates the infection.

Once the sprue patient has regained his health he should continue with a well-balanced diet adequate in vitamins and protein, avoiding alcohol, rich, spiced and sugary foods and condiments. Aperients should be taken with caution, and care exercised to avoid chill and respiratory infection. Sprue relapses may recur after many intervening years of perfect health.

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N. Hamilton Fairley.

MUCO-MEMBRANOUS COLIC

Definition.—In nervous individuals constipation is sometimes associated with the constant or intermittent passage of membranes of coagulated mucus and with attacks of pain, the condition being known as muco-membranous colic. This name is preferable to muco-membranous colitis, as no true inflammation of the colon is present.

Ætiology.—Muco-membranous colic was formerly a common condition in women of the educated classes, and was occasionally also observed in men. For no obvious reason its incidence has greatly diminished since 1914, and well-marked cases are now rarely seen.

Pathology.—Two predisposing factors are invariably present—constipation and an abnormally irritable nervous system. Retention of fæces in an individual with an abnormally irritable nervous system may result in reflex over-activity of the motor and secretory fibres of the colon, leading respectively to painful spasm and to excessive secretion of mucus. The former may occur alone; the resulting spasm of the colon is analogous to pure spasmodic asthma, and, in contrast with muco-membranous colic, it is still comparatively common (p. 617). If the mucus is retained sufficiently long, coagulation takes place and a membrane forms. This is analogous with the formation of Curschmann's spirals in asthma. The mucus contains no pus cells or red corpuscles and the sigmoidoscope reveals a perfectly normal mucous membrane. Some catarrh may be present if the condition has been injudiciously treated with irritating purgatives or injections. In rare cases of allergic origin large numbers of eosinophil cells, sometimes with red blood corpuscles, are present in the mucus.

Symptoms.—In some cases the patient constantly suffers from abdominal discomfort and passes membranes. In others definite attacks, which are often emotional in origin, occur at intervals of weeks or months; the pain may be confined to the attacks, or there may be abdominal discomfort in the intervals. It is, however, not uncommon for the presence of membranes in the stools to be the only symptom.

The pain is situated most frequently in the left flank and iliac fossa and just above the pubes; at the same time the descending and iliac colon are often tender and can be felt as a contracted cord, in which scybala can sometimes be distinguished. Less frequently there is pain and tenderness in the cæcum and ascending colon, which are felt to be more firmly contracted than usual; the condition may then closely simulate appendicitis, but no relief follows appendicectomy. The passage of fæces and membranes or of the latter alone, whether spontaneously or as the result of treatment, generally gives temporary relief.

The constipation present in the intervals becomes much more severe during an attack. The stools consist of hard, small scybala, which may occasionally be moulded into thin or flat pieces as a result of anal spasm.

The mucus is passed as very thin membranous shreds, which may form long tubular casts of the colon, which are sometimes rolled into a ball. The mucus may be transparent like ordinary mucus or opaque like fibrin and grey-white, but it is often stained by fæces and rarely by blood. The membranes

may be passed alone or with scybala. They are sometimes mistaken for shreds of mucous membrane and for tape-worms.

Various symptoms resulting from the associated neurasthenia or anxiety neurosis are generally present, and the patient always tends to become depressed and hypochondriacal.

Intestinal Sand.—The passage of intestinal sand is generally associated with muco-membranous colic. Small quantities of sand, which would otherwise escape detection, can often be discovered by running water on the fæces until the greater part is washed away. True intestinal sand must be distinguished from the sand formed of wood-cells, which is sometimes passed by individuals who have eaten a large quantity of pears or bananas. It is composed of pale yellow or reddish-brown granules, irregular in shape and never crystalline. Their most characteristic constituents are the insoluble calcium soaps of palmitic and stearic acids; an approximately equal quantity of calcium phosphate is also present.

Prognosis.—Muco-membranous colic is a very chronic condition. If treatment is begun at an early stage recovery generally follows, but when it has been present for many years the pasage of membranes is likely to persist even if the accompanying symptoms disappear as a result of treatment.

Treatment.—A patient suffering from muco-membranous colic should be treated with the object of removing the two underlying factors—the abnormal condition of the nervous system and the constipation. The former calls for simple psychotherapy. The patient should be discouraged from making minute investigations of his stools; she should be told to be satisfied if she feels better without looking to see how much mucus is passed. She may feel perfectly well in spite of the presence of mucus; but she will often remain so only as long as she is unaware that she is passing it.

The constipation requires treatment by diet, massage, drugs and enemata. The best results are generally obtained with a generous mixed diet containing a plentiful supply of those articles which have already been described as useful in uncomplicated constipation on account of their chemically stimulating properties, but excluding raw vegetables in salads and pickles, fibrous vegetables such as celery, and the skins and pips of fruit. Mustard, pepper and spices of all kinds should be prohibited. Smoking should be restricted, and in severe cases should be entirely prohibited.

At the commencement of treatment any accumulation of fæces in the colon must be removed. This can best be done by an enema of 6 fluid ounces of paraffin given in the evening and retained during the night. Once the colon is empty, the reaccumulation of fæces can often be prevented by the administration of liquid paraffin and isogel or coreine in order to soften the stools. If this does not result in the passage of a satisfactory stool each day, the further treatment depends upon whether the stasis is in the proximal part of the colon, in which case a mild aperient, such as infusion of senna pods, is required, or in the pelvic colon, when treatment by paraffin enemata without aperients is indicated.

As in the case of uncomplicated colon spasm, belladonna is the most useful drug for combating the pain; small doses of bromide may also be given to diminish the irritable condition of the nervous system.

Local treatment of the mucous membrane of the colon by Plombières douches should be used only in the exceptional cases in which other treatment

has failed to give relief. As the patients are always self-centred, it is of the utmost importance to avoid encouraging them to concentrate upon their bowels and their excreta by irrigating the colon unless this is absolutely necessary. Intestinal lavage can be given at home; but it is generally more effective at one of the spas, such as Harrogate, Llandrindod Wells, Bath or Buxton, at which there are special facilities for carrying it out with the natural waters. Normal saline solution should be used if the treatment is given at home, and injections of soap and water, antiseptics and astringents should be avoided, as they tend to aggravate the condition by irritating the mucous membrane.

INTESTINAL CARBOHYDRATE DYSPEPSIA

Definition.—Intestinal carbohydrate dyspepsia is a condition in which discomfort results from the presence of excess of gas in the colon owing to the fermentation of carbohydrates which have escaped digestion in the small intestines.

Pathology.—Under normal conditions starch is digested by the ptyalin of the saliva and the amylopsin of the pancreatic juice. The ptyalin is the less important, as it is rapidly destroyed by the first trace of free hydrochloric acid with which it comes into contact in the stomach. It was formerly believed that the starch in vegetable food could be digested only when the cellulose had been broken up by cooking, or, if eaten raw, after it had been dissolved by the action of a hypothetical cellulose-splitting ferment in the small intestine or of bacteria in the colon. It is now known that the cellulose walls of vegetable cells are not broken by cooking, a cellulose-splitting ferment does not exist in the human alimentary tract, and bacteria do not normally take any part in the digestion of carbohydrates, which is almost confined to the upper part of the small intestine. Ferments penetrate the unbroken walls of vegetable cells and digest the starch within them, the sugars produced passing out into the surrounding media, from which, owing to the absence of bacteria, they are absorbed without undergoing fermentation.

Normally starch is completely digested in the upper part of the small intestines so that very little reaches the terminal ileum and none reaches the cæcum. When the rate of passage through the small intestines is excessive, there is time for free starch and starch in cells with broken walls to be digested, but the starch in intact cells reaches the terminal ileum and cæcum unaltered. Here the amylopsin penetrates the cells, and the sugars pass into the surrounding media, where they are attacked by bacteria, which are present in very large numbers, and undergo fermentation before there is time for much absorption to take place. The symptoms of intestinal carbohydrate dyspepsia are caused by the carbon dioxide and acetic and butyric acids produced by this fermentation.

In most cases of intestinal carbohydrate dyspepsia there is a history of food-poisoning or of some intestinal infection which has caused enteritis. The latter may still be present, but more commonly it has given place to a functional irritability of the small intestine, which results in excessive motor activity.

Symptoms.—The chief symptom of intestinal carbohydrate dyspepsia is a widespread feeling of discomfort and fullness in the lower part of the abdomen, caused by distension of the colon with carbon dioxide. During the day gas often collects in the splenic flexure, which is the highest point in the colon: the discomfort produced in this way may be mistaken by the patient for gastric flatulence, and aerophagy often results from his attempt to relieve himself by belching. During the night the gas passes to the rectum, which is then as high as any other part of the colon; consequently the greater part is passed during the night and on waking in the morning. The discomfort is generally increased by meals as a result of exaggeration of the gastro-colic reflex. It is often greatest during the night, and is a very common cause of insomnia, which can be cured at once by a suitable diet. The excess of gas produces borborygmi, the noise of which may itself be enough to keep a patient awake. The irritation of the bowel caused by the gas and organic acids may cause spasm; the patient then complains of acute pain. Excessive quantities of odourless flatus are passed, and some relief is always felt after its escape.

The abnormally rapid passage of the chyme through the small intestine can be demonstrated with the X-rays, even when the irritation of the colon is insufficient to cause any diarrhœa, and the X-rays show no change in the normal rate of passage through the colon. In severe cases attacks of mild diarrhœa are common, much gas being always passed with the stools, which are acid and have an unpleasant sour, but not putrefactive, odour when they are liquid. The diarrhœic stools always contain an obvious excess of undigested vegetable matter, and bubbles of gas may continue to form as a result of fermentation of the undigested starch they contain.

A fresh stool should be examined whilst the patient is on his usual diet. Microscopical examination reveals the presence of large numbers of starch granules, which are still within their cellulose envelopes and stain blue with iodine. Few or none are present in normal fæces. In contrast with the stools in pancreatic achylia there is no excess of fat or of striated muscle-fibres. The normal enterococci of the colon are present in considerable excess, but the number of *B. coli* is not increased and no pathogenic organisms are found. On giving a starch-free diet the excess of enterococci rapidly disappears; it is clear, therefore, that the enterococcal excess is not the cause of the condition, but is the result of the excellent culture medium afforded by the excess of carbohydrates present in the colon. If a small quantity of fresh fæces is mixed with water and incubated for 24 hours, any gas given off being collected, the fermentation which has been taking place in the colon in intestinal carbohydrate dyspepsia continues *in vitro*. A considerable quantity of odourless gas is evolved and the fæces become very acid, whereas no gas is evolved from normal stools. If the examination of a stool is delayed for 6 hours or more, all undigested starch may have disappeared and no further gas is evolved on incubation. In the much less common putrefactive diarrhœa, which is due to insufficient digestion of meat, a smaller quantity of foul gas is evolved and the fæces become strongly alkaline.

Treatment.—All root vegetables (potatoes, carrots, onions, beetroot, artichokes, parsnips), green peas and lentils, bananas, rice, tapioca and sago, and porridge are prohibited. Bread, toast and biscuits, and puddings containing starch are allowed in small quantities, and there is no need to restrict

the intake of sugar. If diarrhœa is present, it is necessary to exclude all vegetables and fruit, whether cooked or raw. Within a week the excess of enterococci disappears from the stools, which no longer ferment on incubation. It may be necessary to avoid potatoes and other root vegetables for a considerable period and sometimes permanently.

If a diastatic ferment of vegetable origin is taken with each meal, less restriction in diet is required, as in contrast with the amylopsin of pancreatic preparations it is very slowly destroyed by the gastric juice so that more digestion of starch can occur in the stomach.

A tablespoonful of powdered activated charcoal may be given in a small quantity of water morning and evening to absorb any gas which is still produced, but this should be unnecessary if a sufficiently strict diet is ordered. It is much better to prevent the production of gas than to provide for its absorption, as the condition can be permanently cured only by curing the irritable condition of the small intestine, which is aggravated by the mechanical irritation of undigested vegetable matter and the chemical irritation of the products of bacterial activity on starch.

In severe cases, especially those associated with diarrhœa, excess of gas may still be passed in spite of a strict diet and the use of vegetable diastase and charcoal. This can generally be overcome by giving sufficient codeine to reduce the rapid passage through the small intestine to the normal. A dose of $\frac{1}{4}$ grain of codeine phosphate given three times a day before meals with 5 minims of tincture of belladonna is generally sufficient.

As the excess of enterococci present is a result and not the cause of the condition, vaccine treatment is quite useless. I have seen many patients rapidly cured by diet alone after having undergone many months of treatment by inoculation without the slightest benefit. Colonic lavage, which is almost as popular a treatment, is, of course, equally futile.

ORGANIC DISEASES OF THE INTESTINES

ENTERITIS

Acute Enteritis

Acute enteritis forms part of the picture in most cases of acute food poisoning. Acute gastritis may be present alone when vomiting is severe; more commonly gastro-enteritis occurs with diarrhœa with or without vomiting. The poison is generally so diluted when the colon is reached and its evacuation is so rapid that the colon escapes and gastro-entero-colitis is consequently rare. Acute enteritis may also accompany the gastritis of acute infections, such as gastric influenza; in such cases there is diarrhœa as well as vomiting. If the affected individual happens to be one of the 10 per cent. of normal people with hypochlorhydria, the gastritis is likely to lead to achlorhydria, to which the symptoms caused by the enteritis are often erroneously ascribed.

Chronic Enteritis

Chronic enteritis is a common sequel of acute gastro-enteritis caused by food poisoning and acute infections. It may follow infestation with worms, especially tapeworms. It is frequently caused by indigestible food, especially among people who take excess of "roughage" in the mistaken belief that it is good for their health. The small intestines are often irritated by food which reaches them without undergoing the normal preparation in the stomach in achlorhydria and after gastro-jejunostomy and partial gastrectomy. Chronic enteritis is frequently caused by irritation produced by the habitual use of aperients, psyllium seeds and drugs such as arsenic. The loss of the antiseptic acid barrier of the gastric juice in achlorhydria may lead to infection of the small intestines by swallowed bacteria when oral and naso-pharyngeal sepsis is present. Lastly, the stasis which results from chronic small intestine obstruction leads to a great increase in bacterial activity with the production of chemical irritants which cause severe enteritis. This explains why diarrhœa is commonly present instead of constipation in chronic obstruction of the small intestine.

As the chief symptom of enteritis is diarrhœa, the diagnosis and treatment of which are considered on pp. 625, 627, it is unnecessary to give a separate description here.

REGIONAL ILEITIS

Synonym.—Crohn's Disease.

Ætiology.—Regional ileitis is by no means rare. It occurs between the ages of 4 and 40 and is most common in young adults. Males are more often affected than females.

Morbid Anatomy.—The terminal part of the ileum is generally first involved. The disease may spread into the cæcum, and any part of the small intestine and colon may be attacked. The mucous membrane is inflamed and eventually ulcerates, and all the coats of the affected segment become thick, œdematous and rigid. Active inflammation is followed by fibrosis, and the lumen of the rigid bowel becomes progressively more narrowed. The mesentery is thickened and the lymphatic glands are enlarged. Adjacent parts of the bowel adhere together and fistulæ form between them and occasionally open on the surface of the abdomen. Microscopically acute, subacute and chronic inflammation are found with giant cells, so that the appearance closely simulates tuberculosis, with which it has generally been confused in the past. But tubercle bacilli are never found in the wall or lumen of the bowel, and animals inoculated with the tissue never develop tuberculosis. The condition is probably infective, but nothing is known as to the nature of the infection.

Symptoms.—The symptoms are those of progressive small intestine obstruction. The patient complains of attacks of colicky pain of gradually increasing severity and frequence round the umbilicus and in the right lower quadrant of the abdomen, the whole of which is distended with gas. The attacks may be associated with watery diarrhœa and occasional vomiting, but constipation is often present in the intervals. The stools always

contain occult blood; when they are loose, shreds of mucus are present.

The affected segment of the ileum may form a sausage-shaped tumour, which can be felt in the right iliac fossa.

Mild pyrexia with slight polymorphonuclear leucocytosis is often present. After a time anorexia develops, and the patient loses weight and becomes anæmic. Occasionally, general symptoms such as lassitude and loss in weight may precede the intestinal symptoms by some months.

An X-ray examination should be made hourly from 1 to 6 hours after an opaque meal. In addition to the evidence of small intestine obstruction afforded by the presence of loops of dilated bowel containing fluid and gas, filling defects in the terminal ileum and sometimes in the cæcum may be seen. Most characteristic is the "string sign"—a thin, irregular linear shadow passing from dilated coils of ileum through the filling defect to the cæcum. A better view of the terminal ileum is sometimes obtained after a barium enema, which runs through the incompetent ileo-cæcal sphincter.

Diagnosis.—Pain in the right lower quadrant of the abdomen associated with distension, local tenderness, and possibly a tumour and pyrexia should always raise a suspicion of regional ileitis in addition to subacute appendicitis, ileo-cæcal tuberculosis, carcinoma and, when fistulæ are present, actinomycosis.

Treatment.—The affected segment of bowel should be excised. Simple short-circuiting is generally insufficient, as the disease tends to spread in both directions if it is not eradicated. Short-circuiting is, however, required when extensive lymphatic involvement at the base of the mesentery makes excision impossible and as a preliminary operation when fistulæ are present.

COLITIS

Inflammation of the colon may be general or localised to one segment. Thus inflammation of the cæcum (typhlitis), cæcum and ascending colon, pelvic colon, rectum (proctitis), or pelvic colon and rectum (pelvi-rectal colitis) may occur alone, but except in the case of the two last, localisation is rarely absolute.

Although enteritis frequently causes secondary colitis, the reverse is very rare, as infective and irritating material from the ileum must pass along the colon before it is evacuated, whereas the ileo-cæcal sphincter prevents the spread of infection from the cæcum to the ileum.

The inflammation is generally limited to the mucous membrane and submucous tissue, but it occasionally involves the deeper tissues and may spread to the peritoneum (pericolitis). The inflammation may be catarrhal or ulcerative, and chronic or acute.

The term *mucous colitis* should be abandoned, as mucus is passed in all forms of colitis; moreover, most cases so diagnosed are not suffering from colitis at all, the excess of mucus being the response of the mucous membrane of the normal intestines to irritation by purgatives or of that of the pelvic colon and rectum to irritation by scybala. The term *muco-membranous colitis* should also be replaced by muco-membranous colic, as it is a functional condition and not a form of colitis at all (p. 642).

Acute Catarrhal Colitis

Ætiology.—Acute catarrhal colitis occurs most frequently as a result of food poisoning, either alone or associated with acute gastritis and enteritis. It may also be a symptom of specific fevers and various toxæmias, especially uræmia.

Symptoms.—The chief symptom is diarrhœa, the stools being frequent, fluid and offensive; they contain mucus, sometimes traces of blood, but no excess of food residue unless the small intestine is simultaneously affected. Abdominal discomfort is present, and paroxysms of colicky pain are frequent. In severe cases there may be well-marked general symptoms with a high temperature and a rapid pulse. As a rule the condition rapidly improves, but it may develop into chronic colitis.

Treatment.—The treatment is the same as that for Acute Diarrhœa (p. 627).

Chronic Catarrhal Colitis

Ætiology.—The most common cause of chronic catarrhal colitis is the habitual use of purgatives, which are frequently taken even in the absence of constipation. Infection of the bowels with pathogenic organisms, introduced in the food or water or coming from some septic focus in the mouth, pharynx or appendix, may cause a chronic infective, catarrhal colitis, which may also be the sequel of an attack of acute colitis or the colitis of some specific infection, such as amœbic or bacillary dysentery.

Symptoms.—Diffuse discomfort and a sensation of fullness are commonly present in the lower part of the abdomen. Slight attacks of colic may occur, but in many cases there is no actual pain. The abdomen is often somewhat distended and tender. The discomfort is generally worse after meals and is relieved if the bowels are well opened. In infective cases and those following an attack of acute colitis, diarrhœa is generally present, mucus and occasionally traces of blood being found in the fluid stools, but there is no excess of food residue unless enteritis is also present.

The presence of mucus in the stools is often regarded as sufficient evidence to prove that colitis is present. But it is a function of the healthy mucous membrane to secrete mucus to protect itself against mechanical and chemical irritants. Consequently the unformed, clear mucus passed with hard fæces in constipation, and especially in dyschezia, does not indicate that colitis or proctitis is present, and the same is true of the mucus passed with fluid stools, when irritating aperients have been taken. Only if mucus is passed with soft fæces when no purgative has been given can it be regarded as of any diagnostic importance. On the other hand, pus and red blood corpuscles generally indicate the presence of either ulcerative colitis or carcinoma, though the possibility of hæmorrhoids or polypoid adenoma as the source of the latter must, of course, be remembered.

Treatment.—The teeth should be put into good order and any other source of infection should be removed. The food must be thoroughly masticated and should be of an unirritating character. The use of purgatives should be avoided, though liquid paraffin or a vegetable mucilage should be given if hard scybala are passed. In infective colitis a liquid culture of *B. acidophilus* should be taken, and an autogenous vaccine occasionally proves of value if

definitely pathogenic organisms, which are agglutinated by the patient's serum, have been isolated from the stools. Belladonna should be given before meals with the addition, if diarrhœa persists, of codeine.

Ulcerative Colitis

Ætiology.—Ulcerative colitis is a common disorder in England. Young adults are most frequently affected, and men and women with equal frequency.

Pathology.—Bacillary dysentery, the "bloody flux," has always been endemic in Great Britain, and it still occurs sporadically and in small groups in country districts and in larger epidemics in asylums and other institutions. The epidemic summer diarrhœa of infants is also generally due to infection with a dysenteric organism. The many cases of chronic ulcerative colitis give a history of an acute onset with "bloody flux," which may have lasted only a few days but recurred after intervals of varying length. In the only case in which to my knowledge the stools were examined at the acute onset Flexner's bacillus was isolated. It seems likely that the majority of cases are primarily the result of infection with a dysentery bacillus or some allied parenteric organism. The condition may become chronic owing to secondary infection with (1) the normal *B. coli* or enterococcus of the colon, which may develop toxic properties as a result of the excess of soluble protein and the blood and pus in the surrounding medium; (2) parenteric organisms, such as Gaertner's or Morgan's bacillus or *B. asiaticus*, swallowed at the same time as the original *B. dysenteriæ*, or subsequently; (3) streptococci from the throat as a result of an incidental attack of tonsillitis. The organism which caused the original infection often dies out just as it does in cases of chronic dysentery, which are clinically and pathologically indistinguishable from ulcerative colitis except for their known origin as acute bacillary dysentery. In 15 per cent. of my cases of ulcerative colitis and in many others of which I have knowledge, a dysentery bacillus was isolated from the stools, swabs from ulcers, or a scraping of the floor of an ulcer obtained with a sharp spoon. In a further 30 per cent. of my cases a parenteric organism has been isolated from the stools, and the patient's blood has agglutinated it.

Symptoms.—The onset is sometimes acute with severe diarrhœa and fever. More commonly it is subacute and insidious, the first symptom noticed being the passage of blood and mucus with or without diarrhœa. Even in cases which appear to begin acutely a history can often be obtained of slight intestinal irregularity with the occasional passage of mucus or blood for many months or even several years before the onset of severe symptoms.

Diarrhœa is always present; as many as twenty stools, most of which are quite small, may be passed in the day. Blood, pus and mucus are passed with semi-fluid fæces and also alone. In quiescent periods they may appear to be absent, but microscopical examination of the stools shows that this is not the case. Blood may be passed in large quantities by itself, but it is generally mixed more or less intimately with the mucus and pus. It is bright red, and never produces black tarry stools, such as are seen with gastric and duodenal ulcer. It is mostly fluid, but small clots are often present. The mucus is clear or opaque owing to the presence of pus; membranes are never passed. In most cases small collections of pus are easily recognised with the naked eye in addition to that mixed with the mucus and fluid fæces.

Abdominal discomfort is often, but not always, present. Actual pain is rare except immediately before defæcation, when colic may occur; this disappears as soon as the bowels are opened, especially if flatus is passed. Tenesmus is unusual and occurs only if the anal canal is involved. The abdomen is sometimes slightly distended, but in many cases it is retracted. Tenderness is often completely absent, even in severe cases, but pressure over the colon, especially in the left iliac fossa, may cause discomfort. If the tenderness is considerable, the inflammation has generally spread to the peritoneum and local peritonitis is present. A moderate degree of muscular rigidity is often found in severe cases, especially when there is any local peritonitis.

Digital examination of the rectum is painful only when the anal canal is inflamed. The thickened mucous membrane and the ulcers can be felt with the finger when the rectum is involved.

An examination should always be made with a long proctoscope; in the rare cases in which the rectum is healthy a sigmoidoscope must be used. An anæsthetic is never required, and if the instrument is carefully introduced under visual guidance without inflation and only as far as it goes without difficulty, there is no danger. The mucous membrane is bright red, thick and sometimes granular. It bleeds very readily when touched, and small submucous hæmorrhages are frequently seen. Its surface is covered with blood-stained, purulent mucus, some of which should be removed on a sterile swab for bacteriological and cytological examination. Superficial ulcers are invariably present; but in early cases they may be so small that they are difficult to recognise without a magnifying eye-piece if a sigmoidoscope and not a proctoscope is used. Later they are large, and are sometimes so extensive that only small islets of mucous membrane are left, which may feel like small, flat polypi on rectal examination, the floor of the confluent ulcers being mistaken for the surface of the mucous membrane. The ulcers are always superficial with irregular edges; the thick mucous membrane may be undermined. The floor of the ulcers appears greyish-yellow when the blood and mucus are wiped from their surface.

In acute cases, and in acute exacerbations of more chronic cases, irregular fever is generally present. Apart from this, the patient has generally a good appetite. The constant diarrhœa leads to progressive emaciation and weakness; but in mild cases the patient may feel so well that he is unwilling to undergo treatment in bed. The loss of blood leads to secondary anæmia, which may be severe; the hæmoglobin is often only 50 per cent. of normal, and may fall to 20 per cent. In such cases œdema of the ankles and ascites may develop.

Complications.—In the course of healing, strictures, which may be multiple and of considerable length, may develop, especially in cases of long standing. The symptoms do not alter with the development of the strictures, as the stools are so fluid that they pass without difficulty through the narrowed bowel. A narrowing can sometimes be recognised with the sigmoidoscope, but the exact degree and localisation can only be discovered with the aid of the X-rays. A stricture does not require surgery unless it causes stasis, which can be recognised with an opaque meal, but not with an enema. The X-rays also give some idea of the extent of colon involved, as the normal "haustration" produced by the constant activity of the muscularis mucosæ

disappears when it is paralysed by inflammation spreading from the mucous membrane to the submucous tissue. In the majority of early cases the distal half of the colon or the pelvic colon and rectum are alone affected.

Healing may also be associated with the development of multiple small polypi. The majority of the "polypi" are tags of inflamed mucous membrane, but true adenomatous polypi, which may later undergo malignant degeneration, also occur.

General peritonitis is a very rare complication, and is generally not due to perforation, but to direct spread of infection through the wall of the colon. Localised abscesses are still more unusual except in the perianal region, multiple fistulæ-in-ano being not uncommon; if undiscovered, they may give rise to recurrence after apparent recovery.

In rare cases non-suppurative multiple arthritis develops, as it does in bacillary dysentery.

In advanced cases with much anæmia and toxæmia the malnutrition and vitamin deficiency, which result from an unwisely restricted diet, may give rise to severe trophic lesions in the skin and eyes which recover rapidly when an adequate diet is given.

Diagnosis.—The association of blood in the stools with pus and mucus indicates the presence of ulcerative colitis or a growth of the pelvic colon or rectum. A growth can be excluded by rectal and abdominal palpation, and by the sigmoidoscope. Even if the growth is too high to be reached by the instrument, its presence is rendered very probable when the accessible part of the colon appears normal, and blood, mucus and pus are seen coming from the inaccessible part.

If the patient has been in the East the possibility of amœbic dysentery should be considered, though the absence of such a history does not exclude it, as I have seen several cases in people who have never been out of England. The endoscopic appearance is so distinct that a definite diagnosis can be made from this alone. Small, round, red elevations are seen on the otherwise normal-looking mucous membrane, corresponding with the collection of broken-down material in the submucous tissue caused by the invasion of *Entamœba histolytica*. In the centre of each elevation is a depressed yellowish ulcer, where the submucous abscess has broken through the mucous membrane.

I have seen a case of thrombocytopenic purpura with only a few cutaneous petechiæ, in which the passage of blood in the stools had led to a diagnosis of ulcerative colitis, but the sigmoidoscope revealed innumerable minute submucous hæmorrhages without any actual inflammation.

Prognosis.—Very acute ulcerative colitis may cause death in a few weeks. More commonly it becomes chronic with periodic acute exacerbations, and thus approximates to the ordinary form of ulcerative colitis, in which the onset is insidious and the course very prolonged. In private practice the mortality is about 10 per cent., but in hospital it is at least three times as great. Death is generally the result of exhaustion from prolonged diarrhœa, anæmia caused by constant bleeding and toxæmia.

Relapses tend to occur with acute infections, especially tonsillitis, food poisoning, dietetic indiscretions, exposure to cold and damp, worry, and fatigue from mental or physical overwork.

Treatment.—The most important factors in the successful treatment

of ulcerative colitis are patience and perseverance on the part of both doctor and patient. Even in early cases several weeks of strict treatment are generally required; in chronic and late cases the patient may have to be in bed under continuous supervision for a year or more. He should be kept at rest in bed so long as there is any pyrexia and so long as more than two or three stools are passed in 24 hours. After that he may be allowed to get up for a warm bath and to lie on a couch during the day, if possible in the open air, but he must take no more exercise than is involved in walking from one room to another until recovery is complete.

The small intestines are rarely involved in ulcerative colitis. It is, therefore, quite unnecessary to make any restriction in diet beyond the avoidance of pips and skins of fruit and fibres of vegetables. Too limited a diet results not only in loss of weight and strength, but the food may contain insufficient iron to compensate for the loss of blood in the stools so that microcytic anæmia develops. The anæmia and malnutrition, and particularly any deficiency in vitamins, aggravate the colitis and may lead to serious cutaneous and ocular complications, all of which respond rapidly to a change to a more liberal diet. Patients with ulcerative colitis often have quite a good appetite, and there is no reason for limiting their allowance of meat and other foods containing no indigestible residue. Fruit is best given in the form of strained juice and purées and green vegetables as purées.

Except in the most acute stages local treatment is often useful. The fluid should be run in through a soft catheter introduced only just beyond the anal sphincter. The quantity injected depends upon the extent of the disease as shown by X-ray examination. If the whole colon is involved a pint is needed; when introduced slowly at a pressure not exceeding 18 inches of water, it reaches the cæcum without difficulty and is almost as effective as if given through an appendicular stoma. If only the distal half is involved, half or three-quarters of a pint are sufficient, and the patient should remain in a semi-sitting position so that the fluid cannot run into the more proximal part of the colon. The most useful solution is tannic acid, the strength of which is gradually increased from half to two grains to the fluid ounce; it should be retained, if possible, for half an hour.

The most satisfactory method of giving local treatment in cases of hæmorrhagic proctitis, and of ulcerative colitis in which only the more distal parts of the colon are involved, is by injecting an emulsion of 5 grains of bismuth subgallate to the ounce of an unirritating vegetable mucilage made from isogel or coreine, which is neither affected by bacteria nor absorbed. The emulsion can generally be retained for several hours and should be given directly after the bowels have opened in the morning or at night. For proctitis 4 fluid ounces are required; when the pelvic colon is involved 6 or 8 fluid ounces should be injected. Some patients are able to retain 10 or 12 fluid ounces; this quantity is often sufficient to spread through the whole colon, so that the treatment can be tried as a substitute for injections of tannic acid solution in all cases of ulcerative colitis. Occasionally water is absorbed and difficulty is experienced in evacuating the emulsion in the morning; in such cases one or two fluid ounces of paraffin should be incorporated in the emulsion.

When the diarrhœa is severe the patient is likely to become exhausted by want of sleep. A dose of codeine sufficient to keep the bowels from acting

more than once in the night should be given at 10 p.m. and a smaller dose may be given before meals and immediately before the injection of a retention enema. In most cases the muscular coat of the colon is extremely irritable, and healing is retarded by its continuous activity. Tincture of belladonna should therefore be given every 4 hours, the dose being gradually increased from 5 minims to the maximum the patient can take without getting his mouth uncomfortably dry.

Pain is not a common complaint in ulcerative colitis. Colicky pains may, however, occur owing to distension with gas, especially shortly before the bowels act. They can always be relieved by giving a tablespoonful of activated charcoal two or three times a day.

Most patients with ulcerative colitis are more or less anæmic; 30 grains of iron and ammonium citrate should be given three times a day till the hæmoglobin is at least 80 per cent. If the hæmoglobin percentage is less than 70, repeated small transfusions not only improve the patient's general condition, but often greatly hasten the healing of the ulcers.

The injection of polyvalent anti-dysenteric serum is occasionally followed by dramatic improvement, but in many cases little or no benefit follows. After preliminary desensitisation 20, 40, 60, 80 and 100 c.c. are injected intravenously on consecutive days. Alternatively 10 c.c. of serum can be injected intramuscularly daily for about 10 days; good results are sometimes obtained, though less frequently than with intravenous injections. The great disadvantage of treatment with serum is the possibility of dangerous anaphylactic reaction, which may occur during the injection but is occasionally delayed several hours. Prompt treatment with solution of adrenaline, 1 minim of which should be injected every half minute after an initial injection of 3 minims until complete recovery takes place, is almost always effective. Though the improvement which follows serum treatment is probably in part due to protein shock, especially in cases in which there is much general reaction, yet in some cases it appears to be specific.

I have never seen the slightest benefit follow any form of vaccination, and in some cases the local condition has been definitely aggravated. Several American physicians have told me that they have been quite unable to confirm Bargen's enthusiastic reports about treatment with the vaccine and serum (so-called "ulcerative colitis serum") produced from his diplostreptococcus, which is regarded by most bacteriologists as a non-pathogenic variant of the normal enterococcus of the colon.

The danger of recurrence is much reduced if treatment is continued until endoscopy shows no trace of inflammation, even if symptoms have already disappeared for some weeks. Associated conditions, such as oral and pharyngeal infections and anal complications, must be treated, as a relapse may follow an acute sore throat or the development of a peri-anal abscess or a fistula-in-ano. The patient should keep permanently on a roughage-free diet and, when necessary, take sufficient paraffin to keep his stools soft.

As the whole of the colon can be satisfactorily washed out with 1½ pints of fluid introduced per anum, and as in many cases only the distal half is involved, appendicostomy and cæcostomy are never indicated. There are three indications for ileostomy. (1) It gives the only chance of recovery in the very rare acute fulminating cases with high temperature and passage of

large quantities of pus and blood. The divided ileum can be rejoined some weeks later. (2) When continuous treatment under good conditions for nine months has led to no improvement, and (3) when fibrous strictures or polypi have developed, the terminal ileum should be divided and both ends brought to the surface. The ileostomy causes very little trouble and the patient is soon able to lead a life of normal activity. When there is no longer any anal discharge and washings through the colon contains no pus cells or red corpuscles, diluted fæces from the ileostomy should be injected into the colon in increasing strength. If there is no reaction, it is generally safe to rejoin the ileum unless strictures or polypi are present, in which case the colon should be excised up to about 9 inches from the anus. Some months later the ileum can be joined to the cut end of the pelvic colon after any polypi present have been destroyed and strictures dilated per anum.

TUBERCULOUS ENTERITIS AND COLITIS

Ætiology.—Miliary tubercles may be present in the intestines in general tuberculosis, but they have no clinical importance. Primary infection of the bowels from tuberculous milk is not infrequent in children, but is comparatively rare in adults. Secondary infection from swallowing tuberculous sputum is very common, ulceration being present in 50 per cent. of fatal cases of pulmonary tuberculosis. The lower end of the ileum and the cæcum, where the rapid passage of chyme along the alimentary tract is first arrested so that there is time for the muco-pus in which the tubercle bacilli of the sputum are enmeshed to be digested, are the parts most frequently affected.

Symptoms.—In many cases no symptoms are present, although extensive ulceration may be found *post mortem*. Tuberculous enteritis should be suspected in children suffering from diarrhœa with fever, abdominal distension, enlarged glands, anæmia, wasting and weakness. It should also be suspected when pulmonary tuberculosis is associated with diarrhœa, especially if abdominal pain and tenderness are present and blood is found in the stools. Tubercle bacilli are often present as a result of swallowing infected sputum even with healthy intestines. In the absence of abdominal pain the diarrhœa in advanced phthisis is sometimes due to the achlorhydria which is commonly present.

Perforation of a tuberculous ulcer is rare owing to the adhesions which form between the coils of intestine. Cicatrisation of ulcers may lead to single or multiple strictures of the small intestines; as these are incomplete and the contents of the bowel are fluid, obstruction is rarely produced. External adhesions and the formation of bands may, however, lead to acute intestinal obstruction.

Tuberculous ulceration of the last few inches of the ileum may produce reflex dyspepsia. In such cases when the terminal ileum is visualised with the X-rays it is found to be tender; its lumen may be irregular and thickening may be recognised on palpation. The X-rays may show a group of opaque glands in the ileo-cæcal angle. The stools generally contain occult blood, and there is often mild intermittent pyrexia. At a later stage small intestine peristalsis may become visible, and palpable stiffening of a coil of ileum, which disappears with a gurgle, sometimes occurs, although the bowels may

remain regular until acute obstruction supervenes. In a case under my care multiple strictures of the colon were recognised with the X-rays; recovery followed partial colectomy, and the strictures were found to be caused by cicatrisation of tuberculous ulcers.

What has been described in the past as *hyperplastic tuberculosis of the cæcum* is probably a form of regional ileitis (p. 647) in which the cæcum is involved as well as the end of the ileum. It was always recognised that the condition was not associated with tuberculous foci elsewhere and tubercle bacilli were never found in the stools; there was in fact no evidence that the condition was tuberculous in origin.

Treatment.—The treatment is that of tuberculosis in general, combined with the dietetic restrictions required for non-tuberculous entero-colitis.

POLYPI OF THE COLON: POLYPOSIS

Ætiology and Pathology.—Solitary polypi of the colon are common, and cases with two to twelve are not infrequent. True polyposis, in which the whole or part of the colon is studded with innumerable polypoid adenomata, is very rare.

The polypi generally begin as small flat patches of mucosal overgrowth which soon become polypoid. Exactly similar polypi may develop in the process of recovery from ulcerative colitis; they are generally present in small numbers, but occasionally a condition of generalised polyposis develops which is indistinguishable from the primary condition.

Most cases of primary generalised polyposis are familial, several members of one or more generations of a family being affected. Less frequently single polypi are also familial.

Males are more often affected than females, and the symptoms generally begin before the age of 30.

Symptoms.—Recurrent passage of bright red blood, unmixed with mucus or pus, sometimes with and sometimes independent of fæces, is generally the first and often the only symptom. In adults internal hæmorrhoids give rise to similar symptoms, but in children polypi are the only common cause. In polyposis diarrhœa always develops sooner or later as a result of secondary infection and inflammation, and the fluid fæces are mixed with mucus, pus and bright blood, being indistinguishable from those passed in ulcerative colitis. The hæmorrhage may lead to severe anæmia, and the diarrhœa to malnutrition and, when it begins in childhood, to infantilism. Tenesmus and abdominal pain are uncommon.

The polypi can often be felt on rectal examination and can generally be seen with a proctoscope or sigmoidoscope, but occasionally they are situated too far from the anus, when the X-rays are the only means of making a definite diagnosis. Their exact extent can be estimated by means of an opaque enema which gives a characteristic picture, showing rounded semi-translucent areas in the shadow of the colon. Sometimes they are best demonstrated by inflation of the colon with air after the greater part of the opaque enema has been evacuated.

Polypi are the most common exciting cause of chronic intussusception.

Both single and multiple polypi show a considerable tendency to become

malignant, and the majority of patients with familial polyposis ultimately die of carcinoma. In most cases of carcinoma of the rectum and colon the lesion is probably grafted on a simple polypous adenoma. Thus in 75 per cent. of 33 specimens of carcinoma of the rectum and pelvic colon removed at operation simple adenomata were also present (Dukes), and in nearly all very early cases of carcimona the adenomatous origin can be recognised. Malignant degeneration may occur in more than one polyp either at the same time or after an interval.

Treatment.—Single and multiple polypi in the rectum and pelvic colon can be removed with a diathermy snare or destroyed by a diathermy cautery through a proctoscope or sigmoidoscope. The patient should be re-examined every 4 months for at least 10 years, so that any new polypi which develop can be destroyed before they have time to undergo malignant degeneration. Multiple small polypi sometimes disappear when treated with deep X-rays. When the whole colon is involved, the terminal ileum should be anastomosed with the lower end of the pelvic colon, the rest of the colon being excised. The polypi present in the remaining part of the pelvic colon and in the rectum are removed or destroyed by diathermy.

CANCER OF THE COLON

Ætiology.—Primary columnar-celled carcinoma of the colon attacks men with slightly greater frequency than women. It is most common between the ages of 40 and 65, although cases have been recorded in early childhood.

Pathology.—Only a little over 1 per cent. of cases of intestinal cancer affect the small intestine. Of the remainder 50 per cent. are in the rectum and at the pelvi-rectal flexure, and 25 per cent. in the iliac and pelvic colon; thus 75 per cent. of cases occur in parts of the colon where the fæces are solid. Nearly half of the remainder are in the cæcum and ascending colon.

The adenomatous origin of colonic carcinoma is discussed in the previous section.

Extension to the peritoneum and secondary deposits in the lymphatic glands, liver and other organs develop later and rather less frequently with cancer of the intestine than with cancer in most other situations, obstruction occurring in more than 50 per cent. of cases before the glands are involved. The prospect of a radical cure by operation, if an early diagnosis is made, is therefore comparatively good. The rectum has a moderate supply of lymphatics and gives operative results intermediate between gastric and colonic carcinoma.

Symptoms.—The possibility of cancer of the intestine should be considered whenever an individual over the age of 35, whose bowels have previously been regular develops, without change of diet or habits, constipation or diarrhœa, or when a patient of the same age, who is habitually constipated, becomes more so without obvious reason. Constipation occurs earliest in the common annular form of intestinal cancer, which narrows the circumference of the bowel while the actual size of the growth is still very small. Less obstruction is caused by papillomatous carcinoma, which forms

a friable and ulcerated mass, projecting into, but not obliterating, the intestinal lumen; constipation is at first intermittent and relieved by purgatives, which gradually become less effective and cause more pain. Enemata are generally of use for a longer period, but they also finally fail to act. Sometimes, however, there is persistent diarrhœa from the start, especially when the growth is situated in the pelvic colon. More frequently the initial constipation is interrupted by attacks of diarrhœa. In the majority of cases the constipation becomes steadily more severe until it ends in complete obstruction, which is sometimes hastened by the impaction of a hard mass of fæces in the narrowed lumen.

The stools do not generally differ in shape from those seen in ordinary constipation. Occasionally thin pieces, resembling the fæces formed in some cases of constipation associated with spasm, are passed, especially when the growth is in the pelvic colon or in the rectum; they sometimes owe their shape to spasm of the anal sphincter, produced reflexly by the growth or by the irritating discharge from its surface, but I have also seen ribbon-shaped fæces appear through a stricture six inches from the anus during a sigmoidoscopic examination. The stools in cancer of the rectum and lower part of the pelvic colon generally contain obvious blood, pus and mucus. In rare cases the passage of a large quantity of bright red blood is the first symptom. The stools may closely resemble those of simple ulcerative colitis, but fæcal matter is often absent and fragments of more or less solid fæces can sometimes be recognised, whereas in ulcerative colitis unformed fæces are almost always present. When the growth is proximal to the middle of the pelvic colon, blood and pus can rarely be recognised with the naked eye, but occult blood can always be found by the guaiac test. The spectroscope often shows that acid hæmatin as well as hæmatoporphyrin is present in contrast with the occult blood of gastric and duodenal origin, which gives the latter spectrum alone unless the quantity present is unusually great.

Vague discomfort in the lower part of the abdomen is often present, sometimes without any irregularity of the bowels, and slight attacks of colic occur when constipation becomes severe, but they rarely reach any great intensity until the obstruction is almost complete. In some cases, especially in cancer of the cæcum, hepatic flexure and splenic flexure, the pain may travel in a definite direction to a certain point, where the patient occasionally feels a rumbling sensation; this generally corresponds with the situation of the growth. When the pelvic colon is involved, the pain is always below the umbilicus and is often most marked on the left side.

The over-activity of the colon above the obstruction leads to hypertrophy of its musculature. When the obstruction becomes complete, failure of the muscle ultimately occurs and extreme paralytic distension results; ulceration and perforation, especially of the cæcum, may follow.

When the obstruction is sufficient to give rise to severe colic, strong spasmodic contractions of the colon, but not peristaltic waves, are often visible and palpable. They never occur in the colic associated with lead poisoning or colitis, and very rarely with obstruction due to simple impaction of fæces.

In cancer of the cæcum and ascending colon general symptoms, especially anæmia, are often present for a considerable time before any change takes

place in the activity of the bowels. Severe anæmia may indeed develop in the absence of any symptoms pointing to an abdominal disorder.

In about 30 per cent. of cases when the patient is first seen, a tumour is palpable either on abdominal or rectal examination. In some of the remainder the growth is inaccessible to palpation owing to its situation at the splenic flexure; in others the tumour is too small to be palpable. It is often impossible to reach a growth in the lower end of the pelvic colon or at the top of the rectum either by abdominal or rectal examination, though it may be accessible to bimanual palpation. In such cases the sigmoidoscope alone makes an early diagnosis possible. If acute obstruction is not an early occurrence, the growth develops into a large and easily palpable tumour, which invades the neighbouring peritoneum and viscera. The tumour often varies in size from time to time, as it is formed not only by the growth itself, but partly by impacted fæces or by thickened peritoneum and adherent coils of intestine, with perhaps a localised abscess. The disappearance of a tumour after treatment with purgatives or enemata does not therefore mean that cancer is absent, even if its disappearance is associated with improvement in the symptoms. For a mass of fæces can become impacted above a cancerous stricture and produce obstruction, which may be partially relieved when the fæces are removed. A diagnosis of cancer can only be excluded when the disappearance of the tumour is accompanied by complete and lasting cure of all the symptoms. The tumour produced by a growth is hard; it is rarely very tender, unless complicated by local peritonitis. When situated in the ascending, descending or iliac colon it is generally fixed; in the cæcum and transverse colon it is frequently very movable.

The X-rays often afford considerable help in diagnosis. The shadow of the colon may be visible as far as the seat of obstruction unusually soon after the opaque meal; little or no barium may pass beyond this point for a considerable time, but this may also occur in simple constipation. The passage of an opaque enema is often obstructed at a period in the disease when an opaque meal is not delayed. In most cases, especially when an enema is used, a filling defect caused by the tumour can be observed. When a tumour is present, the combination of abdominal palpation and X-ray examination shows whether any delay in the passage of fæces occurs in the neighbourhood of the tumour and whether the latter arises from some part of the alimentary canal. The X-rays may completely fail to give any evidence of a growth until some months have elapsed since the onset of symptoms, but with modern technique this should happen very rarely.

In exceptional cases symptoms are produced by complications before the intestinal functions become affected. Thus secondary deposits in the brain may cause cerebral symptoms sufficient to overshadow everything else, and an abscess developing in connection with an ulcerated growth or a stercoral ulcer above the obstruction, or general peritonitis resulting from perforation of the ulcer may constitute the earliest clinical manifestation. I have seen two cases in which no symptoms occurred until the development of a gastro-colic fistula.

Diagnosis.—The diagnosis depends upon the history combined with the results of abdominal and rectal palpation, examination of the stools for visible or occult blood, sigmoidoscopy and the X-rays. A tumour in the right iliac fossa may be caused by an inflammatory mass developing round a

small chronic appendicular abscess, by regional ileitis and by actinomycosis of the cæcum as well as by cancer. In the left iliac fossa confusion with diverticulitis is likely to occur. In the latter occult blood is often absent, and the diagnosis can generally be settled by means of the X-rays. The chronic obstruction caused by a local band of adhesions may simulate that caused by a growth, the difficulty being increased by the fact that the stools may contain occult blood.

Prognosis.—Improved methods of examination have made it possible to diagnose the large majority of cases of cancer of the colon as soon as symptoms appear and before any serious degree of obstruction has developed. As glandular involvement and secondary deposits in the liver and other organs occur comparatively late, in most such cases the growth can be completely removed, and many of my patients are still in perfect health several years after the operation. If operation be delayed until acute obstruction is present, the immediate prognosis is very bad, but in subacute obstruction a two-stage operation is often successful.

Treatment.—Cancer of any part of the large intestine proximal to the middle of the transverse colon is best treated by the removal of all the colon up to three inches beyond the growth, an ileo-colostomy being simultaneously performed. Beyond this point resection of the growth and of a sufficient margin on each side with end-to-end anastomosis is more satisfactory. If the slightest obstruction is present, the operation should be performed in two stages, excision being only performed after the patient recovers from a preliminary colostomy.

DIVERTICULOSIS: DIVERTICULITIS

Ætiology and Pathology.—Diverticulosis, the presence of diverticula in the colon, occurs in about 5 per cent. of men and women over the age of 40. They are especially likely to occur if aperients have been habitually used for many years. Owing to the atrophy of the muscular coat of the colon which occurs in old age, pressure from within produces diverticula more readily than in earlier life. The presence of fat diminishes the resistance of the intestinal wall, so that diverticula are especially likely to occur in the obese and they often form in the appendices epiploicæ.

The diverticula increase in number and size as the lower end of the pelvic colon is approached, but they are very rare in the rectum owing to the thickness of its muscular coat. A large number are generally present; some are so small that they are barely visible to the naked eye, whilst others attain a diameter of half an inch. They very rarely become larger than this, as secondary pathological changes interrupt their growth. In the walls of the smaller diverticula all the coats of the bowel are represented. As they grow larger the muscular layer gradually disappears and the mucous membrane frequently becomes atrophied.

Symptoms.—*Diverticulosis*, the simple presence of diverticula of the colon, is a very common condition and gives rise to no symptoms. Inflammation of diverticula, *diverticulitis*, occurs in about 15 per cent. of cases. Most frequently the patient complains of discomfort in the lower part of the abdomen and, after a time, attacks of colic, which gradually increase in

severity and in frequency. The discomfort is generally most marked in the left iliac fossa. At the same time the constipation, for which the patient has taken aperients for many years, may become more severe. Aperients aggravate the pain, which is relieved to some extent by the passage of flatus or fæces. Mucus may be present in the stools, and pus cells can occasionally be discovered on microscopical examination, but obvious and occult blood is generally absent.

The temperature is sometimes slightly raised, and in acute exacerbations it may be very high and accompanied by severe constitutional symptoms with polymorphonuclear leucocytosis.

The bladder is often irritable, the patient having to pass urine with abnormal frequency. At a later stage adhesions with the bladder may develop and lead to cystitis, and in rare cases gas and fæces are finally passed *per urethram* owing to the development of a vesico-colic fistula, diverticulitis and not cancer of the colon being the cause of the majority of cases of this condition.

Diverticulitis, like appendicitis, may cause reflex gastric dyspepsia.

Tenderness is most marked in the left iliac fossa and occasionally immediately above the pubes. The rigidity of the abdominal wall over the tender area may make palpation difficult, but in most cases it is possible to feel the irregularly thickened and extremely tender iliac colon. Digital examination of the rectum generally reveals nothing abnormal, but I have felt a mass suggestive of a secondary malignant deposit in Douglas's pouch which was caused by thickening round inflamed diverticula of the pelvic colon. The sigmoidoscope often cannot be passed farther than the pelvi-rectal flexure or an inch or two beyond, the bowel at this point appearing to be abnormally fixed and its lumen narrowed. I have never been able to see the mouths of diverticula at the lower end of the affected portion of the pelvic colon.

An opaque meal shows that there is generally little or no delay in the passage through the bowel till the iliac colon is reached. The presence of diverticula can often be recognised when the barium reaches the affected part, as some of it enters and remains in them after the rest has been evacuated. A barium enema should also be given, as whenever diverticula are present their number and localisation can be more accurately determined in this way than by any other method. They may be discovered directly the enema is given, but more often only after it has been evacuated, a double row of small rounded shadows representing the diverticula being then seen, especially in the position of the iliac and pelvic colon. They often remain visible for several days.

Diagnosis.—Discomfort and colicky pain in the lower part of the abdomen in middle-aged and elderly patients, especially if associated with increasing constipation, should raise the suspicion of diverticulitis or a growth of the colon. If the pain is most marked in the left iliac fossa and if it is associated with bladder irritability, the former is the more probable diagnosis. A tender tumour in the left iliac fossa, associated with muscular rigidity is much more frequently due to diverticulitis than to cancer. An X-ray examination after an opaque meal and an opaque enema generally settle the diagnosis. Diverticulitis is not a pre-cancerous condition, as the occasional association with cancer is no more frequent than can be explained by coin-

cidence, and the incidence of cancer in simple diverticulosis is as great as in diverticulitis. When cancer is present the stools contain pus and blood, whereas even occult blood is usually absent in uncomplicated diverticulitis, and an opaque enema reveals a filling defect in addition to the diverticula, which do not necessarily involve the same part of the colon.

Treatment.—The accidental discovery of diverticulosis in the course of a routine X-ray examination indicates the necessity for keeping the stools permanently soft by means of paraffin or an unirritating vegetable mucilage, and the avoidance of pips and skins of fruit, pickles and salads, and cooked green vegetables except as purées. No aperients should be used, as they tend to force the fluid fæces into the diverticula. In very mild diverticulitis the same treatment is effective. In more severe cases with pyrexia and abdominal rigidity the patient should be kept in bed till all signs of active inflammation have disappeared. The diet already mentioned should be given together with an ounce of paraffin three times a day. Belladonna in frequent and maximal doses may be required to control the secondary spasm. Six fluid ounces of paraffin should be injected into the rectum every evening and retained during the night. If the bowels do not act satisfactorily in the morning, water should be run into the rectum slowly and under low pressure in quantity insufficient to cause pain. By this means the accumulation of fæces generally present is gradually evacuated, and the pain and inflammation subside.

Very few cases require operation. Large inflammatory masses associated with a high temperature and leucocytosis often completely disappear with medical treatment, and a considerable degree of obstruction may be overcome. I have seen only one case requiring operation in the last fifteen years. Only if the symptoms become worse in spite of treatment, or if the condition is complicated by the development of an abscess, signs of spreading peritonitis, or intractable cystitis suggesting that a vesico-colic fistula is about to form, is an operation indicated. It is sometimes possible to excise or short-circuit the whole of the affected portion of the bowel, but more often a colostomy has to be performed.

CHRONIC INTUSSUSCEPTION

Ætiology.—Chronic intussusception is a rare disease occurring only in adults. Twenty per cent. are secondary to innocent and 15 per cent. to malignant tumours, most of which project as polypi into the lumen of the bowel. A case of mine was associated with chronic uræmia in a man suffering from nephritis due to lead poisoning.

For Acute Intussusception *vide* Acute Intestinal Obstruction, p. 671.

Symptoms.—A chronic intussusception may last for a month, a year or longer before it terminates in an attack of acute obstruction or of general peritonitis from perforation. It may finally reach the anus, from which it may project for some inches without preventing the passage of fæces. The onset is generally insidious; occasionally it is acute, but the severity of the symptoms generally diminishes and the subsequent progress of the case is chronic. Only about half of the cases are accompanied by constipation, diarrhœa being present in the majority of the others. The most prominent

symptom is colic, occurring in attacks which steadily increase in frequency and severity, and which may be brought on by taking food or by aperients; constipation is present during the attack, and blood and mucus may be passed at frequent intervals in entero-colic and colic, but not in enteric, intussusceptions. A palpable tumour is present in half the cases; it becomes harder and longer during an attack of colic, and appears to recede in the intervals. Severe attacks are accompanied by vomiting, especially in the enteric form. Visible peristalsis and dilatation may occur in the intestines above the intussusception. An opaque enema, given for suspected chronic obstruction, may reveal the presence of an intussusception by the typical appearance produced when a small quantity of fluid penetrates between the intussusceptum and the intussuscipiens.

Treatment.—The treatment is always surgical.

ANAL ACHALASIA AND MEGACOLON (HIRSCHSPRUNG'S DISEASE)

Definition.—Megacolon is a condition in which the rectum and pelvic colon and sometimes the whole of the large intestine are dilated and hypertrophied, although no organic obstruction is present.

The name Hirschsprung's disease, which is generally used to describe megacolon in children, should be discarded, as von Ammon gave a good description of two cases in 1842, forty-four years before Hirschsprung, and no clear dividing line can be drawn between the megacolon of children and that of adults, to which the name of Hirschsprung's disease is never applied.

Megacolon must be distinguished from a colon of abnormal length—*dolichocolon*. The pelvic colon varies greatly in length, but although a very long pelvic colon may predispose to volvulus, there is no reason to believe that it predisposes to megacolon.

Ætiology and Pathogenesis.—Megacolon in children is rare; I have seen only 10 cases compared with 36 in adults. Whereas in children it occurs almost exclusively in boys (9 out of 10 of my cases), the incidence is about equal in the two sexes in adults: there were 19 males and 17 females in my series. It is probable that the majority of cases observed in adult life do not date from childhood, as otherwise it would not occur so often in women, and the history of the onset of symptoms, though generally very vague, supports this view. There is, however, no doubt that many children with "Hirschsprung's disease" attain adult life, although the megacolon remains.

I believe that the primary factor in the pathogenesis of almost all cases of megacolon is achalasia of the sphincter ani—absence of the relaxation of the sphincter, which normally occurs when the rectum contracts during defæcation. Simple absence of normal relaxation without any added spasm of the sphincter is sufficient to prevent the easy evacuation of fæces, which are consequently retained. Under normal conditions gas can escape from the rectum by voluntary relaxation of the sphincter at any time; when achalasia is present voluntary relaxation is no longer possible, so gas as well as fæces accumulates in the rectum and pelvic colon.

The pelvic colon and rectum attempt to overcome the resistance offered by the closed anal sphincter by increased peristalsis with the result that their walls gradually become hypertrophied. This is at first sufficient to prevent any serious accumulation of fæces and gas, but after a time the amount of retention gradually increases. The thick walls of the fixed rectum give way less readily than the comparatively thin walls of the freely movable pelvic colon, so that the rectum does not show the same degree of dilatation as the pelvic colon, and in many cases it is only slightly enlarged. The distension of the pelvic colon results in an increase in its length as well as its diameter; as it contains a great excess of gas the dilated and elongated loop rises during the day when the individual is in the erect position, and eventually its upper extremity generally reaches the left dome of the diaphragm.

In adults the extreme degree of hypertrophy and dilatation does not as a rule extend beyond the pelvic colon, though some slight dilatation and hypertrophy are often present in parts or all of the rest of the colon. The same was true in most of the cases I have seen in children, but in only a third of the neglected cases which come to post-mortem is the extreme dilatation confined to the pelvic colon and rectum.

Megacolon is the result of disturbance in the normal balance between the sympathetic and parasympathetic nerve supply to the sphincter. This might theoretically be due to overactivity of the sympathetic, stimulation of which inhibits the movements of the pelvic colon and rectum and causes spasm of the sphincter ani, or to under activity of the parasympathetic, stimulation of which causes contraction of the pelvic colon and rectum and relaxation of the sphincter. The great hypertrophy of the muscular coat of the pelvic colon is clearly the result of overactivity and not of inhibition, which would tend to produce atrophy. Moreover, in the large majority of cases the examining finger meets with normal resistance on rectal examination, spasm being present only in exceptional cases. Long-continued spasm would lead to hypertrophy of the sphincter, but no hypertrophy can be recognised on palpation, and *post mortem* the absence of hypertrophy of the sphincter is in striking contrast with the hypertrophy of the wall of the pelvic colon and rectum. In all probability, therefore, the disturbed innervation which gives rise to megacolon takes the form of underactivity of the parasympathetic. In most cases the parasympathetic deficiency is confined to the fibres supplying the anal sphincter with the production of achalasia; the changes in the pelvic colon and rectum are a result of the obstruction offered by the closed sphincter. The parasympathetic deficiency is the result of inflammation, simple degeneration, or fibrosis of the myenteric (Auerbach's) plexus, which have been found in several cases of megacolon both in children and adults.

If, at the onset of dilatation of the pelvic colon, the fold of mucous membrane at the pelvi-rectal flexure is unusually prominent, the dilatation of the part immediately proximal to it may exaggerate the kink and prevent the passage of fæces and gas into the rectum. Although the primary condition is still the anal achalasia, the secondary obstruction caused by the kink at the pelvi-rectal flexure prevents the rectum from becoming distended with gas and fæces. In spite of this it always appears much enlarged when an opaque enema is given, showing that it must have been greatly distended at first, but that when the pelvi-rectal kink developed and gas and fæces

ceased to accumulate in the rectum, it contracted down without, however, losing the abnormal distensibility caused by the earlier distension.

In the majority of cases the sigmoidoscope can be passed its full length of 12 inches blindly without meeting any resistance, whereas in normal individuals it is very rarely possible to pass it beyond the pelvi-rectal flexure without having to withdraw the obturator and guide the instrument with the aid of direct vision. Endoscopy shows the end of the instrument in the centre of an enormous cavity. On withdrawing it no dividing-line can be recognised between the pelvic colon and rectum, the dilatation of which extends to the entrance of the anal canal. In some cases the rectum is only slightly dilated or is normal in size, and occasionally its walls have collapsed to obliterate the lumen. It is then difficult to pass the sigmoidoscope round the pelvi-rectal flexure into the pelvic colon. If, however, the window of the instrument is removed, the patient being in the knee-elbow position, air enters and the rectum dilates. No difficulty is now experienced in passing the sigmoidoscope into the pelvic colon. Nothing suggesting the presence of a pelvi-rectal sphincter, closed as a result of either achalasia or spasm, is ever observed.[1]

In well-compensated cases and in patients under treatment the rectum is either empty or contains a small quantity of fæces. Small, soft scybala or unformed collections of soft fæces are often seen sticking to the mucous membrane at different points in the enormously dilated pelvic colon. Presumably they are propelled along the mucous membrane by the activity of the hypertrophied muscularis mucosæ.

Megacolon, secondary to spasm of the anal sphincter, is in rare cases associated with spasm of the sphincter of the bladder with dilatation and hypertrophy of the bladder and ureters. The lesion in such cases must be situated either in the central nervous system or in the large sympathetic plexuses, from which fibres pass to both the rectal and bladder sphincters.

Symptoms.—In children with megacolon there is almost always a history of constipation dating from birth or from the first few months of life. At an early stage the bowels cease to act spontaneously, and drugs gradually lose their effect until an evacuation can be procured only by means of enemata. The stools are generally soft, but in early cases hard scybala may be passed. Soon after the onset of constipation the abdomen, which is normal in appearance at birth, begins to increase in size owing to distension of the colon with gas and fæces, the size varying from time to time according to the extent to which the bowels are opened. Enormously dilated segments of colon can often be recognised through the stretched abdominal wall; they are dull on percussion, and palpation shows that they are filled with soft unformed fæces. The rectum is generally much dilated and filled with soft fæces or less frequently with a large solid fæcal ball. If secondary obstruction has developed at the pelvi-rectal flexure, the rectum is empty and fæces can be felt in the pelvic colon through its anterior wall. With proper treatment the child can lead an ordinary life and has no symptoms of toxæmia.

[1] In most discussions on the pathogenesis of megacolon it is assumed that a sphincter exists at the pelvi-rectal flexure. Sigmoidoscopy and radiology in normal individuals show, however, that there is never any uniform constriction at the pelvi-rectal flexure such as would be produced by a sphincter, the lumen of the pelvic colon being separated from that of the rectum by the uppermost Houston's fold and by nothing else.

If neglected, enormous accumulations of fæces collect, and formerly, before the true nature of the condition was recognised, the bowels sometimes ceased to act at all and death occurred from chronic fæcal obstruction.

Megacolon in adults may give rise to no symptoms beyond a mild degree of constipation. The abdomen is often not obviously distended.

The gas in the dilated pelvic colon is under considerable pressure. In small children it pushes the diaphragm up and the abdominal wall forward, but in older children and in adults the appearance of the abdomen is generally less abnormal and is sometimes quite normal, as the diaphragm, which receives no support from above owing to the negative intra-thoracic pressure, gives way earlier than the abdominal muscles. The increase in the capacity of the upper part of the abdominal cavity produced in this way provides sufficient space for the greater part of the dilated colon. In spite of the fact that the diaphragm is almost completely out of action and that the capacity of the chest is much reduced, there is no complaint of dyspnœa. Several of my patients were able to take strenuous exercise without difficulty, and the majority were physically well developed. In most cases the left dome of the diaphragm is alone involved; it may reach the level of the third or fourth rib and is always higher than the right dome. In 2 of my cases the heart was pushed over to the right. In 5 the pelvic colon was so long and dilated that its upper extremity crossed the middle line after reaching the diaphragm on the left side and passed upwards in front of the liver so as to intervene between its upper surface and the right dome of the diaphragm. Its gas-containing cavity was seen with the X-rays to be in contact with the diaphragm on both sides.

Eventration of the Diaphragm.—As the diaphragm in megacolon is displaced into what is normally part of the thoracic cavity, the condition present might with justice be called eventration of the diaphragm. This name is, however, generally reserved for a condition in which the high position of the diaphragm is the result of a congenital defect in the musculature of the left half of the diaphragm, which is represented by a fibrous membrane containing only a few scattered muscle fibres. In deep respiration it moves passively up in inspiration and down in expiration—*i.e.* in the reverse direction to that taken by the normal right half of the diaphragm. When the high position of the diaphragm is secondary to megacolon there is a small movement in the normal direction.

The eventration of the diaphragm which results from maldevelopment of its musculature is very rare compared with that due to megacolon, as I have seen only 2 cases of the former compared with 42 of the latter.

If the term "eventration of the diaphragm" is to be retained at all, it would be more logical to include all cases in which the diaphragm is abnormally high, instead of confining it to those in which it results from a congenital defect in development. Cases would then be classified as follows:

(1) Primary and due to maldevelopment of one-half of the diaphragm. This is always left-sided.

(2) Secondary to atrophy following interference with the nerve supply. This may, of course, occur on either side. It is a result of (*a*) disease, most commonly secondary carcinoma, but occasionally primary carcinoma of the lung, tuberculosis, Hodgkin's disease and aneurysm; and (*b*) therapeutic division or avulsion of the nerve.

(3) Secondary to (*a*) aërogastrie bloquée (p. 575) and (*b*) aërocolie bloquée in megacolon.

Radiological Examination.—Every X-ray examination should begin with an inspection of the patient in the erect position before he has had an opaque meal or enema. The possibility of a megacolon is at once suggested by the discovery of eventration of the diaphragm. The abnormally high position of the left dome of the diaphragm presents such a striking appearance that it can hardly be missed. I have already pointed out that it is much more frequently caused by megacolon than by primary atrophy of the diaphragm, in which the left side moves upwards during inspiration while the right side moves downwards in the normal manner. It is generally possible in megacolon to recognise the outline of the enormously dilated air-containing loop of pelvic colon and to distinguish it from an abnormally large gas-bubble in the fundus of the stomach, which is always limited below by the horizontal upper border of the shadow of the gastric contents. When a gas-containing cavity is seen under the right dome of the diaphragm, as well as the left, the diagnosis of megacolon is certain.

An opaque meal does not help greatly in the diagnosis of megacolon, but it is a very valuable corrective for the false conclusions which are likely to be drawn from an examination after an opaque enema. It shows how much of the colon is undilated, the degree of stasis present and where the stasis occurs. The small intestine is always normal, and in most cases the large intestine as far as the end of the iliac colon is normal in size and shows little or no stasis. When the barium passes beyond the iliac colon it is lost in the large cavity of the pelvic colon, small spots of opaque material being scattered over the whole of the enormous area it occupies. Stasis of varying degree is always present in the pelvic colon. In well compensated cases, in which the bowels are opened daily, there is no delay in the evacuation of the greater part of the opaque meal, but a small quantity generally remains scattered through the pelvic colon for many days or even weeks.

An X-ray examination after an opaque enema gives the only means of recognising the exact anatomical condition present in megacolon. It is, however, essential to watch the fluid being run in, as it is otherwise impossible to interpret a radiograph owing to the large amount of overlapping of different segments of the bowel caused by the enormous dilatation of the pelvic colon, the uppermost loop of which is often mistaken for the splenic flexure. The fluid is seen to run straight upwards through a greatly dilated rectum and pelvic colon to the left dome of the diaphragm. Even if the rectum is not found to be dilated on digital examination; it is always distensible and no resistance in the passage of the enema into the pelvic colon is encountered; it is, in fact, often impossible to recognise where the rectum ends and the pelvic colon begins. After reaching the diaphragm, the fluid passes downwards again, but often not until it has made a more or less complicated loop, which may reach the right dome of the diaphragm in front of and above the liver. It finally reaches the left brim of the pelvis, where it passes upwards again along the iliac and descending colon to the splenic flexure and thence without difficulty to the cæcum. The splenic flexure, together with that of most of the transverse colon and all of the descending colon and iliac colon, is entirely obscured by the pelvic colon, which lies in front of it. Very large quantities of fluid are required to visualise the whole colon, and the pelvic colon alone

may have a capacity of 6 to 12 pints. The colon in children may hold as much as 4 to 6 pints, and in babies 1½ to 2 pints.

The size of the colon, as shown in a radiograph taken after the injection of an opaque enema, is not an indication of its actual size nor a measure of its tonicity, but an indication of its distensibility. Even if the fluid is injected at a pressure insufficient to cause discomfort, the size of the various segments is often much greater than what it is when seen with the sigmoidoscope or after an opaque meal. The radiographic appearance after an opaque enema does not correspond with the condition present immediately before it is given, because the walls of the colon relax in order to allow more and more fluid to enter until the maximal size which has been present at any recent time is attained. This explains why the pelvic colon in a case of megacolon, in which more or less complete relief has followed treatment, often appears to be as large as ever when examined after an opaque enema, though any abdominal distension present before the treatment may have disappeared and an opaque meal and sigmoidoscopic examination show no abnormality.

Prognosis.—Megacolon is compatible with perfect health. The majority of my patients came on account of nothing more than constipation, which was generally no more severe than that occurring in many individuals with no organic disease of any kind; in four it was accidentally discovered in the course of a routine investigation on account of abdominal symptoms caused by some other condition. Toxic symptoms are rare unless aperients have been taken in excess. Only in exceptional cases, in which the X-rays show that severe stasis occurs in the cæcum and ascending colon as well as in the pelvic colon, may true intestinal toxæmia occur. As 16 out of the 36 private cases were over 50 and an additional 9 were over 40 when I first saw them, although the condition had presumably been present for many years, if not from infancy, megacolon does not as a rule shorten life.

Only three of my patients died directly as a result of the intestinal condition—all after operation; a fourth patient died after excision of a carcinoma, which had developed in the dilated colon. Of the three fatal cases a woman of 22 died after colectomy in 1912, and a boy of 5 died after ileo-sigmoidoscopy performed as a preliminary to colectomy in 1914. With our present knowledge of the condition both of these patients could have been relieved by non-surgical means. The third case was a man of 55, who died after an operation for volvulus of the cæcum five years after I saw him.

All the children I have seen since the war with megacolon are developing normally and appear to be none the worse either physically or mentally for having had a dilated colon.

Complications.—*Volvulus.*—In a small proportion of cases the patient complains of sudden attacks of very severe pain with abdominal distension. Slight attacks, in which the pain is not very severe and the distension is slight, occur much more frequently; they are probably of the same nature as the severe attacks and are caused by the twisting of a loop of the dilated pelvic colon. Both types of attack may last a few hours or a few days, and almost always subside spontaneously.

Carcinoma.—In one of my patients—a man of 64—a carcinoma had developed in the dilated colon.

Treatment.—The main object in the treatment of megacolon is to lessen the resistance offered by the closed anal sphincter to the passage of fæces

and gas. Rapid stretching of the sphincter is not as a rule effective, as it quickly contracts again to its original state. For a permanent result to be obtained the postural tone of the muscle fibres of the sphincter must be permanently reduced. This can best be attained by the use of a conical ebony bougie, which is passed every morning just after the first attempt to open the bowels has been made. The bougie is pushed slowly in as far as it will go without causing discomfort and kept in position for half an hour. Patients soon learn to pass it for themselves, and the mother or nurse can pass it for children. A second attempt to defæcate is made immediately afterwards. At the end of about a week the bougie need be kept in position for only a quarter of an hour; at the end of a month it is passed on alternate days, then once a week, and finally it is used only from time to time if a slight return of symptoms should occur.

When a child with megacolon comes under treatment there is generally a large accumulation of fæces in the pelvic colon and in about 50 per cent. of cases in the rectum as well. The latter cases are easier to treat, as when the rectum is empty and a secondary kink has developed at the pelvi-rectal flexure, treatment of the anal achalasia does not help until the pelvic colon has been kept comparatively empty for some time so that its contents can pass without difficulty into the rectum. In adults such an accumulation is less frequently found, though in neglected cases and in all of the comparatively small number which have come to autopsy, huge quantities of fæces are present. In both children and adults there is always a very large accumulation of gas in the dilated segment of bowel. Before any permanent improvement can be attained, the fæces and gas must be evacuated as completely as possible. Aperients are quite useless, and enemas are not always effective, as a good deal of the water injected is often retained. In neglected cases in children the best results are obtained by evacuation under a general anæsthetic, partly by lavage with simultaneous abdominal kneading and partly by the finger. The fæces are generally soft, but sometimes a secondary cause of obstruction is present in the form of a solid ball of fæces, which acts as a ball-valve in the rectum and has to be broken up and removed bit by bit under an anæsthetic before the colon can be emptied.

After the colon has been evacuated and the resistance offered by the anal sphincter reduced, the patient is generally able to get his bowels satisfactorily opened every day. No aperient should be given, but it is wise to prevent the fæces from becoming hard by means of liquid paraffin. In many cases no further treatment is required. Sometimes, however, especially if the dilatation has been excessive, there is still a tendency for fæces to accumulate in the pelvic colon in spite of the bowels being opened daily. It is then necessary to give an enema perhaps once a week or once a month. In some cases the best results are obtained with a very large enema, as much as 8 or 10 pints being run in under low pressure; in others, most of the water is retained when large quantities are given, and quite satisfactory results are obtained with a single pint.

When attacks of pain and distension, presumably caused by a partial volvulus, recur in spite of treatment, immediate relief can often be obtained by the passage of a long flatus tube with the patient in the knee-elbow position. If this fails and the pain is severe, morphine and atropine should be injected. Relief almost always follows, but if the attacks are frequent and

severe the dilated loop forming the volvulus should be excised in the free interval.

Such operations as colostomy, ileo-sigmoidostomy and colectomy, which were formerly performed for megacolon, had a very high mortality and rarely led to any appreciable improvement, as the primary seat of obstruction—the anal canal—was left untouched. Various operations on the sympathetic nervous system have been performed with the object of reducing the tone of the anal sphincter, but this object can be very much more simply attained by local treatment. The operation has the further disadvantage of being invariably followed in males by permanent loss of ejaculatory power and consequent sterility.

It has recently been discovered that complete relief may follow spinal anæsthesia, and it is probable that the good effects of sympathectomy were really the result of the anæsthetic used for diagnostic purposes or for the operation. It seems likely that spinal anæsthesia will in the future replace all other methods of treating megacolon.

A. F. Hurst.

ACUTE INTESTINAL OBSTRUCTION

Acute intestinal obstruction is a condition in which the passage of the contents along the intestinal canal is more or less suddenly obstructed either completely or in greater part. Only mechanical causes of intestinal obstruction will be dealt with in this place, conditions of paralysis or spasm causing obstruction being considered elsewhere.

Ætiology.—The causes of acute intestinal obstruction are numerous, and may best be considered under (1) causes within the lumen of the bowel, (2) causes in the wall of the bowel, and (3) causes outside the bowel, while there are two additional conditions—intussusception and volvulus—which do not come under any of these categories.

1. Causes within the lumen of the bowel giving rise to acute obstruction are gall-stones, fæcal accumulations, and, very rarely, true foreign bodies.

Large gall-stones enter the intestine through a fistula between the gall-bladder and duodenum or, more rarely, some other part of the intestinal canal. Gall-stones are generally passed spontaneously; when this does not occur the site of impaction is often the lower part of the ileum near the ileo-cæcal sphincter.

Fæcal accumulation is a common cause of an acute termination to a case of chronic obstruction, but even without any previous narrowing it may cause obstruction. In such cases the fæcal mass may be enormous in size and of a stony hardness; it leads more frequently to the pseudo-diarrhœa of partial obstruction than to complete obstruction.

2. Causes in the wall of the bowel give rise in most cases to chronic rather than acute obstruction; the commonest of such narrowings are those due to cancer. These conditions are discussed elsewhere, and it is only their liability to an acute termination which needs consideration here. Such a final catastrophe may result from the impaction of fæces, or acute paralysis of the intestinal wall with or without peritonitis may develop. Congenital stricture is a rare cause of acute intestinal obstruction in early infancy;

apart from stricture of the rectum, the commonest site is in the duodenum, just above the entrance of the bile-duct, or in connection with Meckel's diverticulum.

3. The most common cause outside the intestine is strangulation of a portion of intestine by congenital or adventitious bands, diverticula or peritoneal adhesions. Such bands may result from old tuberculous or inflammatory disease, or may be a sequel to a laparotomy. They may be produced by the adherence of normal structures, such as the omentum, Fallopian tube or appendix to other abdominal organs, or may result from the presence of a persistent Meckel's diverticulum. The latter may remain attached to the umbilicus, or its free end may become adherent. Such bands may obstruct by bridging across a portion of bowel, or a knuckle of bowel may become twisted round or under them, or, if the band is not long, mere kinking at its point of attachment may be sufficient to obstruct the lumen. Internal herniæ may give rise to strangulation and intestinal obstruction; their commonest sites are congenital or acquired slits or tears in the mesentery or omentum, one or other of the normal peritoneal fossæ, or, more rarely, the foramen of Winslow or congenital or acquired apertures in the diaphragm. The peritoneal fossæ into which such internal herniæ may pass are situated in the neighbourhood of the duodeno-jejunal flexure, in the peri-cæcal region, and in the root of the pelvic mesocolon.

4. *Intussusception.*—By intussusception is meant the passage of one segment of intestine into another immediately below. When this occurs a tumour is formed consisting of three layers, the outermost or intussuscipiens being the portion of bowel into which invagination is occurring, and the inner two constituting the intussusceptum, which therefore consists of an entering layer and a returning layer. Between these latter is the strangled mesentery, interference with the vessels of which speedily occurs and induces changes in the intussusceptum. The apex is the distal part of the intussusceptum, and the neck the narrow part where the returning layer turns to become the sheath or intussuscipiens.

The chief cause of intussusception is undue enlargement of the intestinal lymphatic tissue producing irregular muscular action, aided no doubt by an unusually long mesentery, and by an atonic condition of the ileo-cæcal sphincter. All these three factors, particularly the first, are most common in early childhood, and intussusception is consequently rare at other ages; 70 per cent. of cases occur in infants under a year old. In adults an intestinal polypus or carcinoma is often the starting-point of the invagination, which generally differs from that occurring in infants by being chronic instead of acute.

Various forms of intussusception occur, of which the ileo-cæcal variety, with the ileo-cæcal valve as its apex, constitutes about 70 per cent. Enteric, colic, ileo-colic and multiple intussusceptions are less frequent. An intussusception always increases at the expense of the ensheathing layer, its apex remaining constant.

5. *Volvulus* is a condition in which a coil of intestine becomes twisted on itself around its mesenteric axis, leading to interference with its circulation and with the passage of its contents. It occurs most frequently in the pelvic colon and the ileum, but may affect the cæcum or any part of the intestine with a mesentery. It usually occurs late in life, is commonest in males, and

depends partly upon an abnormally shaped mesentery and partly upon loading of the loop from chronic constipation. The dilated coils above a chronic obstruction are especially liable to become twisted and so bring about an acute termination to the case.

Pathology.—In acute intestinal obstructions the conditions found fall mainly into two groups depending on (1) the occurrence of obstruction of intestine with a previously normal lumen, and (2) acute obstruction terminating a case of gradually increasing chronic obstruction.

1. In most cases in this group a portion of intestine is strangulated in addition to the obstruction to the lumen of the bowel, and consequently the condition of the intestine must be considered in three regions—namely, above the obstruction, below it, and in the strangulated coil itself. An exception occurs in the acute obstruction produced by an impacted foreign body, where, of course, there is no strangulation.

(*a*) The intestine above an acute obstruction is usually greatly distended, its walls are at first pale and thin, and later œdematous and purple in colour, and the extent of these changes rapidly increases upwards as the obstruction persists. The distended coils are full of fluid (partly the normal dammed-back secretion, partly an exudation of serum), and as the case progresses bacteria escape through the distended and paralytic coils, and lead to peritonitis. These changes are far more marked in small intestine obstruction than when the colon is affected.

(*b*) Below the obstruction the coils are, as a rule, empty, contracted and pale.

(*c*) As a result of circulatory interference, the strangulated coil itself becomes distended with effused blood and gas, the latter mainly CO_2, which cannot be absorbed. It is purple in colour, tense, œdematous and paralysed, and it exudes bloodstained fluid both into its lumen and into the surrounding peritoneum. If the strangulation is sufficiently severe to obstruct arteries as well as veins the coil becomes gangrenous in less than an hour. Such a coil is grey and loses its peritoneal sheen; it is flaccid and exudes free gas and stinking fluid into the peritoneum. This condition is, of course, irrecoverable, but in less complete strangulation the intestinal wall quickly returns to normal when the strangulation is released. A strangulated coil soon looses power to prevent the passage of bacteria, and if left alone its vessels inevitably become thrombosed, and its walls become gangrenous and ultimately perforate. The contents of an obstructed loop are profoundly toxic, the toxicity being greater the higher in the course of the alimentary canal the obstruction is situated.

2. When acute supervenes on chronic obstruction, the bowel has already had time to accommodate itself in some degree to the presence of narrowing of its lumen. The final blockage of the passage is most frequently due to impaction of fæces in the narrowed part, or kinking adhesion, volvulus or acute paralysis of the intestine above it. In such cases the already existing hypertrophy above the obstruction gives place to rapidly increasing distension, and as a result the intestinal circulation is interfered with, and gas, being no longer efficiently absorbed, collects within the bowel. The enteritis and ulceration usually present in some degree above a chronic obstruction rapidly increase, and perforation and consequent peritonitis speedily follow.

Symptoms.—The symptoms of acute intestinal obstruction vary to a

certain extent with the particular cause of the condition, but some of them are present in all cases. Of the general symptoms, pain, vomiting, constipation and collapse are the most important.

Pain is an early symptom and is very severe, in many cases a patient in perfect health being suddenly seized with an acute abdominal pain which doubles him up and never remits. At first the pain is stabbing in nature, but later he complains of exacerbations which are colicky in character, and which occasionally serve to localise the obstruction. If the case is allowed to progress until peritonitis supervenes, the continuous pain and tenderness associated with that condition are present in addition.

Vomiting, preceded by nausea and severe retching, usually comes on about an hour after the pain, but it may be delayed for 8 or 10 hours. Once it has begun it continues with increasing frequency, and from the second to the fourth day it becomes fæcal in character. The higher the site of the obstruction is situated in the bowel, the greater the vomiting and the sooner it becomes fæcal. Fæcal vomiting is not due to antiperistalsis, but is caused by the stagnant and excessive secretions of the portions of bowel above the obstruction, gradually extending upward until they overflow into the stomach and cause vomiting. The fæcal character is accounted for by the remarkable speed with which *Bacillus coli* and other organisms multiply in the stagnant contents.

Collapse is early and severe. The patient is prostrated, anxious, and restless, the pulse is rapid, small and thready, the temperature subnormal, and the extremities cold and clammy. The collapse is partly reflex from stimulation of the vagal and splanchnic nerve endings in the abdomen, and is partly due to loss of fluid from sweating and excessive intestinal secretion. A very important part is also played by the toxic intestinal contents; the higher in the bowel the obstruction is situated the greater is the toxicity of the stagnating contents.

Constipation is as a rule absolute, although the bowel below the obstruction may empty itself shortly after the onset of the pain and vomiting. Neither fæces nor flatus are passed, and enemata after washing away any fæcal material present in the bowel below are either retained or return slowly without force.

In addition to these cardinal symptoms the patient presents certain other important signs. The tongue is dry and the teeth are covered with sordes. The abdomen at first is not tender to touch, and sometimes pressure may relieve the pain. It is often not distended, though in some conditions, such as volvulus, the distension may be extreme. If acute obstruction supervenes on chronic obstruction visible peristalsis may be present, and the coils can be felt to harden under the hand. Occasionally a tumour is felt in the abdomen, especially in intussusception, where a sausage-shaped mass can frequently be felt. On auscultation intestinal sounds are present in increased intensity, and are high-pitched in character. If the case goes on until peritonitis supervenes the symptoms of that condition develop and consequently the abdominal picture changes. In acute intestinal obstruction the urine is scanty and highly coloured, and when the obstruction is low in the bowel it contains a great excess of indican. The viscosity of the blood is increased from loss of fluid; this probably accounts for the frequent cramp-like pains in the limbs.

Diagnosis.—The diagnosis of acute intestinal obstruction is usually easy, but the further differentiation of the site and nature of the obstruction, though sometimes fairly simple, is often impossible before operation. The history is of importance in deciding whether the acute symptoms have supervened on those of chronic obstruction, in which case similar but less severe attacks which were relieved by enemata or purgatives may have occurred. A previous history pointing to gall-bladder trouble, particularly if the onset of obstruction is somewhat less acute than usual, suggests gall-stone impaction.

Inquiry should be made for evidence of abdominal attacks suggesting appendicitis, salpingitis, or other conditions, which might produce bands.

The presence in an infant of a sausage-shaped tumour, which can be felt to harden and is situated usually in the upper abdomen, with tenesmus and the passage of blood and slime, acute attacks of colic causing the child to scream and to draw up its legs, with occasional vomiting, forms a characteristic picture of intussusception, and enables a confident diagnosis to be made in many cases. In doubtful cases, examination under anæsthesia may be required, and rectal examination may enable the intussusception to be felt.

In volvulus the onset is acute, but collapse may be absent. Vomiting is not frequent at first, but the characteristic feature is the rapid onset and extreme degree of distension. This distension may at first be localised and indicate the seat of the volvulus, but it soon involves the whole abdomen and may cause severe cardiac and respiratory embarrassment.

Distension implies interference with the blood supply and consequent deficient absorption of gas from the bowel; it is thus a valuable indication as to whether strangulation has taken place as well as intestinal obstruction.

The conditions from which acute intestinal obstruction has to be differentiated are numerous. The most important is hernia, and a careful examination of the hernial apertures should always be made. In some cases of small femoral herniæ in fat persons it is very easy to overlook the condition, and in the rare obturator hernia diagnosis is frequently only possible on opening the abdomen. Fæcal impaction is another important condition to be considered, particularly in view of the grave results of laparotomy mistakenly undertaken for its relief. The history of chronic constipation and the presence of hard or putty-like masses in the rectum or pelvic colon should prevent errors.

Peritonitis is often a source of difficulty. The extreme tenderness and rigidity, the absence of fæcal vomiting, the partial nature of the constipation at first, as well as the temperature, history, and silence of the abdomen on auscultation are distinguishing features. Difficulty may arise from conditions causing acute stimulation of the sympathetic nerve, such as torsion of the testicles, ovary, or omentum, or the passage of a renal or biliary calculus. Careful inquiry of the history, the characteristic distribution of pain in the colics, examination of the scrotum and vagina and of the urine will usually lead to a correct diagnosis. Further, in these conditions enemata generally result in passing of flatus, and the course of the disease does not follow the usual sequence of cases of acute intestinal obstruction. In acute pancreatitis the pain is localised in the epigastrium, while the constipation is usually not absolute.

Lead colic can be distinguished by the blue line on the gums, the history, the blood picture, the absence of fæculent vomiting, and the result of enemata; while a routine neurological examination will distinguish tabetic crises.

Rare conditions which may lead to mistakes are embolus or thrombosis of the superior mesenteric vessels. In embolus some cardiac lesion is usually present, and in thrombosis there may be evidence of cirrhosis, gall-bladder disease or thrombosis of other veins, while hæmatemesis and melæna are common in both conditions.

Prognosis.—Spontaneous cure is remotely possible in all cases of intestinal obstruction, but in the majority of cases, if operation is not undertaken, death occurs at varying intervals, the average being after 6 days. Once the obstruction has been relieved by operation recurrence is uncommon, excepting perhaps in cases due to adhesions following operation. Even when operation is undertaken acute intestinal obstruction has a grave outlook, depending partly on the length of time elapsing before operation and partly on the nature of the lesion present. Other conditions materially affecting the prognosis are the age and general condition of the patient, and the presence of toxæmia, septicæmia, peritonitis, or complicating conditions elsewhere.

Treatment.—Excluding cases of fæcal impaction the treatment of all cases of acute intestinal obstruction is immediate operation. The object of the surgeon is to locate the seat of the obstruction, and to relieve it as quickly as possible with the minimum of handling and exposure of the abdominal contents. When the abdomen is opened a collapsed portion of gut is sought, as it helps to localise the seat of obstruction. When found, the obstruction must be relieved in the simplest possible manner, by reducing a hernia, dividing a band, reduction of an intussusception by manipulation, removing a gall-stone, etc. If, however, the obstruction cannot be relieved, or if the bowel is too severely damaged to return to the abdomen, it is wise simply to establish drainage above the obstruction and to wait till the acute period is passed before undertaking further measures. In cases with much distension, where the obstruction is obviously in the colon, and where an exploration would entail considerable handling, the proper treatment is undoubtedly to perform a blind cæcostomy and to delay further procedures until the distension has been relieved. Apart from operation, saline solution should be given intravenously, by the continuous drip method to combat the loss of chlorides and fluid, and opium may be given to relieve pain once the diagnosis is established and operation agreed to. Gas-gangrene antitoxin (*B. welchii*) is of value in combating toxæmia, and helps to relieve distension. It should be given intramuscularly, the initial dose being 10,000 units, followed by 4000 units on the two next successive days.

APPENDICITIS

Ætiology.—The two sexes are affected equally. No age is exempt, but whereas acute appendicitis is more common in children, chronic appendicitis is more common in adults.

The appendix may become infected either by organisms spreading from the lumen of the cæcum or conveyed by the blood. In the former case, the

original infection may presumably come from infected food, but septic foci in connection with the teeth, tonsils and naso-pharynx are undoubtedly of more importance. The latter are also the chief sources of hæmatogenous infection.

The commonest organism is the *Bacillus coli communis*; next in order of frequency come streptococci and staphylococci. The proteus, tubercle and actinomycosis organisms are rare. Congenital or acquired abnormalities are present in a considerable proportion of cases. In the former the appendix is not fully descended, is of the infantile variety, or is twisted on itself. In the latter, there are adhesions or kinks caused by previous inflammation either of the appendix itself or of neighbouring organs; and in many cases the bands resulting from chronic intestinal stasis lead to kinking of the appendix. Obstruction to its lumen from any of these causes produces stagnation of its contents, and provides the necessary conditions for bacterial invasion. Foreign bodies are another cause, but they occur less frequently than might be expected. Intestinal worms, pins, and fruit pips and stones have all been met with, but by far the commonest foreign body is the so-called "appendicular concretion," formed of inspissated fæcal material moulded into shape by the appendix itself.

Acute Appendicitis

Pathology.—In catarrhal appendicitis the mucosa only is affected, but in the commoner diffuse type all the coats are involved, the organ being hyperæmic, rigid, tense, and swollen, and the mucous membrane being frequently ulcerated. Later the lumen of the appendix becomes filled with pus, and if there is obstruction, empyema of the organ results. Later still, local or general gangrene occurs, the most frequent sites being the tip or the base. Perforation is very liable to take place at any of these stages, leading either to a localised appendicular abscess or to generalised peritonitis. The chief factor in determining which of these two complications will occur is the virulence of the organism, since it requires time for the reaction of the peritoneum to come into play sufficiently to localise the results of perforation to the immediate neighbourhood. If the lumen of the appendix is obstructed by a stercolith, acute appendicular obstruction results, and the tension of decomposing fæcal matter within its lumen leads to rapid gangrene and perforation. In milder cases the inflammation tends to resolve, and the appendix may return to an apparently normal condition, but if the attack has been at all acute, either adhesions or narrowing of the lumen generally remain, leaving it far more liable to further attacks of inflammation. If perforation and abscess formation occur and operation is not undertaken, spreading peritonitis results. Suppurative pylephlebitis may result from spread of infection along the mesenteric veins either with or without perforation of the appendix.

Symptoms.—In nearly all cases the following symptoms are present, though they may vary in degree—(1) sudden abdominal pain, (2) pyrexia, (3) increased pulse rate, (4) gastro-intestinal symptoms, (5) local signs.

1. *Sudden abdominal pain.*—The onset is usually sudden, the patient being seized with severe abdominal pain, often severe enough to produce collapse and vomiting, and often referred at first to the region of the umbilicus, particularly in children. Later the pain becomes more or less local-

ised to the right iliac fossa, and may be of considerable intensity. In the obstructive type of case, colicky pain marks the onset, unassociated with fever or increase of pulse rate, and continues until perforation results, or operation is undertaken. In very severe cases, especially in children, and where early gangrene occurs, the pain may be comparatively slight after the initial onset, and in other cases the affection may progress to abscess formation with relatively little pain. Such cases are, however, the exception, and the pain is usually a prominent symptom.

2. *Pyrexia* is almost always present at some time during the attack, except in cases of the obstructive type, where its absence is apt to lead to mistakes in diagnosis, but its height is no measure of the severity of the lesion in the appendix. There is sometimes a rigor at the onset, and the temperature in an average case varies from 100° to 102°, rarely higher. A rise only to 99° or 100° is not uncommon, but is important, as very few cases occur in which there has not been some pyrexia at some period of the attack. When a localised abscess has formed, and in very severe cases with perforation and generalised peritonitis, the temperature may be normal or subnormal throughout.

3. The *pulse rate* is usually increased and tends to continue to increase as the disease progresses. In cases of appendicular obstruction there may be no increase in the pulse rate until perforation has occurred.

4. *Gastro-intestinal disturbances* are almost invariably present. The tongue is furred and rapidly becomes dry. Vomiting is frequent. There is usually vomiting at the onset of the attack, and though this persists in the severe cases with peritonitis, it may pass off, but nausea usually continues. Constipation is the rule, and in the majority of cases is absolute. Diarrhœa is, however, by no means uncommon, indicating usually a pelvic position of the appendix, in which the inflammation spreads to and irritates the rectum. If the process is allowed to progress, complete constipation resulting from peritonitis and consequent paralysis of intestinal movements ensues. Even before this stage has been reached, auscultation over the region of the cæcum often reveals a complete absence of the usual intestinal sounds, which may be of considerable help in diagnosis.

5. *Local signs.*—There is usually no distension of the abdomen at the onset of the attack, but on inspection it will be seen that the lower abdomen moves less freely than the upper on respiration, and the right side less than the left. There is frequently hyperæsthesia of the skin in the right iliac fossa, and occasionally some œdema can be discovered by loosely picking up the skin and subcutaneous tissues between the fingers and comparing with the other side. There is great rigidity of the right rectus muscle, and this is probably the most important single sign; the rigidity is often too great to allow of any proper deep palpation. In addition to the rigidity there is great tenderness and pain on palpation, which has its maximum at Mac-Burney's point, situated at the junction of the outer and middle thirds of a line drawn from the anterior superior iliac spine to the umbilicus. In children the maximum pain and tenderness are often in the region of the umbilicus. In some cases an ill-defined mass can be felt in the right iliac fossa, and the longer the history, the more likely is such a mass to be present. It is constituted mainly of adherent coils of intestine and omentum surrounding the inflamed or perforated appendix. Rectal examination is often of

value, and in many cases a tender mass can be felt on the right side of the rectum, when none can be made out from above. Considerable irritability of the bladder may be present, especially with a pelvic appendix, and the urine, which is scanty, frequently contains albumin.

A blood count is occasionally of value for purposes of differential diagnosis, and usually shows a leucocytosis of from 15,000 to 20,000.

In many of the worst cases, some or all of these signs and symptoms may be absent, but with a careful examination and a clear history it is usually possible to reach a correct diagnosis.

In some cases an abnormally situated appendix gives rise to characteristic symptoms. With a retro-cæcal appendix, local signs in the right iliac fossa may be absent, there being instead great pain and tenderness in the loin, and rigidity without great tenderness of the right rectus. These cases are specially apt to develop subdiaphragmatic abscess, and later empyema. An appendix running down into the pelvis is apt to give diarrhœa and bladder irritability, local rigidity may be slight and a mass can usually be felt per rectum. An appendix running directly inwards may occasionally give rise to left-sided symptoms.

Course.—Where a correct diagnosis is made, early operation should be undertaken at once, for reasons to be discussed later, but if for any reason operation is delayed the case may take one of three possible courses.

(*a*) Gradual recovery may ensue, and in first attacks this will occur in a large number of cases. Improvement begins about the second or third day and the acute symptoms generally subside in a week. In such cases the patient is extremely liable to have further attacks, a liability which is increased in proportion to the degree of change which has occurred in the appendix.

(*b*) In many cases, as the result of ulceration or perforation of the appendix, the local symptoms not only do not disappear at the end of the first week, but persist and become aggravated. The temperature usually rises and there may be rigors, while at the same time a tumour becomes palpable in the iliac fossa. In some cases the abdominal wall may become œdematous and indurated, and the patient frequently begins to lose weight rapidly, to sweat profusely and to show all the signs of closed suppuration. If an operation be now performed, an abscess is found in connection with the appendix, having definite walls composed of adherent and matted intestine, omentum and parietal peritoneum. Such abscesses often contain large quantities of very foul-smelling pus, and if left alone may burst into the rectum or general peritoneum, or more rarely on to the surface, usually in the neighbourhood of the umbilicus. Spontaneous recovery may follow rupture into the rectum or on to the surface, but in the other cases death is almost certain to ensue.

(*c*) The third result of an unoperated attack of acute appendicitis, and by far the commonest cause of death in this disease, is generalised peritonitis. This may occur either from perforation of the appendix before limiting adhesions have had time to form, as in cases of the obstructive type, or it may occur without any perforation at all. In the latter case bacteria pass through the wall of the inflamed appendix and set up suppuration in the neighbourhood; if the resistance is poor, this involves the neighbouring peritoneum and ultimately leads to a generalised infection. In other cases

a localised abscess may form and later burst into the peritoneum, a result often precipitated by sudden exertion on the part of the patient, injudicious palpation, or the administration of aperients. The great danger of appendicitis, and one that can only be met by immediate operation in all definite cases, is that general peritonitis may occur from the very beginning, and its symptoms may be indistinguishable from those of the acute appendicitis itself. In the hands of competent abdominal surgeons, operation in the early stages is one of almost absolute safety, and in these circumstances any delay, with the shadow of possible peritonitis menacing the patient at any time, is quite unjustifiable.

Diagnosis.—As appendicitis is by far the commonest acute inflammatory condition occurring in the abdomen in people under middle age, it must always be thought of in the presence of acute abdominal disease. In a typical case, with acute onset of abdominal pain, generalised at first and later settling into the right iliac fossa, with vomiting, constipation and local rigidity and tenderness, the diagnosis is easy, but one or more of these signs may be absent, and in such cases it is well to remember that a single positive sign is worth several negative ones. The most constant single sign is tenderness on deep pressure in the iliac fossa, and if this is present even in moderate degree, the case must be carefully watched before a diagnosis of acute appendicitis can be safely discarded.

Rectal examination may reveal bulging of the rectal wall by an abscess, particularly with a pelvic appendix, which, if palpable, is extremely tender.

A general examination of the patient is essential in order to eliminate certain other conditions which sometimes lead to mistakes. Right-sided pneumonia may cause difficulty, as the onset is sometimes associated with considerable pain and rigidity in the right side of the abdomen, but as a rule the accompanying respiratory symptoms and signs, especially the rapid respiration, will prevent error. In children, contraction of the right psoas muscle with flexion of the hip may suggest an acute arthritis or even a psoas abscess, whilst a psoas abscess is occasionally mistaken for appendicitis. Of the abdominal lesions most likely to cause confusion the most difficult to differentiate is acute tubo-ovarian disease in women. In some of these cases, appendicitis coexists from spread of infection, and where doubt remains after a thorough pelvic examination it is safer to operate than to risk leaving a possible acute appendicular lesion.

In perforation of gastric or duodenal ulcers, the general shock is more profound, the rigidity is more general and board-like, and the pain is diffuse and not localised; in biliary, renal, and intestinal colic, the nature and distribution of the pain usually suffice to prevent mistakes. Twisting of a small ovarian cyst may be impossible to differentiate, but operation is called for in either case. In certain cases of typhoid fever the clinical picture may simulate appendicitis very closely. The relatively slower pulse and higher temperature, the constant headache, and the absence of any definitely acute onset, are of the greatest help in distinguishing, and a leucocyte count may be of considerable assistance, as leucopenia is present in typhoid fever in contrast with the leucocytosis of appendicitis.

Prognosis.—If left alone a considerable proportion of cases of acute appendicitis tend to recovery, but it is at present impossible to give an accurate prognosis of the course of any particular case within the first 48 hours. The

chief cause of death is peritonitis, and less often pylephlebitis, septicæmia, or pulmonary embolism. Even if recovery from a first attack does occur, the patient is left with a far greater liability to subsequent attacks, and is in some danger of acute or chronic obstruction from the adhesions which so frequently develop. Successive attacks of appendicitis tend to be more severe, and a patient who has had two is almost certain to have further trouble.

With early operation the prognosis is extremely good, death being rare after operation within 36 hours. Even when operation is undertaken later in the attack, the prognosis is still good, unless general peritonitis has ensued, in which case the prognosis without operation is uniformly bad. A further great advantage of early operation is that drainage of the abdomen can be avoided in these cases, whereas in later operations drainage is frequently necessary with a consequent increased risk of post-operative hernia.

Treatment.—In acute appendicitis operated on within 36 hours of the onset, the mortality in the hands of competent surgeons is negligible, and since it is quite impossible to determine the course which any particular attack is going to take, there can be no doubt that when the diagnosis is definitely established, operation should be undertaken at once. Some surgeons are of opinion that when the case is seen later than 48 hours from the onset and is tending to improve, medical treatment should be undertaken until the attack has subsided, and the appendix should be removed during the quiescent period. Since operation in these cases is, with modern technique, very little more difficult or dangerous than in early cases, such a view has little to recommend it, since it condemns the patient to two tedious periods of sickness instead of one, and there is, in addition, the risk of the patient's natural objection to an operation, when he feels perfectly well, overcoming the advice he has been given and leaving him exposed to all the risks of a further attack. When peritonitis or localised abscess formation has occurred, there are no two opinions as to the necessity of operation. If, for any reason, operation is impossible or refused, the patient should be kept in the Fowler position, should have nothing but water by mouth, and may be given morphine to diminish both pain and intestinal movement, provided always that the question of operation has been finally and definitely decided. Under no circumstances should a purge be given, as there can be no doubt that in far too many cases purgation is the direct cause of perforation.

Where an appendicular abscess has developed, it was formerly held that the abscess should be drained and the appendix removed subsequently. Modern surgical opinion is in favour of doing both at one operation, and in the hands of an experienced operator this procedure is undoubtedly best, but where skilled surgical aid is not available, simple incision and drainage of the abscess meet the immediate emergency.

E. G. Slesinger.

Recurrent Subacute Appendicitis, Chronic Appendicitis and Appendicular Dyspepsia.

At one time I diagnosed chronic appendicitis with confidence, and regarded it as a common cause of abdominal symptoms. In recent years I have diagnosed it with less and less confidence, and am now doubtful

whether such a condition really exists. I have seen hundreds of patients who have had their appendix removed for "chronic appendicitis" without the slightest benefit, and I am inclined to think that there is no justification for performing appendicectomy unless there is a history of subacute attacks, however slight. A considerable proportion of patients suffering from colon spasm and muco-membraneous colic and other abdominal neuroses and abdominal allergy, as well as from chronic cholecystitis, have their appendix removed without benefit before a correct diagnosis is made. Perhaps five per cent. of the patients, who ten years ago would have had their appendix removed for "chronic appendicitis," have recurrent subacute appendicitis and will benefit from appendicectomy. But there is no longer any excuse for ascribing symptoms to a "long," "kinked," "obliterated," "adherent," or "controlling" appendix. Symptoms are not likely to disappear permanently after appendicectomy unless the appendix contains pus or shows other definite signs of inflammation on naked-eye examination.

Symptoms.—A diseased appendix may give rise to gastric symptoms, accompanied by constant discomfort or short attacks of pain in the right iliac fossa. Epigastric pain, which may radiate downwards to the umbilicus or below, and occasionally towards the right iliac fossa, occurs after meals. The time of its onset is very irregular. Most commonly it occurs immediately after meals, but occasionally it may be delayed for 2 or 3 hours. It is at the most only slightly relieved by alkalis, and food rarely gives even momentary relief. It is aggravated by fatigue to a greater extent than is the case with the indigestion of gastric and duodenal ulcer and gall-bladder disease. The degree of discomfort varies from time to time; it is rarely completely absent and may sometimes be sufficiently severe for the patient to go to bed. Nausea is common and is often present in the absence of vomiting. Vomiting may occur, especially after food and when the pain is severe, but it gives much less relief than in gastric ulcer. Heartburn and acid regurgitation are uncommon. Hæmatemesis may occur from an acute gastric or duodenal ulcer secondary to the appendicular infection, which is also occasionally associated with a chronic gastric or duodenal ulcer. I have several times seen lasting benefit follow the removal of the appendix after an acute attack in a patient with a chronic ulcer, which had presumably been kept active hitherto by the presence of latent disease in the appendix.

Tenderness is generally more marked in the right iliac fossa than in the epigastrium, even when there is no spontaneous pain in the former situation. Occasionally the localised tenderness can be discovered only when pressure is exerted directly over the appendix after it has become visualised with the X-rays. In many cases pressure in the right iliac fossa leads to no local pain, but to discomfort in the epigastrium, sometimes with nausea, exactly simulating the spontaneous symptoms. Constipation is commonly present. In rare cases there may be chronic diarrhœa, but more frequently a form of pseudo-diarrhœa, in which frequent small stools are passed owing to irritation of the rectum by a chronically inflamed appendix situated in the pelvis. Pelvic appendicitis may also lead to irritability of the bladder with frequent micturition, and in women to dysmenorrhœa.

An operation is not justifiable for chronic appendicitis, unless the diagnosis has been confirmed by means of the X-rays and, if possible, by Bastedo's inflation sign. The appendix can be visualised in almost all normal individuals

and in about 80 per cent. of cases of appendicitis, and its discovery in the pelvis or immediately under the liver may explain anomalous symptoms. When the appendix is inflamed, all or part of it, especially the base or the tip, is found to be the point of maximum tenderness, definitely more tender than the end of the ileum or the cæcum. By manipulating the cæcum so that the position of the appendix in the abdomen is altered, the tender point moves with it. In some cases pressure on the appendix produces epigastric discomfort, either with or without local tenderness. Indirect evidence of appendicitis is occasionally afforded by the presence of ileal stasis, and by the recognition of adhesions in the right iliac fossa, which are most commonly due to previous attacks of acute or subacute appendicitis.

On inflating the colon with air through a tube introduced into the rectum generalised discomfort is felt in the lower part of the abdomen. Bastedo's sign is the production under these conditions of localised pain in the right iliac fossa with increased tenderness, sometimes associated with or even entirely replaced by epigastric discomfort. This is present in a large proportion of cases, but never in salpingitis, ureteral calculus, gall-bladder disease or other conditions, which might simulate chronic appendicitis. The inflation should be carried out during the X-ray examination, as it raises a pelvic cæcum and brings the appendix within reach of the palpating fingers. It also unravels confusing pelvic shadows and makes it possible to decide to what extent adhesions are present in connection with the terminal ileum, cæcum and appendix. If inflation fails to raise a pelvic cæcum and appendix into the abdomen, the X-ray examination should be repeated with a full bladder, which always brings them within reach of abdominal palpation except in the very rare cases in which they are fixed in the pelvis.

If repeated attempts fail to visualise the appendix it is probable that its mouth is obstructed ; in the presence of suspicious symptoms and tenderness in the ileo-cæcal angle the absence of an appendicular shadow favours the diagnosis of appendicitis. In such cases Bastedo's sign is also negative, as it depends upon distension of the appendix itself, which is only possible when barium can enter it.

Treatment.—Recovery should follow the removal of a grossly diseased appendix, but it is not infrequent for the symptoms to persist for a time or recur after the operation, especially if the disease is associated with some visceral neurosis or with chronic gastritis, gastric or duodenal ulcer, chronic typhlitis or chronic cholecystitis. Such associated conditions require attention both before and after the operation, and if the gall-bladder is diseased it should be removed at the same time.

ARTHUR F. HURST.

DISEASES OF THE LIVER

TESTS FOR HEPATIC FUNCTION

The most practically useful tests for hepatic efficiency in cases of suspected liver disease with or without jaundice are the lævulose tests, the hippuric acid test and the serum choline esterase test. For the lævulose tests 50 g.

of lævulose are taken in 100 c.c. of water on an empty stomach: the blood sugar is estimated immediately before and one and two hours later. Normally the first hour rise is between 0 and 20 mgrm. per 100 c.c.; at the end of the second hour the figure should fall within 5 mgrm. of the fasting figure. A combined rise of more than 25 mgrm. is suspicious, and of more than 30 mgrm. is certain evidence of hepatic insufficiency. If the fasting blood sugar is below 80 mgrm. or all the figures are above 120 mgrm., no definite conclusions can be drawn from the test. This test has recently been improved by substituting the estimation of the lævulose in the blood for that of the total blood sugar.

The hippuric acid test depends on the fact that in hepatic disease the power of the liver to conjugate benzoic and amino-acetic acids to form hippuric acid is reduced. The hippuric acid is estimated in the urine.

In hepatic disease there is also a diminution in the serum choline esterase, an enzyme which destroys acetylcholine with the formation of choline and acetic acid. The esterase is estimated by measuring the amount of CO_2 liberated when acetylcholine is added to a mixture of the blood serum and Ringer's solution; the bicarbonate of the latter reacts with the acetic acid formed to set free CO_2.

In considering the diagnosis of jaundice van den Bergh's reaction for excess of bile-pigment in the blood will be described, and the direct investigation of the bile obtained by means of a duodenal tube will be considered in connection with disorders of the gall-bladder and bile-ducts.

JAUNDICE

Definition.—Jaundice is the condition caused by the presence of bile-pigment in the blood, which manifests itself clinically by yellow coloration of the conjunctivæ and skin.

Ætiology and Pathology.—All cases of jaundice may be divided into three groups—hæmolytic jaundice, hepatic jaundice and obstructive jaundice.

(*a*) Hæmolytic Jaundice.—In hæmolytic jaundice bilirubin is produced in excess from hæmoglobin set free in the general circulation by the destruction of red cells as a result of abnormal fragility, as in acholuric jaundice, or of the presence of hæmolytic toxins in the blood. The hæmoglobin set free is broken down, and bilirubin is formed by the action of the endothelial cells of the spleen, and to a less extent the similar endothelial cells of Kupffer, which lie along the portal capillaries adjacent to the bile capillaries of the liver, and the endothelial cells of other organs. The excess of bile-pigment in the blood is thus formed quite independently of the glandular cells of the liver.

(*b*) Hepatic Jaundice.—This includes the toxic and infective jaundice described under the headings acute and subacute necrosis of the liver (p. 695) and infective hepatitis (p. 698) respectively. The jaundice is the result of damage to the liver cells which are unable to convey the bile-pigment from Kupffer's endothelial cells into the bile capillaries; the pigment consequently passes to the hepatic vein and thence into the general circulation.

(*c*) Obstructive Jaundice.—In obstructive jaundice bile excreted by the hepatic cells is reabsorbed by the hepatic blood capillaries, together

perhaps with the lymphatics, owing to the rise in pressure caused by obstruction of the bile-ducts. The obstruction may occur (1) within the ducts, or it may be due to (2) changes in their walls or (3) pressure from without.

1. *Obstruction within the ducts.*—This is almost always due to gall-stones. In very rare cases a hydatid cyst has ruptured into a duct, which becomes obstructed by a piece of membrane or a daughter cyst, or a round worm has entered the common bile-duct from the duodenum.

2. *Obstruction due to changes in the walls of the ducts.*—Congenital obliteration of the bile-ducts is a rare cause of icterus neonatorum (p. 688). An acquired stricture may result from accidental injury of the common bile-duct during operation. Catarrhal jaundice is due to the obstruction produced by inflammatory swelling at the mouth of the common bile-duct. Infective and suppurative cholangitis also lead to jaundice, but in some cases the obstruction to the ducts is associated with changes in the liver cells, which are in part responsible for the production of the jaundice. Primary carcinoma of the hepatic and common bile-ducts and biliary papilla give rise to jaundice.

3. *Pressure on the ducts from without.*—Malignant tumours of the liver and very rarely gummata and hydatid cysts give rise to jaundice by pressing on the intrahepatic branches of the bile-ducts; if some of the latter escape, bile still passes into the duodenum from other parts of the liver and the fæces remain coloured. The tumour may also project into the portal fissure and give rise to jaundice with colourless stools by pressing upon the hepatic ducts or common bile-duct.

Enlarged glands in the portal fissure may cause jaundice by pressure upon the ducts. The most common cause is primary or secondary cancer of the liver, as these glands drain the liver, but not the other abdominal viscera or peritoneum; for the same reason they rarely become tuberculous. They are very rarely enlarged in Hodgkin's disease and never in syphilis.

Jaundice may occur in cancer of the stomach, even when no secondary deposits are present in the liver or in the glands in the portal fissure. This is due to the pressure of glands in the neighbourhood of the head of the pancreas, or to direct spread of the growth into the lesser omentum, where it compresses the common bile-duct and may invade its walls.

Jaundice is produced by obstruction of the common bile-duct when chronic pancreatitis occurs in an individual in whom the duct is embedded in the head of the gland. It is generally present in cancer of the head of the pancreas, but very rarely with a pancreatic cyst or calculus.

Symptoms.—Jaundice appears first in the conjunctivæ and then successively on the face, neck, body and limbs. The mucous membrane of the lips and palate becomes yellow very soon after the conjunctivæ. In chronic obstructive jaundice the pigment in the skin becomes dark green. In a small proportion of very chronic cases xanthoma develops, but this condition is more common without jaundice (p. 1468). The patches consist of cholesterol, which the blood in jaundice contains in excess. In chronic jaundice there is a tendency for telangiectases to develop over the body and face; they may disappear at the same time as the jaundice. Purpura and hæmorrhage from mucous membranes, especially the nose and gums, may occur.

The urine becomes bile-stained before the conjunctivæ and skin, the interval being sometimes as long as 24 hours, but it generally returns to

normal before the yellow colour of the skin has disappeared. The urine may be yellow, olive, dark brown or even black. The colour can be distinguished from that in urobilinuria, hæmaturia and melanuria, and that produced by rhubarb, senna, santonin and chrysophanic acid by Gmelin's test for bile-pigment.

When obstruction to the bile-ducts is complete, no bile reaches the intestines and urobilin is absent from the urine; when the obstruction is incomplete, decomposition of the bile which reaches the intestines may occur and urobilinuria results. Bile-salts are only present in the urine for the first few days. Their disappearance is due to the fact that they are only produced in very small quantities, being constantly reabsorbed from the bowel and then re-excreted; when the bile-ducts are obstructed the kidneys rapidly excrete all the bile-salts present in the blood. In chronic obstructive jaundice bile-stained casts are almost always present in the urine, and less frequently albuminuria occurs. The urine often reduces Fehling's solution owing to the presence of glycuronic acid.

The fæces are bulky and often extremely offensive. When the obstruction is complete they are clay-coloured, owing partly to the absence of stercobilin and partly to the presence of excess of fatty acids and soaps which require the presence of bile for their complete absorption, and of neutral fat if the pancreatic duct is simultaneously obstructed (p. 688). Loss in weight results, and the excess of undigested food which reaches the colon is likely to cause excessive bacterial decomposition. This may lead to intestinal intoxication if the hepatic cells are damaged and their antitoxic action impaired.

The sweat may contain bile, which is also sometimes present in the tears and in the milk; but the saliva, cerebro-spinal fluid and mucus of the alimentary canal are free from bile, although the salivary glands and other organs are deeply bile-stained. The sputum in pneumonia and the effusion in pleurisy and peritonitis contain bile-pigments. The blood plasma is tinged with bile. Coagulation is considerably delayed in obstructive jaundice owing to deficiency of prothrombin. This is a result of lack of fat-soluble vitamin K ("Koagulation vitamin"), too little of which is absorbed when bile is absent from the small intestine.

In jaundice of recent origin the pulse is slow as a result of the presence of bile-salts in the blood. Pruritus occurs in about 20 per cent. of cases, especially when the jaundice is deep; it may be very severe and interfere with sleep. It is not directly due to the jaundice, as it may occur before the jaundice appears and continue after its disappearance; when present before the jaundice, it may subside with the onset of the latter, and it has also been observed in association with gall-stones when no jaundice was present.

The yellow vision or xanthopsia of jaundiced patients is less marked than that caused by santonin, and is rarely sufficiently obvious for the patient to mention is unless directly asked.

Diagnosis.—(*a*) RECOGNITION OF JAUNDICE: VAN DEN BERGH'S REACTION.—Bilirubin is normally present in the blood. Just as the kidneys in diabetes do not excrete sugar until the concentration in the blood has reached the leakage-point, which is considerably higher than the normal concentration, so no bilirubin passes into the urine until the concentration

in the blood has risen from the normal of 1 in 250,000 to the leakage-point of 1 in 50,000. About the same concentration is required to cause jaundice, but the appearance of a trace of bile-pigment in the urine is easier to recognise with certainty than the first trace of pigmentation of the skin or conjunctiva. Moreover, the pigmentation is somewhat slower to develop, and it remains for a time after all pigment has disappeared from the urine.

Hijmans van den Bergh has shown that excess of bilirubin in the blood can be recognised by a colour reaction, now commonly known as van den Bergh's test, which is given by Ehrlich's diazo reagent. The *direct reaction* may be "prompt," the maximum being reached within 30 seconds; it may be "delayed" for 1 to 15 minutes or be entirely negative; or it may be "biphasic," giving a slight prompt reaction, followed after a delay by gradual deepening of the colour. The *indirect reaction*, obtained after precipitation with alcohol so as to bring the bile into alcoholic solution, is always prompt.

With van den Bergh's test it is possible to distinguish two different forms of bilirubin. The direct reaction is prompt when the bilirubin is reabsorbed into the blood after it has been excreted by the hepatic cells in cases of obstructive jaundice, but is negative or delayed when the excess of bilirubin is a result of over-production, as in hæmolytic jaundice; it is negative, delayed or biphasic when the jaundice is due to inability of the hepatic cells to excrete it, as in toxic and infective hepatic jaundice.

By means of van den Bergh's test it is also possible to recognise latent jaundice. Thus the hyperbilirubinæmia present in pernicious anæmia gives a positive indirect reaction, although there is no jaundice except in occasional acute hæmolytic crises. Excess of bilirubin in the blood at a concentration below the leakage-point may also result from a very slight degree of biliary obstruction, such as may occur with a stone in the ampulla of Vater and in some cases of cirrhosis and of secondary carcinoma of the liver; it is recognised by giving a positive direct van den Bergh's reaction in spite of the absence of jaundice and of bile from the urine. In cases of progressive obstructive jaundice a positive direct reaction may be given at a stage before jaundice develops and bile appears in the urine, and still longer before any change is noticed in the stools.

(*b*) Differential Diagnosis of the Cause of Jaundice.

1. *Age, sex and history.*—Transient jaundice is common in the newly born (p. 688). Obstructive jaundice may result from congenital obliteration of the bile-ducts (p. 734) and congenital syphilis (p. 713). Severe jaundice in infants may be familial (p. 688). Mild infective jaundice may occur sporadically or in epidemics among infants; it is identical with the catarrhal jaundice of older children and adults. Epidemics of very fatal jaundice were formerly common in lying-in hospitals; sporadic cases still occur. The infection may enter by the umbilicus, which is red and swollen and may bleed, or by the alimentary tract; jaundice appears about the fifth day and is accompanied by high fever and severe septic symptoms. Hæmorrhage may occur from the alimentary tract or kidneys.

Jaundice occurring in childhood or before the age of thirty is generally catarrhal. After thirty gall-stones become a more common cause, especially in women, and after forty cancer is the most common cause in both sexes. Jaundice developing in pregnancy should raise a suspicion of acute necrosis of the liver. When more than one member of a family are affected, an

infection, such as spirochætal jaundice, or a toxæmia is probably the cause in acute cases; in chronic cases acholuric jaundice should be considered.

In jaundice of obscure origin the possibility of a toxic origin should be remembered, and inquiries made whether the patient has recently received treatment with organic arsenical preparations, atophan, etc.

2. *Colour.*—In hæmolytic anæmia the skin has a characteristic lemon-yellow colour, though the conjunctivæ are unaffected. In acute and sub-acute hepatic necrosis, such as the toxic jaundice caused by arsenobenzene, the skin assumes a very bright yellow colour, which is quite distinct from that of ordinary jaundice caused by obstruction of the bile passages. The former is probably produced by the form of bilirubin which gives only an indirect van den Bergh reaction, and the latter is produced by the form which also gives a positive direct reaction. A dirty yellow or greenish-yellow colour occurs only in chronic and more or less complete obstructive jaundice.

3. *Course.*—Jaundice of short duration is generally catarrhal or due to the passage of a gall-stone. Obstructive jaundice, which progresses until it becomes extremely deep, suggests cancer or chronic pancreatitis, whilst chronic jaundice, which varies from time to time, and intermittent jaundice are generally due to a stone in the ampulla of Vater, but may also be due to cancer of the ampulla of Vater.

4. *Condition of the gall-bladder.*—Enlargement of the gall-bladder indicates obstruction of the cystic or common bile-duct, though the former is not likely to be associated with jaundice. The enlargement is present in over 90 per cent. of cases in which obstruction is due to causes other than gall-stones, but in only 20 per cent. of cases of calculous obstruction. This difference is known as Courvoisier's law, and is due to the contraction of the gall-bladder caused by chronic inflammation in cholelithiasis, in which, moreover, the obstruction is often incomplete.

5. *Condition of the liver.*—Jaundice associated with great enlargement of the liver is generally due to growth if it is irregular, and to chronic obstruction of the common bile-duct if the liver is smooth; the irregular enlargement due to syphilis is less extreme, and, like that due to hydatid cysts or an abscess, is rarely associated with jaundice. The presence of ascites points to a growth or to cirrhosis, but the jaundice is generally more marked in the former.

6. *Examination of the stools.*—The presence or absence of stercobilin in the stools shows whether the common bile-duct is incompletely or completely obstructed. Slight excess of fatty acid and soap without any striated meat fibres or starch occurs in uncomplicated jaundice; excess of neutral fat, as well as fatty acid and soap, together with striated meat fibres, points to obstruction of the pancreatic duct. Complete absence of both bile and pancreatic juice from the intestinal contents indicates obstruction of the common bile-duct by a growth. Incomplete obstruction of the bile-ducts without interference to pancreatic digestion points to gall-stones, catarrhal jaundice or chronic pancreatitis.

7. *Pain.*—Constant pain suggests growth, attacks of pain gall-stones, and absence of pain catarrhal jaundice, acute or subacute necrosis, infective hepatitis or chronic pancreatitis; but many exceptions to this general statement occur.

8. *Syphilis.*—Active signs of syphilis or scars of old lesions indicate the possibility of a syphilitic origin, or of poisoning by an organic arsenical preparation which a patient may be having for syphilis without his own doctor's knowledge.

Treatment.—The treatment of jaundice is the treatment of the condition which causes it. The subject, therefore, requires no further consideration here, except for the pruritus and tendency to hæmorrhage, which are results of the jaundice itself. Thyroid, ½ gr. three times a day, and fractional doses of calomel may give relief to the pruritus, which is also helped by a warm alkaline bath, or moistening the irritable parts of the skin with 1 in 40 carbolic acid, 1 in 50 ichthammol, or 1 in 70 solution of menthol in spirit. The tendency to hæmorrhage can be controlled by the administration of vitamin K and bile-salts by mouth. Calcium, which is present in the blood in normal amount, is without effect.

Simple Jaundice in Infants (Icterus Neonatorum)

Ætiology.—Simple jaundice occurs in about 50 per cent. of infants, especially among the premature.

Pathology.—The number of red corpuscles is high in the newly born, but quickly falls during the first few days of life. The excessive blood destruction is associated with an excess of bile-pigment in the blood, as shown by van den Bergh's reaction, which gives a positive indirect but negative direct reaction in all new-born infants. The jaundice is therefore hæmolytic, and when death occurs from some independent cause nothing abnormal is found in the liver or bile-ducts.

Symptoms.—The jaundice generally begins on the second or third day of life; it increases in intensity for 2 or 3 days and then gradually diminishes until it disappears after 1 or 2 weeks, but occasionally it lasts for a longer period. The jaundice begins on the face and spreads over the whole of the body; unlike other forms of jaundice, the conjunctivæ are affected after the skin, and in mild cases they are not stained at all.

Diagnosis.—If the jaundice is slight, its presence can be recognised only by pressing the blood out of the cutaneous vessels, when the normal redness of the infant disappears and the yellow colour remains. Its short duration and the absence of enlargement of the liver and spleen distinguish simple icterus neonatorum from congenital obliteration of the bile-ducts, and the healthy condition of the infant distinguishes it from the infective forms of jaundice.

Prognosis and Treatment.—Rapid recovery always occurs, and no treatment is required.

Familial Icterus Gravis Neonatorum

The jaundice, which affects successive members of the same family, though the first-born often escapes, begins within a few hours of birth. The colour rapidly deepens till the skin is deep bronze. The infants are drowsy and take the breast badly. The stools are normal in colour. The urine is dark and contains urobilin and often bilirubin in excess. The liver and spleen are generally enlarged.

The quantity of bilirubin in the blood at birth is greater than normal; the blood contains no hæmolysin, but the cells show a slight increased tendency to hæmolysis.

In fatal cases death generally occurs within a few days and almost always within 3 weeks: *post mortem* nothing abnormal is found. Hampson has shown that complete recovery follows the injection of 15 c.c. of the mother's blood serum daily for 3 or 4 days into the infant's muscles.

ACHOLURIC JAUNDICE[1]

Synonym.—Chronic Splenomegalic Hæmolytic Jaundice.

Ætiology.—Acholuric jaundice is a familial disease, in which an hereditary abnormality of the red corpuscles is transmitted as a Mendelian dominant. It may occur in as many as four generations and may be transmitted through healthy parents. The abnormality presumably exists from birth, but the symptoms of the disease, though sometimes present from early infancy, may not manifest themselves till a much later age and may even remain in abeyance throughout life. It is often stated that there is a non-hereditary form of the disease, the so-called *acquired acholuric jaundice*, but it is probable that the familial nature of the condition could always be demonstrated if a sufficiently thorough investigation of the family were made.

Pathology.—The essential abnormality is an increase in the fragility of the red corpuscles, which leads to excessive hæmolysis with liberation of hæmoglobin and the formation of excess of bilirubin, so that jaundice develops and the patient may become anæmic. There are no abnormal hæmolysins in the blood, nor is there any evidence that the hæmolysis is dependent on over-activity of the spleen.

Symptoms.—The severity of the disease is extremely variable. There may be no symptoms at any time, the condition being recognised only on a routine examination of the blood. Most patients have a mild degree of jaundice, and give a history either that they have always been jaundiced, or that they have always been liable to attacks of jaundice. There is no pruritus. Irregularly recurring attacks or "crises," in which jaundice appears or in which an existing jaundice grows deeper, are characteristic of the disease. Such crises are usually mild, and apart from the jaundice the patient merely notices that he is slightly out of sorts. Occasionally they are more serious and are accompanied by the symptoms of an acutely developing severe anæmia; there is then often a high temperature with nausea and vomiting. Between the crises the jaundice and anæmia may be very slight or even disappear; but in some cases they persist, and the anæmia may be sufficient to interfere seriously with the patient's mode of life. It not infrefrequently happens that a crisis suddenly develops in an adult who gives no history of previous jaundice; in such cases the crises are particularly liable to be severe. Crises may follow over-exertion or infection.

Calcium bilirubinate gall-stones may develop as a result of the chronic bilirubinæmia. These may give rise to attacks of biliary colic, which may be accompanied by an increase in the jaundice, which is quite independent

[1] I am indebted to Dr. R. L. Waterfield, Clinical Pathologist to Guy's Hospital, for this article.—A. F. H.

of the hæmolytic crises. An unexplained complication is chronic ulceration of the legs, which may be the chief and sometimes the only symptom of the disease.

Splenomegaly is usually present; though occasionally extreme, it is commonly of moderate degree. The spleen may increase in size during a crisis, and may be painful and tender.

The fæces are normal in colour, and the urine, though dark as the result of the presence of urobilin, contains no bile.

In normal fully oxygenated blood the red corpuscles show no hæmolysis in a 0·50 per cent. solution and only slight hæmolysis in a 0·45 per cent. solution of sodium chloride. In acholuric jaundice the fully oxygenated corpuscles show gross hæmolysis in a 0·45 per cent. solution and lesser degrees of hæmolysis in stronger solutions, sometimes even as high as a 0·80 or 0·85 per cent. solution. The corpuscular diameter is usually diminished and often very markedly so, but occasionally it is normal or even above normal. But the corpuscles are disproportionately thick, so that the corpuscular volume and colour index instead of being diminished are normal or above normal; they may be higher than in any disease except pernicious anæmia. This discrepancy between corpuscular volume and colour index on the one hand and corpuscular diameter on the other occurs in no other disease and immediately distinguishes acholuric jaundice from pernicious anæmia. In stained films there is gross irregularity in the size of the corpuscles; the small ones tend to be deeply stained, while the large ones are feebly stained and often polychromatic. In shape they are of a remarkably uniform roundness, and stippled corpuscles are unusually scarce. Yet reticulocytes frequently constitute over 10 per cent. of the red corpuscles and are sometimes much more numerous. In severe crises large numbers of nucleated red corpuscles, mostly normoblasts, may appear. There is often a polymorphonuclear leucocytosis, which may reach 40,000 or more per c.mm., and among the cells there may be myelocytes and even myeloblasts. As the jaundice is hæmolytic the van den Bergh test gives only an indirect reaction. Occasionally, however, obstructive jaundice is present as well owing to the presence of a pigment stone in the common bile duct; a direct reaction is then present as well.

Diagnosis.—The diagnosis is suggested by the association of splenomegaly with long-standing jaundice or recurrent attacks of jaundice. It is strengthened by a history of jaundice in other members of the family. Its confirmation depends on finding increased fragility of the red corpuscles and the characteristic blood picture, particularly the discrepancy between the corpuscular volume and diameter and the increased fragility. The blood picture distinguishes the condition from other hæmolytic anæmias, from pernicious anæmia, chronic myelogenous leukæmia and splenic anæmia. Chronic ulceration of the legs should always call to mind the possibility that the underlying cause may be acholuric jaundice, even in the absence of jaundice and splenomegaly. Finally it must be remembered that attacks of biliary colic may occasionally be a complication of acholuric jaundice.

Prognosis.—If in the early stages the symptoms are mild they do not generally become more severe at a later period. Even severe crises generally end spontaneously. Very rarely the anæmia proves fatal, especially when severe crises occur in adults who give no previous history of the disease.

Treatment.—In mild or latent cases no special treatment is required, but patients should avoid undue exertion and treat with care any minor infection they may contract. When the anæmia or other symptoms are sufficient to interfere with the patient's activities splenectomy should be performed. At the same time the gall-bladder should be examined for calculi and any stones present removed, but there is no indication for cholecystectomy. In very severe crises transfusion may be necessary to prepare the patient for operation. The effects of splenectomy are dramatic: the jaundice and the anæmia quickly disappear and the leg ulceration heals. The increased fragility persists, though it may be slightly lessened. The disproportionate thickness of the corpuscles and the resulting discrepancy between the corpuscular volume and the diameter remain, but the reticulocytosis and leucocytosis, which are secondary to the anæmia, usually disappear.

CONGESTION OF THE LIVER

Ætiology.—When the outflow of blood from the hepatic vein is impeded as a result of right-sided heart failure, following primary disease of the heart or obstructive pulmonary disease, passive congestion of the liver may result. It is also produced by thrombosis of the hepatic veins, which is a rare condition generally secondary to some neighbouring malignant, syphilitic or inflammatory disease.

Pathology.—The sublobular and intralobular veins are dilated. The centre of each lobule thus appears as a dark spot, whilst the outer part is pale owing to fatty infiltration; the mottled appearance resembles the section of a nutmeg and has led to the name "nutmeg liver."

Symptoms.—In addition to the symptoms of the cardiac or pulmonary disease, which has led to the right-sided heart failure, special symptoms result from the passive congestion of the liver. The capsule of the liver is stretched and pain results, especially if the enlargement is rapid. When the increase in size is more gradual, there is a feeling of fullness and weight in the right hypochondrium. The liver can be felt to extend considerably lower than normal, its size varying from time to time according to the condition of the heart. It is firm and tender, especially if the congestion is recent and acute. Distinct expansile pulsation can sometimes be felt by placing one hand in the loin and the other just below the right costal margin; this corresponds with ventricular systole if tricuspid regurgitation exists and with auricular systole if there is tricuspid stenosis. It must be distinguished from the non-expansile pulsation transmitted through the diaphragm from the hypertrophied and labouring right ventricle.

The congestion of the liver leads in turn to congestion of the organs which are drained by the portal vein. Anorexia, discomfort immediately after food, flatulent distension of both stomach and intestines from deficient absorption of the gas swallowed with the food or produced by fermentation, and constipation are commonly present. The combination of slight jaundice with cyanosis produces a characteristic dusky green colour of the face. The jaundice, is, however, often latent, a positive indirect but negative direct van den Bergh reaction being obtained.

Ascites is common, but is rare in the absence of general œdema, being

mainly due to the same causes; it is also in part a direct result of portal congestion and sometimes of chronic peritonitis. The spleen is very rarely enlarged in spite of the interference with the outflow of blood in the splenic vein by the hepatic congestion.

Diagnosis.—When the heart disease is obvious, the diagnosis is easy. Sometimes, however, the most prominent symptoms are due to the congestion of the liver, and the diagnosis from cirrhosis may be difficult. In congestion of the liver the spleen is not enlarged, and the symptoms rapidly improve and the liver diminishes in size with rest and cardiac tonics; moreover, hæmatemesis, though common in cirrhosis, very rarely occurs in passive congestion in spite of the congestion of the gastric mucous membrane.

A history of alcoholism does not necessarily point to cirrhosis; if the heart is failing and there is no valvular disease, the enlargement of the liver is probably due to congestion and the heart failure in part to alcoholic poisoning. The diagnosis would be confirmed if the ankle-jerks are lost, as latent neuritis is frequently associated with an alcoholic heart and congested liver, but rarely with cirrhosis.

Treatment.—Apart from the treatment of the primary condition the local pain and discomfort are rapidly relieved by the application of six leeches over the hepatic region. Mild purgation with Epsom salts also helps to relieve the portal congestion.

GLYCOGEN DISEASE (VON GIERKE'S DISEASE)[1]

This rare disease, first described by Von Gierke in 1929, is characterised by an abnormal deposition of glycogen in the tissues, the liver being the organ principally affected.

Ætiology.—Glycogen disease occurs in both sexes. It is congenital and may be familial. The relatively high incidence of cousin-marriages amongst the parents of affected patients suggests that the condition may possibly be inherited as a Mendelian recessive character.

Pathology.—Deposition of glycogen in the liver, kidney, heart and other organs gives rise to distension of the individual cells and gross enlargement of the affected organs. The blood glycogen content (principally the glycogen contained in the red cells) is also raised. Whereas glycogen normally disappears from the tissues rapidly after death, in glycogen disease it is peculiarly stable. Possibly this is due to an abnormal linkage with protein, but more probably to a congenital deficiency of a factor acting between the glycogen and the glycogen-splitting ferment. Pituitary dysfunction has been suggested as the underlying cause. The glycogen of the tissues can only be mobilised with difficulty during life, with the result that the fasting blood sugar is low and acetonuria occurs. This delayed mobilisation is demonstrated by the adrenaline test, the normal rise of blood sugar following the injection of adrenaline being absent or delayed. That there is usually some delay in glycogen storage also is shown by an abnormal glucose tolerance test. The blood cholesterol is raised.

[1] I am indebted to Dr. R. W. B. Ellis, Assistant Physician to the Department for Children's Diseases, Guy's Hospital, for this article on Glycogen Disease.—A. F. H.

Symptoms.—The most striking symptom is lack of growth and development, the older patients often showing well-marked infantilism. The large size of the liver causes abdominal distension, but seldom any discomfort. Obesity of local or generalised distribution has been described. Occasionally convulsions occur, which are probably attributable to the hypoglycæmia, but may be associated with local depositions of glycogen in the brain. Whilst some of the patients are of low vitality with poor resistance to infection, others suffer very little disturbance of normal health and activity. In a few instances the condition appears to have undergone spontaneous cure. Involvement of the heart (cardiomegalia glycogenica) may result in sudden death.

Diagnosis.—The presence of a large, smooth, non-tender liver, in the absence of splenic enlargement, jaundice or other evidence of cirrhosis, will suggest the diagnosis, which is confirmed by the low fasting blood sugar, acetonuria and abnormal response to the adrenaline test.

Treatment.—There is at present no method known by which glycogen mobilisation can be restored to normal in this disease. If hypoglycæmic symptoms occur, the diet should be relatively high in carbohydrates. Injections of combined anterior pituitary hormones have been tried, but the results have been disappointing.

INFECTIONS OF THE LIVER

Infection may be conveyed to the liver by (1) the hepatic artery, (2) the portal vein, and (3) the bile ducts.

(1) *Systemic blood infections.*—Hepatitis forms part of the clinical picture of yellow fever and spirochætosis ictero-hæmorrhagica. Infective hepatitis may also occur in malaria, in typhoid and paratyphoid fever and similar, but non-specific infections, and very rarely in influenza, streptococcal septicæmia, especially in association with erysipelas, and in lobar pneumonia. Acute hepatitis of infective origin may occur sporadically and give rise to both small and extensive epidemics (p. 694).

(2) *Portal infections.*—Acute, subacute and chronic amœbic hepatitis (p. 709) and suppurative pylephlebitis (p. 721) result from infection conveyed by the portal vein.

(3) *Ascending cholangitis.*—Hepatitis may be caused by infection ascending the bile ducts when stasis is produced by obstruction to the common bile duct. Very acute cases, especially when associated with gall-stones, may result in suppurative cholangitis with formation of innumerable minute abscesses in the liver. In chronic cases perilobular (or " biliary ") cirrhosis is the final result (p. 698).

CATARRHAL JAUNDICE

Two separate conditions are commonly described as catarrhal jaundice, both of which may occur in sporadic and epidemic form. The term is correctly applied only to the first; the second is more accurately called acute hepatitis (p. 698).

Ætiology and Pathology.—Catarrhal jaundice is more common in children and young adults than in older people. Single cases are quite common, but groups may occur in houses, institutions and villages, but large epidemics, such as that which developed in the autumn of 1915 in Gallipoli, are rare.

The majority of cases diagnosed in England as catarrhal jaundice are probably correctly labelled and depend upon obstruction to the flow of bile secondary to acute gastro-duodenal catarrh. The obstruction may be caused in various ways. (1) The swelling of the mucous membrane of the duodenum may itself be sufficient to obstruct the mouth of the common bile-duct. (2) The duodenitis is probably often associated with an ascending cholangitis; the swollen mucous membrane of the mouth of the duct where it is surrounded by Oddi's sphincter must increase the obstruction. (3) In most of the recorded autopsies the mouth of the common bile-duct was found to be obstructed by a plug of mucus and epithelial debris. (4) The inflammation of the duodenum and terminal part of the common bile-duct would be likely to cause achalasia and in more severe cases spasm of Oddi's sphincter and so add a functional element to the organic obstruction already present.

Catarrhal jaundice is so rarely fatal that the number of recorded autopsies is very small. The following *post-mortem* report from the case of a girl of 19, who died from an accidental injury at the height of an attack, is typical of the small number on record. The mucous membrane of the stomach and duodenum was swollen and showed submucous ecchymoses, and the papilla of Vater was unusually prominent; there was no bile pigment in the duodenal contents, but the common bile-duct, hepatic ducts and gall-bladder were moderately dilated and contained dark, sticky bile; the mouth of the common bile-duct was completely obstructed as a result of inflammatory swelling of its wall with overgrowth of lymphoid tissue, and no bile passed into the duodenum on compressing the gall-bladder; the liver and pancreas were macroscopically and microscopically normal (Eppinger).

The liver is affected only in the comparatively rare cases, in which the jaundice persists for a considerable period, when the usual degenerative changes which follow obstruction to the flow of bile gradually develop.

Symptoms.—The clinical picture of true catarrhal jaundice shows remarkably few variations, and is exactly what might be expected with the pathogenesis just described. The initial symptoms are those of acute gastritis. The patient complains of epigastric discomfort, which rarely amounts to pain, with anorexia and nausea. Pressure in the epigastrium produces acute discomfort. If the patient attempts to eat he is generally sick. Diarrhœa may occur. He feels ill and his temperature is raised. In two or three days improvement sets in, but just when he thinks he has almost recovered his urine becomes dark, his stools pale, and his conjunctivæ and subsequently his skin becomes jaundiced. His temperature falls, and by the time the jaundice has fully developed he feels perfectly well, except that he is still likely to be nauseated or to vomit if he eats fatty food, especially if he does not remain in bed. At this stage examination shows that the epigastric tenderness had disappeared, but that the liver is a little enlarged and slightly tender. The gall-bladder may be palpable—an important sign that the jaundice is obstructive and not of hepatic origin, and in severe cases the spleen is slightly enlarged. The jaundice generally begins to fade

within a week, and by the end of a fortnight all symptoms and signs have disappeared. In epidemics mild cases occur in which no jaundice follows the initial symptoms caused by the acute gastro-duodenitis.

In the majority of cases the lævulose test shows no hepatic insufficiency. When, however, recovery is delayed, secondary hepatic degeneration occurs and the lævulose test may show a moderate degree of insufficiency. In the early stages the material obtained through a duodenal tube contains excess of mucus and cells, but no flow of bile follows the injection of magnesium sulphate. As the jaundice decreases bile is obtained, and for a short time it contains leucocytes, epithelial cells and pigment granules.

Diagnosis.—When jaundice, unaccompanied by pain and with very slight constitutional symptoms, develops in a patient with mild gastric symptoms of a few days' duration, catarrhal jaundice is the probable diagnosis. When the symptoms do not abate with the onset of jaundice and much constitutional disturbance is present, especially if the spleen is enlarged, the possibility of acute infective hepatitis, including spirochætosis ictero-hæmorrhagica, requires consideration. When the initial gastric symptoms are absent and the jaundice persists for more than a fortnight, catarrhal jaundice can be excluded. When pain of any severity occurs, especially after the onset of jaundice, and when the gall-bladder is tender, fever persists or the jaundice recurs, gall-stones are probably present.

Treatment.—The patient should be kept in bed on a plain diet containing as little fat as possible, and his bowels should be opened daily with Epsom salts, which at the same time promote biliary drainage. He should not be allowed to get up until the jaundice is beginning to disappear.

ACUTE AND SUBACUTE HEPATIC NECROSIS

Ætiology.—Hepatic necrosis may be caused by a large variety of intrinsic and extrinsic toxins, of which the following are the most important.

(*a*) *Intrinsic toxins.*—i. An unknown toxin which may develop in the later months of pregnancy, causing the toxic jaundice of pregnancy.

ii. An unknown intrinsic toxin is probably the cause of the rare cases of acute necrosis in which no extrinsic cause can be found.

(*b*) *Extrinsic toxins.*—i. Acute alcoholic poisoning.

ii. Delayed chloroform poisoning. This is probably the cause of most cases of death a few days after childbirth in the absence of sepsis, but an overdose during prolonged labour is much less common than it was twenty-five years ago. I know two anæsthetists who developed a mild form of toxic jaundice as a result of inhaling chloroform in small doses day after day.

iii. Delayed bromethol (avertin) poisoning. Bromethol is dangerous only if the liver is already damaged. I know of several cases in which death occurred a few days after an operation on a jaundiced patient from what was described as "shock," but which was, I believe, really the result of delayed avertin poisoning.

iv. Carbon tetrachloride used in treatment of ancylostomiasis.

v. Trinitrotoluene and tetrachlorethane, which caused an epidemic of jaundice in munition and aeroplane workers respectively during the War of 1914–1918 (pp. 385 and 389).

ACUTE INFECTIVE HEPATITIS

Widespread epidemics of a non-spirochætal acute hepatitis occurred in Sweden in 1926 and 1927, and small epidemics of a mild character are common in Great Britain, where they are generally confused with true catarrhal jaundice. The condition is infective and probably caused by a virus, which is transmissible from man to swine and swine to swine.

It is clinically indistinguishable from the infective hepatitis which is a very rare complication of typhoid and paratyphoid fever and of influenza ; in the former it generally appears about the third week and in the latter towards the end of the first week.

Symptoms and Diagnosis.—In most cases there are no pre-icteric symptoms of any kind, in contrast with the indigestion which constantly precedes the onset of catarrhal jaundice. The patient first notices that his urine is becoming dark, then that his stools are pale, and finally that he is jaundiced. The onset of jaundice is accompanied by symptoms of general toxæmia—anorexia, headache and weakness, and occasionally vomiting and diarrhœa. The temperature is generally slightly raised. There is no epigastric tenderness, but the liver is tender and slightly enlarged, and the spleen is often palpable. The jaundice is generally less deep than in catarrhal jaundice, and bile is always present in the stools. The jaundice lasts anything between a week and 2 or 3 months, the average duration being greater than in true catarrhal jaundice. Instead of the rapid complete recovery which is characteristic of the latter, convalescence is often prolonged and the patient may become very weak and emaciated. In rare cases the jaundice persists and the patient becomes increasingly toxic, dying eventually with all the symptoms of acute hepatic necrosis.

From the onset the lævulose test shows the presence of well-marked hepatic insufficiency. This is occasionally present many years after clinically complete recovery, whereas true catarrhal jaundice leaves the liver quite undamaged.

When the infective jaundice is secondary to some acute infection the primary illness runs its usual course, but instead of a normal convalescence after the former subsides, the above symptoms develop. The temperature is generally normal and the illness is mild in type, but the jaundice may last for several weeks. Symptoms of hepatic insufficiency rarely develop and complete recovery is the rule.

CIRRHOSIS OF THE LIVER

Cirrhosis of the liver is a condition in which the liver hardens as a result of the development of new fibrous tissue. Three entirely distinct forms occur.

(1) *Pericellular cirrhosis.*—This is invariably the result of congenital syphilis (p. 712).

(2) *Perilobular cirrhosis.*—This is the late result of the chronic hepatitis caused by ascending infection of the bile ducts (cholangitis), and is therefore also known as *biliary cirrhosis.* It is always associated with jaundice. It is

generally the result of infection following chronic obstruction of the common bile duct by a gall-stone, cicatricial stenosis (resulting from an injury during cholecystectomy), chronic pancreatitis, or carcinoma of the head of the pancreas, the common bile duct or ampulla of Vater. Cellular infiltration and new fibrous tissue form around the bile ducts and between the lobules of the liver with the final production of perilobular cirrhosis.

In these conditions the enlargement and hardness of the liver and the jaundice, which are primarily the result of retention of bile in the intra-hepatic ducts caused by obstruction to their outflow into the duodenum, may also be caused by the secondary perilobular cirrhosis. Consequently, if the obstruction is eventually relieved, the liver remains hard and large and the jaundice does not disappear. A measure of the degenerative changes in the liver can be obtained from the lævulose test, which shows no hepatic insufficiency at the onset of obstruction but a slowly increasing insufficiency if the obstruction is not overcome. In the more acute cases changes similar to those of subacute hepatic necrosis occur and death may ensue from hepatic failure.

A condition has been described as Hanot's biliary cirrhosis, which is said to affect children and young adults, often several members of a family, and to be characterised by enlargement of the liver and spleen, with chronic jaundice and febrile attacks, but rarely ascites. I have never seen a case which answered to this description, and I am exceedingly doubtful whether such a clinical entity exists. Even in France, where it was first described, it is now said to be exceedingly rare. The term has probably been used to include the biliary cirrhosis described above and also cases of splenic anæmia with cirrhosis and of acholuric jaundice.

ALCOHOLIC HEPATITIS

A. Pre-Cirrhotic Alcoholic Hepatitis

Definition.—In the early stages of chronic alcoholic poisoning of the liver complete or almost complete recovery may take place if the patient becomes teetotal. Not only do the symptoms disappear, but the liver becomes smaller and softer, and the lævulose test, which originally showed gross hepatic insufficiency, shows little or no abnormality and a positive van den Bergh reaction may become negative. Though there is no pathological evidence as to the exact condition of the liver before and after treatment, it is clear that actual cirrhosis cannot have taken place. It is therefore reasonable to regard the condition as pre-cirrhotic and to call it alcoholic hepatitis.

Ætiology.—Whereas the fully developed picture of cirrhosis of the liver has become rare since the War of 1914–1918, alcoholic hepatitis has become increasingly common, especially among the well-to-do. Whilst the poor man's beer is more expensive and weaker than it was before 1914, many people celebrate their newly acquired wealth by excessive indulgence in cocktails, champagne and whisky. Some have been drinking in obvious excess, though they may never get drunk, but with others it is the concentration of the alcohol and the fact that it is drunk when the stomach is empty rather than the total quantity consumed which are mainly responsible for

the damage done to the liver. Consequently alcoholic hepatitis is not at all uncommon among young adults of both sexes, though fully developed cirrhosis is now, as it has always been, rare before middle age. In older patients a sedentary life is an important predisposing factor.

The condition has long been recognised as common among Europeans living in tropical countries, where the consumption of highly spiced food and repeated attacks of malaria, together sometimes with amœbiasis and enteric fever, are additional factors.

Symptoms.—A feeling of discomfort, rarely amounting to actual pain, is felt in the region of the liver. Symptoms of alcoholic gastritis, especially morning anorexia and nausea, are often present with hypochlorhydria or achlorhydria and excess of mucus in every fraction of a test-meal. The patient's complexion is sallow, and there is sometimes a slight degree of jaundice. The liver is hard, moderately enlarged and tender, and the spleen may be just palpable. The patient says he is "liverish"; he is irritable and depressed, and complains of a feeling of general unfitness, headache and drowsiness. Intestinal flatulence may occur as a result of deficient absorption of gas secondary to slight portal obstruction, which may also cause occult blood to appear in the stools, though actual hæmatemesis and melæna are rare.

Periods of comparative well-being may alternate with acute exacerbations or "liver attacks," which are generally caused by increased alcoholic excess and to a less extent by over-eating, and sometimes by exposure to cold. During such an attack the liver becomes larger and more tender, and the stretching of the capsule may cause acute pain. In rare cases hæmatemesis occurs. With suitable treatment an attack generally subsides within a fortnight, and even in severe cases a month or six weeks is generally sufficient to restore the patient to good health. If he becomes teetotal complete recovery may occur; otherwise cirrhosis will eventually develop.

Ascites never occurs in the pre-cirrhotic stage.

Treatment.—The patient should be kept in bed on a diet of citrated milk until all the symptoms have disappeared and the liver is no longer tender. If gastritis is present, the stomach should be washed out every morning (p. 586). The diet can then be gradually increased, but the patient should continue on the diet described on p. 706 for several months. It is essential that he should become completely teetotal and should remain so for the rest of his life. It should be pointed out to him that his liver has become abnormally vulnerable, and that even a small quantity of alcohol is a poison for him. He should be warned of the danger of cirrhosis if he does not follow the advice given him. It is remarkable how easily the majority of such patients can become teetotal; fortunately they have none of the craving for alcohol experienced by dipsomaniacs, but only take it because they like it or for the sake of conviviality.

B. Cirrhosis of the Liver

Synonyms.—Portal or Multilobular Cirrhosis; Laennec's Cirrhosis.

Definition.—The portal or multilobular form of cirrhosis of the liver is so much the most common that it is generally described shortly as cirrhosis of the liver. It is a disease in which degeneration of the hepatic cells occurs

in association with fibrosis spreading from the portal spaces to enclose various numbers of lobules.

Ætiology.—Cirrhosis of the liver is generally fatal about the age of fifty, but a distinct group of cases occurs in childhood. It is three times more common in men than in women, but only slightly more so in boys than in girls. Cirrhosis is in very rare instances familial, presumably as a result of an inborn defect of the liver cells which renders them abnormally vulnerable to toxins and liable to premature degeneration; this may then be associated with chronic lenticular degeneration (Wilson's disease). It is more common in individuals who follow a sedentary occupation than in those who lead an active life, and among the poor than the well-to-do, though since the War of 1914–1918 it has become less common among the former and more common among the latter.

A very large majority of patients with cirrhosis of the liver have indulged excessively in alcohol; it is three times more common among people connected with the liquor trade than among the general public. Any condition, such as syphilis, amœbiasis and malaria, which can damage the liver predisposes to the development of alcoholic cirrhosis. Cases occur, however, especially in India, Egypt, and Dutch East Indies, and in children, in which alcoholic excess can be excluded with certainty. Thus cirrhosis is not infrequent among Brahmins, the majority of whom indulge in large quantities of ginger, cardamoms, red pepper and other spices, but never touch alcohol. I have seen a typical case with severe ascites in a lady of thirty, who was teetotal, had never suffered from malaria, and had always taken an ordinary diet. The multilobular cirrhosis which develops as a complication of splenic anæmia as the result of the action of a poison produced in the spleen is almost indistinguishable pathologically from that associated with chronic alcoholism.

Pathology.—Cirrhosis very rarely develops experimentally in animals as a result of chronic alcoholic poisoning, although fatty changes and occasionally necrosis with a slight degree of small-celled infiltration may be produced. It occurs in less than 3 per cent. of drunkards dying from the effect of alcoholism, and its geographical distribution does not correspond with that of chronic alcoholism, cirrhosis being rare, for example, in Scotland and Ireland; and when excessive indulgence in alcohol leads to nervous or cardiac symptoms, cirrhosis of the liver is rare. It is probable, therefore, that alcohol produces cirrhosis of the liver indirectly by leading to gastro-enteritis; the poisons produced in the alimentary canal are absorbed and pass to the liver. As ordinary gastro-enteritis does not lead to cirrhosis, an additional factor must be present. This is probably the direct poisonous action of alcohol and occasionally of other toxins, such as that of malaria, on the liver cells, which thus become more liable to injury by gastro-intestinal toxæmia.

Cirrhosis of the liver may result from the action of poisons which reach it from the spleen. This is the cause of the cirrhosis of splenic anæmia, as the liver does not become affected if the spleen is removed at a sufficiently early stage. In a typical early case under my care a fragment of liver removed when splenectomy was performed showed no pathological changes.

It is probable that the poisons which cause cirrhosis of the liver lead both to degeneration of the hepatic cells and to irritative hyperplasia of the connective tissue; the degeneration of the hepatic cells is increased by the

connective-tissue hyperplasia, which in turn is exaggerated by replacement fibrosis following atrophy of the hepatic cells.

The size of the liver varies greatly; it may be much smaller or much larger than normal. The large liver is due to compensatory hyperplasia of the liver cells and to a less extent to fatty degeneration.

The surface of the liver is irregular. The projections may be as small as those of a granular kidney, but more frequently they give rise to a hob-nailed appearance.

The obstruction to the intrahepatic branches of the portal vein produces a rise in pressure in its tributaries; this results in dilatation of the collateral circulation which normally exists between the portal and general venous systems. This compensatory circulation is carried out by the following groups of vessels.

1. An anastomosis may develop within the liver between the branches of the portal vein and the intralobular veins. Large branches pass from the liver and its capsule to the phrenic and intercostal veins, where the liver and diaphragm are uncovered by peritoneum. Occasionally a single large vein passes from the liver in the falciform ligament by the side of the obliterated umbilical vein to join the veins of the abdominal wall at the umbilicus; the subcutaneous veins around and above the umbilicus are consequently dilated, and a large bunch of dilated veins may form at the umbilicus.

2. The gastric veins anastomose with the œsophageal veins, which open into the azygos veins; the veins in the lower end of the œsophagus may become greatly dilated.

3. The inferior mesenteric vein communicates through the superior and middle hæmorrhoidal veins with the inferior hæmorrhoidal vein, which is a branch of the internal iliac vein; this might be expected to give rise to hæmorrhoids, but they are hardly more common among patients with cirrhosis than in individuals with healthy livers.

4. The veins of Retzius unite the radicles of the portal veins in the intestines and peritoneum with the inferior vena cava and its branches. These include the retro-peritoneal veins, which are often greatly enlarged, especially in the neighbourhood of the kidneys.

Symptoms.—About 50 per cent. of patients with cirrhosis of the liver die from some intercurrent disease or accident. Such cases are generally described as latent; but in the majority symptoms due to the condition were probably present before death, and the fatal result of the intercurrent disease or accident was often due to the diminished power of resistance to toxæmia which results from cirrhosis. In some cases, however, the disease may be genuinely latent, owing to compensatory hyperplasia of the liver cells and to the development of an efficient collateral circulation between branches of the portal vein and systemic veins.

In a large majority of cases the symptoms caused by cirrhosis are preceded by those of pre-cirrhotic hepatitis, which have already been described (p. 700), and alcoholic œsophagitis and gastritis have generally been present for many years. The patient habitually wakes in the morning with a feeling of nausea and no desire for breakfast; violent retching often occurs, and he then vomits a small quantity of alkaline watery fluid, after which some bile-stained mucus may appear. A sense of uncomfortable fullness is also felt in the epigastrium after other meals, and the nausea and vomiting may recur. The

appetite is poor, and there is a special repugnance for meat. When cirrhosis develops, the symptoms due to catarrh are exaggerated by the congestion of the gastric and intestinal mucous membrane caused by portal obstruction; this leads to the secretion of still more mucus, and by preventing absorption of gas leads to flatulence, which aggravates the feeling of distension already present. Flatulence is a constant early symptom and is the earliest sign of portal congestion; it is " le vent avant la pluie."

The complexion is generally sallow and bloated with dilated capillary or arterial angiomata, especially over the nose and cheeks. In the later stages the face is drawn, the cheeks and eyes are sunken, and the conjunctivæ are congested and often slightly tinged with bile. The skin of the body is dry and inelastic; numerous spider angiomata appear on the face, neck and back as the disease progresses, and red or purple areas of skin may be produced by the uniform distension of small venules. Purpura and various forms of erythema may occur.

The tongue is flabby and furred, the gums readily bleed, and pharyngitis is common owing to chronic irritation by alcohol. The breath is often offensive as a result of oral sepsis.

The patient is generally constipated, but attacks of diarrhœa may occur, especially during the last few weeks of life.

In a large proportion of cases the liver is enlarged. Its lower border can generally be felt below the costal margin in the right nipple line; but ascites and occasionally flatulent distension of the intestines or obesity may render it impalpable. It is always very hard; its edge can consequently often be felt even when it is not enlarged. In rare cases an enlarged liver can be observed to shrink as the disease progresses until it ceases to be palpable, and after death it may be found to be considerably smaller than normal. The irregular surface of the liver can occasionally be recognised by palpation, The liver is insensitive in contrast with its tenderness in pre-cirrhotic alcoholic hepatitis.

Discomfort is often felt in the right hypochondrium, but pain only occurs if the disease is complicated by an attack of perihepatitis.

In about 35 per cent. of cases jaundice occurs. It is generally slight and is often transient. In the absence of jaundice van den Bergh's test may give a positive indirect reaction with a delayed or biphasic direct reaction.

In 80 per cent. of cases the spleen is enlarged. Owing to its hardness it is easily felt unless it is obscured by ascites or intestinal flatulence. Discomfort or pain may result from stretching of the capsule if rapid enlargement occurs; more frequently it is due to perisplenitis. When both the liver and spleen are much enlarged, the left lobe of the former may overlap the latter.

Hæmatemesis occurs in about 25 per cent. of cases. It is generally an early symptom, and is often the first indication of the presence of serious disease, though it is generally preceded by symptoms of gastritis. It is uncommon after ascites has developed. The hæmatemesis generally takes the form of a single large hæmorrhage; but sometimes a smaller quantity is vomited during the next few days. It is generally repeated only after a considerable interval. The blood collects slowly in the stomach and often passes into the intestine, causing melæna without hæmatemesis. When a considerable quantity has collected in the stomach, the distension causes it to be vomited; small quantities are not brought up unless vomiting occurs

from some independent cause. The blood collects more slowly than in gastric ulcer and is therefore generally more clotted and darker, as there is more time for digestion to occur; for the same reason fainting occurs less frequently. Death from hæmatemesis is very unusual in cirrhosis and accounts for less than 5 per cent. of the mortality.

In the majority of cases the hæmorrhage is a result of rupture of varicose œsophageal veins in the lowest 3 inches of the œsophagus, when they can be easily demonstrated with the X-rays. The blood runs into the stomach, though in severe cases it may well up directly from the œsophagus. Hæmorrhage may also occur from minute erosions secondary to acute gastritis, sometimes associated with varicose veins. The erosions are very difficult to discover *post mortem*, and possibly in some cases there is no actual loss of surface, the hæmorrhage corresponding with the bleeding which occurs from other mucous membranes as a result of the toxæmia. In very rare cases melæna may result from thrombosis of the portal vein or one of its branches (*vide* p. 721).

Epistaxis is common. The hæmorrhage generally comes from a point on the anterior part of the septum. In the late stages oozing from the nose may occur, as well as from the gums, lungs, kidneys and uterus, as a result of the toxæmia caused by hepatic insufficiency, and small hæmorrhages often occur under the skin. Hæmoptysis, however, is generally due to the cirrhosis being associated with pulmonary tuberculosis.

Ascites is present in most cases of cirrhosis which run their full course; it is a late symptom in uncomplicated cases, and is often absent if the patient dies from some independent cause or from hæmatemesis at a comparatively early stage. The onset is generally gradual, but it occasionally develops suddenly after a blow on the abdomen, a chill or an acute infection; it is also acute in portal thrombosis. It sometimes disappears spontaneously shortly before death. It is a result of portal congestion, as the intrahepatic branches of the portal vein are compressed, some being completely obliterated; occasionally others are thrombosed, and in rare cases thrombosis of the portal vein itself occurs. This is not the sole cause of ascites, as the fluid may collect with extreme rapidity instead of *pari passu* with the changes in the liver, and it is often absent when the portal pressure is high as shown by the occurrence of hæmatemesis. In many cases it is secondary to chronic peritonitis.

The ascitic fluid is clear and sometimes slightly bile-stained. Its reaction is alkaline, its specific gravity between 1008 and 1015, and a large proportion of the cells it contains are endothelial. When the ascites is due to chronic peritonitis the specific gravity is greater than 1015, more albumin is present, flakes of fibrin may form on standing and polymorphonuclear cells are found. When 50 per cent. or more of the cells are lymphocytes, tuberculous peritonitis is probably present. In rare cases the ascites is chylous or chyliform; still more rarely it is hæmorrhagic.

Œdema of the ankles is frequent, but it is rarely very marked, though occasionally it speads up the legs to the abdomen and back. It often develops before or at the same time as the ascites, in which case it must be toxic in origin, but most frequently it follows it and is caused by pressure of the ascitic fluid on the inferior vena cava and the abdominal lymphatics; it rapidly diminishes when the abdomen is tapped.

Muscular weakness and loss of energy may be the earliest symptoms; they are constant in the late stages. The muscles are flabby and atrophied, and marked wasting of the whole body occurs.

The rise in intra-abdominal tension caused by flatulent dyspepsia and later by ascites is frequently followed by the development of hernias.

The urine is diminished in quantity and the specific gravity is high. It is very acid and high coloured, and a large deposit of urates generally forms on standing. It contains excess of urobilin, but even when slight jaundice is present bile-pigment is often absent. In the late stages the percentage of nitrogen excreted as ammonia increases at the expense of urea; this is due to ammonia being required to unite with the excess of organic acids present, and not to inability of the liver to form urea, as ammonia given by the mouth is still excreted as urea. In the last days of life leucin and tyrosin are sometimes found.

Albuminuria is occasionally present as a result of the hepatic toxæmia, nephritis, or congestion of the kidneys from heart failure. Glycosuria is rare, as the glycogenic function of the liver is maintained to a certain extent even in advanced cases, but the lævulose test for hepatic efficiency generally shows considerably impairment throughout the course of the disease, though owing to compensating hyperplasia this is often less than might be expected.

The blood is generally normal, except when severe hæmorrhages have led to secondary anæmia. I have seen two cases in which the achlorhydric gastritis caused by chronic irritation of the stomach by alcohol led to the development of typical pernicious anæmia in patients with cirrhosis.

The temperature is often raised in rapidly progressing cases apart from complications such as tuberculosis and infective endocarditis.

In the late stages of cirrhosis the toxæmia which results from hepatic insufficiency gives rise to restlessness, irritability, muttering delirium, and finally to coma.

Nervous symptoms may also be present as a direct result of chronic alcoholism. Delirium tremens may follow a drinking bout and occasionally hæmatemesis; slight mental disturbance and muscular tremor are not uncommon, but neuritis is a rare complication.

Active tuberculous disease is found more frequently in patients dying with cirrhosis of the liver than with other diseases. This is probably due to the diminished resistance to tuberculous infection caused by chronic alcoholism. The lungs are most often affected, phthisis being the cause of death in 15 per cent. of cases of cirrhosis, and tuberculous pleurisy is not uncommon. Either the cirrhosis or the phthisis may be completely latent and remain undiscovered until death.

Tuberculous peritonitis is found in 10 per cent. of cases; the accompanying ascites is often thought during life to be due to the cirrhosis. The lungs are generally also involved. The majority of cases of tuberculous peritonitis in adult males are associated with cirrhosis.

Diagnosis.—A regularly enlarged, hard liver in an alcoholic individual is generally the result of cirrhosis. The occurrence of hæmatemesis, enlargement of the spleen, slight jaundice or a positive indirect van den Bergh reaction, makes the diagnosis still more probable. The enlarged hard liver, which is produced by chronic venous congestion in heart failure, may be difficult to distinguish from cirrhosis if the patient is seen when the heart is no

longer failing. A history of heart failure with pain in the hepatic region and any evidence of existing heart disease point to congestion.

The diagnosis from syphilis and from malignant disease of the liver is discussed elsewhere (p. 714 and p. 719).

Splenic anæmia with hæmatemesis can be distinguished from cirrhosis by the much greater enlargement of the spleen and the presence of leucopenia. It must, however, be remembered that cirrhosis of the liver always develops sooner or later in untreated splenic anæmia.

The symptoms in the last stages are often indistinguishable from those of uræmia, and the diagnosis may be very difficult in the absence of a full history. But a much increased blood urea with high blood pressure, albuminuric retinitis or the presence of a large quantity of albumin with casts in the urine would prove that uræmia is present.

Prognosis.—If an individual with cirrhosis permanently gives up alcohol in the pre-ascitic stage, there is a good chance that the disease will not progress and that his symptoms will disappear. Even the damage done to the liver can be repaired to some extent by hyperplasia of its cells, a large liver being therefore a favourable sign, and the danger of hæmatemesis, together with the other ill-effects of portal congestion, may be overcome by a sufficient development of the anastomoses between the portal and general venous systems.

Much, therefore, depends upon the patient's character, as, if he is unable to control his desire for alcohol, the disease is certain to advance to a fatal issue. The younger the patient the more chance there is for functional compensation to occur, but the prognosis is always bad in children. However completely latent the disease may become, much of the damage to the liver is of course permanent, and the patient's power of resisting acute infections and all other diseases is materially reduced.

Fever is a serious symptom, as it indicates rapid advance of the disease or the presence of some complication. When the patient becomes drowsy death is almost certain to follow rapidly, but I have seen complete restoration to health occur in a semi-comatose, tremulous, apparently moribund man, who had drunk champagne in great excess for many years but remained completely teetotal after recovery from the acute illness.

In rare cases the disease runs a subacute course, death occurring within a few months of the onset of symptoms. Such cases are most frequent in comparatively young adults who are heavy drinkers. The liver is painful and tender, fever is present, emaciation is rapid, and multiple hæmorrhages are likely to occur. Such cases, however, are really examples of subacute necrosis of the liver.

Treatment.—Alcohol must be absolutely prohibited for the rest of the patient's life, and no medicine containing alcohol should be prescribed. Curries, pickles, ginger, all highly-seasoned food, vinegar, mustard, pepper, high game and ripe cheese must be permanently avoided.

Apart from these restrictions the diet in the early stages should be that required for the treatment of the associated chronic gastritis. In the late stage, when symptoms of hepatic insufficiency are present, the diet should consist entirely of milk, milk foods, vegetable purées and fruit, and even when improvement occurs very little animal food should be allowed. Half a pound of dextrose in a pint of lemonade should be given daily.

The bowels should be kept regular by means of Epsom salts. No other drugs are required in uncomplicated cases. The treatment of the gastritis, ascites and hæmatemesis is considered elsewhere. Recurrent severe hæmorrhage can sometimes be controlled by ligature of the coronary veins just below the diaphragm or by direct injection of varicose œsophageal veins with sclerosing fluid through an œsophagoscope.

The regular life led at a spa, such as Harrogate, combined with the use of a mild aperient water, is often very beneficial

The treatment of the drowsy toxæmic condition of the late stage is the same as that of subacute hepatic necrosis (p. 697).

HÆMOCHROMATOSIS

Synonyms.—Pigmentary Cirrhosis ; Bronzed Diabetes.

Ætiology and Pathology.—Hæmochromatosis is a very rare disease, in which large quantities of hæmosiderin, an iron-containing pigment, are deposited in various parts of the body, especially the liver, upper abdominal lymph glands, pancreas, suprarenal glands and skin, but very little in the kidneys and spleen. The deposition of pigment is associated with ordinary multilobular cirrhosis of the liver and cirrhosis of the pancreas, and the latter, by involving the islands of Langerhans, may give rise to diabetes mellitus. It occurs in about 7 per cent. of cases of cirrhosis of the liver in males and hardly ever in females. There is no excessive hæmolysis ; the quantity of iron deposited is much greater than in hæmolytic anæmias, in which the excess of iron is chiefly in the liver and kidneys, whereas in hæmochromatosis it is chiefly in the liver, pancreas and abdominal glands, to which it passes from the liver and pancreas.

The disease is extremely chronic. In advanced cases 30 grm. of iron may be deposited in the body compared with the normal of 0·3 grm. ; as the ordinary daily intake of iron in the food is about 10 mgrms. it would take 3000 days to accumulate, even if no iron were ever excreted. There must clearly be a failure in the elimination of iron, but it is unknown whether this is primary or the result of excessive deposition. Possibly the liver cells are affected by an unknown toxin responsible for the disease in such a way that they become incapable of dealing with the iron which comes to them in the food, which is consequently deposited in the cells of the liver and other organs as hæmosiderin. It is, however, equally likely that the cirrhosis of the liver, like that of the pancreas and lymphatic glands, is secondary to the excessive deposit of iron pigment, which in any case must aggravate the cirrhosis. In support of this theory is the observation that a patient of mine with aplastic anæmia developed typical hæmochromatosis in the course of seven years during which he received 270 transfusions.

Primary carcinoma of the liver occurs in hæmochromatosis somewhat more frequently than in simple cirrhosis of the liver.

Symptoms.—The symptoms are those of cirrhosis and diabetes associated with pigmentation. The liver and spleen become progressively larger. Ascites may occur and the subcutaneous veins are sometimes enlarged. The skin is generally pigmented a slaty colour, especially in the exposed parts of the body. The lesion of the suprarenal cortex may give rise to symptoms of Addison's disease, the pigmentation of the skin being sometimes due to

melanin and not to hæmosiderin, and pigmentation of the buccal mucous membrane may occur. In the rare cases in which no pigmentation is present the nature of the disease is only discovered after death. In most cases symptoms of severe diabetes with acidosis appear suddenly, but they may be absent to the end.

Diagnosis.—The disease can only be diagnosed with certainty when pigmentation, diabetes and cirrhosis are associated together. When two of these conditions are present alone, a definite diagnosis is impossible. It can, however, be made with a considerable degree of probability if well-marked bronzing is associated with cirrhosis even in the absence of diabetes. In doubtful cases biopsy of a pigmented area of skin will settle the diagnosis.

Prognosis.—So long as no diabetes is present the prognosis is not worse than that of uncomplicated cirrhosis, but the onset of diabetes is always a very grave event; with insulin treatment, however, a normal life can generally be led for several years, death being finally caused by the cirrhosis.

Treatment.—The treatment is that of cirrhosis and diabetes. The latter requires large doses of insulin, with the aid of which the diet can be balanced without special difficulty.

AMŒBIC HEPATITIS AND HEPATIC ABSCESS

Ætiology.—Amœbic hepatitis is very rare before the age of 20 and is most common in the third and fourth decades. Amœbic hepatitis and amœbic abscess of the liver are invariably secondary to amœbic dysentery (*vide* p. 264). In 98 per cent. of fatal cases Rogers either obtained a history of dysentery or found amœbic ulcers or scars of ulcers in the large intestine. The patient had had dysentery in the past or was still suffering from it in about 75 per cent. of acute and subacute cases, and in an additional 15 per cent. there was a history of diarrhœa, which was doubtless a mild form of amœbic dysentery. In the remaining cases amœbic ulcers had probably been present in the cæcum or ascending colon, situations in which they do not necessarily give rise to any symptoms. Dysentery may precede the development of an abscess by months or even years—in one of my cases by 16 years. When hepatitis develops during an attack of dysentery, the latter generally becomes less severe as the inflammation in the liver progresses.

The geographical distribution of the disease is identical with that of amœbic dysentery, but as it may develop in chronic cases and long after the onset of dysentery, it is not uncommon, especially in the chronic form, among individuals who have returned to Europe from the tropics. Chronic alcoholism is an important predisposing cause.

Pathology.—The amœbæ, which collect in the thrombosed veins at the base of dysenteric ulcers, pass to the liver by the portal vein. Nothing more is known as to the pathology of non-suppurative amœbic hepatitis, as death does not occur unless an abscess forms, but the hepatic insufficiency, which is always found to be present by the lævulose test, indicates that the infection is widespread and uniform through the liver. An abscess forms if a local accumulation of amœbæ gives rise to thrombosis in a portal radicle. The circulation is obstructed and necrosis of the surrounding tissue occurs;

at the same time pus is secreted as a result of the irritant action of the amœbæ on the liver tissue. The wall of the abscess is at first formed by necrotic liver tissue, but the cavity gradually becomes limited by a fibrous capsule produced by the inflammatory reaction. In 70 per cent. of cases a single abscess is present; in nearly half of the others there are 2 abscesses, in a quarter there are 3, and in the remainder there are 4 or more. A single abscess is found five times as often in the right as in the left lobe of the liver.

The contents of the abscess consist of necrosed liver cells, leucocytes, red corpuscles, fat droplets, and generally amœbæ but no bacteria. In chronic cases all the amœbæ may have died, but they can still be found in the material obtained by scraping the wall of the abscess. In rare cases an amœbic abscess becomes spontaneously sterile, and its dried remains have been found at a post-morten examination years afterwards. When an hepatic abscess reaches the surface, adhesions form between the liver and the adjoining structures, so that the contents of the abscess may burst into the lung, stomach or bowel, or open externally without infecting the serous cavities.

Acute and Subacute Amœbic Hepatitis and Hepatic Abscess

Symptoms.—About one-tenth of the cases of acute amœbic hepatitis occurring in India are of a fulminating type, in which the whole liver is riddled with small collections of pus with no fibrous tissue separating them from the surrounding liver substance—a condition which rarely, if ever, occurs outside the endemic areas. The liver rapidly increases in size; it is very painful and extremely tender. Slight jaundice may be present. The temperature is high with rapid remissions, the rise being often accompanied by rigors and the fall by copious sweating. Leucocytosis is well marked. Death generally occurs between 6 and 18 days from the onset of symptoms.

As most cases of subacute amœbic hepatitis subside completely with injections of emetine, it is clear that in the early stages no suppuration is present. Discomfort and a sense of weight are felt in the right hypochondrium in the slighter cases, but in the more severe ones the pain may be so great that the patient is hardly able to move, and he is often unable to lie on his left side owing to the dragging pain caused by the change of position. Pain may also be referred to the right shoulder and occasionally to the right arm, especially when the upper part of the liver is involved. The liver is enlarged and tender, but the rigidity of the abdominal muscles may be so great that it is impossible to feel its edge. Pressure exerted on the lower part of the right thorax, with one hand behind and the other in front, gives rise to pain. Slight jaundice is occasionally present in the severer cases. The appetite is impaired or lost, and the patient rapidly becomes weak and emaciated.

The temperature is generally remittent, varying between 100° in the morning and 103° or 104° in the evening. In severe cases it remains high with only small remissions, but in more chronic cases, especially when the abscess bulges through the capsule of the liver and the tension within its cavity consequently falls, the fever is less marked; it may then be low, continued or relapsing, and may finally disappear. Copious sweating is

common in the more severe cases. Moderate leucocytosis is always present, and the proportion of polymorphonuclear cells is considerably increased, especially when actual suppuration has occurred; if the percentage is less than 70, simple hepatitis, and not an abscess, is probably present.

The upper part of the liver is most frequently involved, and the main increase in dullness is then in the upward direction, but the lower border is also abnormally low. The lower ribs bulge, and the intercostal spaces become wider; the edges of the ribs become less clearly defined, and the skin may be œdematous even in acute hepatitis without suppuration. At an early stage the breath-sounds become feeble and the percussion note impaired at the right base; the X-rays show that the right side of the diaphragm is abnormally high, and when suppuration occurs its movements are diminished and finally cease completely. If the diaphragm is perforated by an abscess of the liver, a pulmonary abscess, or less frequently an empyema, develops. In the former case large quantities of thick reddish pus are expectorated, and, if emetine is given, rapid recovery generally results.

An abscess in the anterior and lower part of the right lobe produces a tender tumour in the right side of the epigastrium, the lower ribs become prominent, and the lower border of the liver can either be felt or is found by percussion to be displaced downwards. A rub may be heard when an abscess reaches the surface of the liver, but it disappears on the formation of adhesions with the anterior abdominal wall. In advanced cases the skin becomes œdematous, fluctuation is present, and the abscess may open externally just below the costal margin. Less frequently the abscess reaches the under surface of the liver, when it may rupture into the duodenum or hepatic flexure. Pus is then passed by rectum, and the tumour suddenly diminishes in size. The general condition of the patient immediately improves, the temperature falls, and spontaneous recovery may follow.

An abscess in the left lobe of the liver generally gives rise to a tender tumour in the epigastrium. An abscess bulging from the lower or upper surface of the left lobe is less easily diagnosed; it may escape recognition till it ruptures respectively into the stomach, when the characteristic thick reddish pus is vomited, or into the left lung or pericardium.

In some cases the X-rays show a localised increased density in the hepatic shadow, especially if the abscess is in the left lobe or if it is large and surrounded by a thick fibrous capsule. Localised subdiaphragmatic, subhepatic and retroperitoneal abscesses are uncommon complications, and general peritonitis rarely develops.

Diagnosis.—The possibility of amœbic hepatitis or hepatic abscess should be considered whenever an individual, who has been in the East, is suffering from progressive deterioration in health with more or less pyrexia, especially if the latter is remittent and accompanied by chills and sweats, and if obscure abdominal symptoms are present.

Subacute hepatitis is most commonly confused with malaria; but the rise of temperature in hepatitis is generally in the evening instead of during the day, and the liver is enlarged out of proportion to the spleen instead of *vice versa*, leucocytosis is present with a relative increase of polymorphonuclear cells and only 2 to 4 per cent. large mononuclear cells in contrast with the normal or subnormal count with 15 to 20 per cent. large mononuclear cells found in malaria; the malarial parasite cannot be found in

the blood, and the injection of emetine is followed by improvement, whilst quinine fails to influence the pyrexia.

A localised tumour in the liver in a man who has been exposed to amœbic infection is generally an abscess and more probably amœbic than a suppurating hydatid cyst. It is elastic or fluctuating, unlike the hard solid tumour formed by a gumma and a growth.

Prognosis.—Until 1907 hepatic abscess was the second commonest cause of death in the British Army in India, but the incidence of the disease has become much smaller since amœbic dysentery has been treated by emetine injections, and the mortality has been greatly reduced since the necessity for operation has become comparatively rare owing to the frequency with which treatment is instituted in the pre-suppurative stage.

Treatment.—In acute hepatitis without suppuration very rapid improvement follows the subcutaneous injection of 1 grain emetine hydrochloride on 12 or more consecutive days; the hepatic tenderness diminishes within 8 hours of the first injection, and the temperature may fall to normal in 24 hours. As there are no definite signs which distinguish acute hepatitis without suppuration from hepatic abscess unless a definite tumour is present, no local treatment should be adopted until emetine injections have been given daily for a week without producing any improvement. Even a small abscess may be completely absorbed without aspiration after the amœbæ in its walls have been killed by subcutaneous injections of emetine.

The most satisfactory treatment of an abscess is evacuation by aspiration, emetine being injected subcutaneously in order to kill the amœbæ in the abscess wall and in any ulcers which are still present in the colon. If the pus reaccumulates, a grain of emetine hydrochloride dissolved in a fluid ounce of water should be injected into the abscess cavity after it has been aspirated. The results with this treatment are so successful that the open operation, which is frequently followed by prolonged convalescence or death owing to secondary infection, is required only in the comparatively rare cases, in which the situation of the abscess cannot be determined, or bacteriological examination of the pus obtained by aspiration shows that the abscess already contains pyogenic bacteria. When an abscess has been opened or has ruptured into the lung, stomach or bowel, subcutaneous emetine injections should be continued until the temperature has remained normal for a week.

Chronic Amœbic Hepatitis

Amœbic dysentery is almost always associated with hepatic insufficiency as demonstrated by the lævulose test, although in a large majority of cases there is no sign of hepatic disorder. As acute and subacute hepatitis and hepatic abscess are common complications of amœbic dysentery, it seems reasonable to assume that the functional deficiency of the liver in these cases is caused by a mild and latent form of amœbic hepatitis.

Symptoms.—It is not uncommon to find hepatic insufficiency in patients complaining of unfitness since returning from a country in which amœbic dysentery is endemic. Some have had definite dysentery, but others have had nothing more than a few attacks of diarrhœa, and occasionally they have never had intestinal symptoms of any kind.

The patient complains of general unfitness and is easily fatigued. Very often he rightly describes himself as liverish. He generally suffers from a constant ache over the liver. His appetite is poor, and he is pale and sallow, though generally not anæmic, and true jaundice is never present. There is no pyrexia, and the leucocyte count is normal. The whole of the exposed surface of the liver is tender, and the lower border is often more easily palpable than normal, but there is little or no enlargement. Amœbic cysts are very rarely found in the stools, but in a small proportion of cases, in spite of the absence of intestinal symptoms, the sigmoidoscope has revealed the presence of small but typical amœbic ulcers—raised red spots with a necrotic centre on a normal pink mucous membrane, very closely resembling boils on the skin. Not infrequently the cæcum and ascending colon are tender, and the stools may contain traces of occult blood, presumably the result of chronic amœbic typhlitis.

Diagnosis and Treatment.—The diagnosis is quickly confirmed by the result of treatment. The injection of 1 grain of emetine hydrochloride every night for twelve nights results in the disappearance of all symptoms, and the lævulose test shows that there is no longer any hepatic insufficiency. In one case, for example, the rise in the blood sugar was 55 mgrm. per 100 c.c. one hour after taking 50 g. of lævulose and in two hours it had only fallen 25 mgrm.; after treatment the one-hour rise was 6 mgrm. per 100 c.c., and in two hours the blood sugar was the same as before the lævulose had been taken.

Further courses of six or more injections should be given 3, 6 and 12 months later in order to prevent recurrence. This treatment is more efficacious and far less upsetting to the patient than the administration of the various other drugs which have been recommended for the treatment of amœbiasis.

SYPHILIS OF THE LIVER

Congenital Syphilis (Pericellular Cirrhosis)

Ætiology and Pathology.—The liver is affected in 50 per cent. of infants with congenital syphilis. This great frequency is probably due to the *Spirochæta pallida* passing through the placenta and the umbilical vein direct to the fœtal liver, which is the first organ it reaches, and which is consequently found to contain it in larger numbers than any other organ.

Congenital syphilis produces diffuse changes in the liver very different from the focal lesions of acquired syphilis, except in rare cases occurring in later childhood, in which caseous gummata are found. The liver is smooth and uniformly enlarged and is firmer and paler than normal. The changes are due to pericellular cirrhosis, the result of diffuse infiltration with embryonic connective-tissue cells between the individual liver cells. These may be associated with small collections of round cells, or miliary gummata, which resemble tubercles when seen by the naked eye.

The spleen is generally enlarged and hard. Diffuse small-celled infiltration or fibrosis may be found in the kidneys, pancreas, testes, suprarenal glands and lungs.

Symptoms.—Symptoms pointing to disease of the liver are not often present in infants with congenital syphilis, but on examination the liver

and spleen are found to be enlarged and abnormally firm. The liver normally extends farther down in young children than in adults owing to its relatively larger size and the more horizontal position of the ribs. Only definite enlargement and abnormal hardness of the liver can, therefore, be regarded as important in the absence of other evidence of congenital syphilis. Jaundice is rare; it may be present from birth or, less frequently, it develops a few weeks later.

Diagnosis.—The diagnosis is generally easy owing to the well-marked signs of congenital syphilis present in other parts of the body together with a positive Wassermann reaction. In the absence of such signs the diagnosis must be made from rickets, tuberculosis and gastro-intestinal infection, and, when jaundice is present, from the other more common causes of icterus neonatorum (p. 688).

Prognosis.—The prognosis depends upon the general condition of the infant. The disease is less amenable to anti-syphilitic treatment if the liver and spleen are greatly enlarged, and if hæmorrhages occur or jaundice is present. The prognosis in delayed congenital syphilis is less favourable than in acquired syphilis owing to the changes being generally more widespread.

Treatment.—The treatment is that of congenital syphilis.

Acquired Syphilis

1. *Secondary Syphilis.*—Jaundice formerly occurred in about $\frac{1}{4}$ per cent. of cases of syphilis at the same time as the roseola and enlargement of glands, but it is now almost unknown. Rapid recovery generally followed treatment with mercury, but occasionally death occurred from acute hepatic necrosis. It must, of course, be distinguished from the toxic jaundice caused by treatment with organic arsenical preparations (p. 212).

2. *Tertiary syphilis.*—**Ætiology.**—Gummata of the liver are found in only 0·3 per cent. of autopsies; but in more than half of the cases in which other active syphilitic lesions are found the liver is affected.

Syphilis affects the liver three times as frequently in men as in women. The disease is generally discovered between 10 and 20 years after infection, but in rare instances it has occurred within a year.

Pathology.—In the early stages a mass of pink syphilitic granulation-tissue, sharply separated from the healthy liver, is found; necrosis soon occurs in the centre, which becomes yellowish-white. The caseous mass is later surrounded by a fibrous capsule; as this contracts, the liver becomes more and more deformed. The capsule of the liver in the neighbourhood of a gumma is thickened, and adhesions often develop between it and the adjacent organs, the diaphragm and anterior abdominal wall. Unless they are very large, gummata are slowly absorbed till they may finally be represented by nothing more than scars, from which fibrous tissue radiates into the capsule. Gummata are generally multiple; much less often a large part of the liver is diffusely infiltrated. The condition is often associated with some degree of diffuse syphilitic hepatitis, which produces cirrhotic changes in long-standing cases, especially if the patient is alcoholic or has been treated with arsphenamine derivatives for primary and secondary syphilis.

Symptoms.—Gummata and cicatrices are sometimes found after death

without having led to any symptoms. The nature of the symptoms they produce depends upon the size, extent and position of the lesions. Before any localising symptoms appear the patient often complains of general ill-health, which is often associated with gastro-intestinal symptoms. The first symptom pointing to disease of the liver is generally pain in the right hypochondrium, the result of perihepatitis over a gumma. The pain may radiate to the right shoulder and is sometimes associated with local tenderness.

Irregularities on the anterior surface of the liver produced by gummata and by the contraction of cicatrices are easily palpable. The diagnosis from malignant disease can be made by the presence of a positive Wassermann reaction and the rapid disappearance of a gumma with anti-syphilitic treatment; jaundice and ascites are much more common in malignant disease, in which the constitutional symptoms are generally more severe, and there may be evidence of a primary growth in some other situation. In hyatid disease the liver is smooth apart from the tumour itself, but in syphilis it is often irregular, owing to the contraction of cicatrices. The presence of eosinophilia points to hydatid disease. A gumma near the gall-bladder or in the left lobe of the liver may simulate a growth of the gall-bladder or of the stomach respectively.

Irregular fever sometimes occurs. The general symptoms may simulate pylephlebitis, tuberculosis, typhoid fever or malaria, but they generally disappear under anti-syphilitic treatment. In rare cases an infected gumma may break down, when the symptoms and sequelæ do not differ from those of other forms of hepatic abscess.

Jaundice is infrequent in syphilis of the liver, but it is occasionally produced by the pressure of a gumma or of a syphilitic cicatrix; in very rare cases this is associated with attacks of pain indistinguishable from biliary colic due to gall-stones.

Ascites is uncommon, and I have seen only one case in which it was severe and recurred rapidly after paracentesis. It may result from pressure of gummata or cicatrices on the intrahepatic branches of the portal vein or less frequently on the vein itself in the portal fissure, in which cases thrombosis is likely to occur.

When a gummatous liver is associated with lardaceous disease, the clinical aspects of the latter may be so prominent that the presence of a gumma is overlooked. The liver and the spleen are enlarged, ascites and œdema are present, and the urine contains albumin and casts.

Diagnosis.—The possibility of syphilis should always be remembered in obscure hepatic disorders. Apart from a history of infection and the presence of other syphilitic lesions, the Wassermann reaction should always be tested in doubtful cases. As, however, infection with syphilis does not prove that every lesion present is syphilitic, the final proof of the nature of the disease is obtained only if great improvement or complete recovery results from anti-syphilitic treatment. The diagnosis from cirrhosis of the liver is suggested by the greater irregularity in the enlargement of the liver. Hæmatemesis, dilated veins on the abdominal wall, jaundice and symptoms of gastritis are much more common in cirrhosis, and the nutrition suffers at an earlier stage than in syphilis of the liver.

Prognosis.—The prognosis of syphilitic lesions of the liver is good if treatment is actively carried out at an early stage. In the rare cases in

which the symptoms are due to pressure exerted by cicatrices and not by gummata little or no improvement can occur.

Treatment.—As soon as the possibility of syphilis is recognised, large doses of iodide should be given. I have very rarely found ill results follow the administration of as much as 60 grains of potassium iodide every 6 hours; a patient is more likely to suffer from iodism if the dose is gradually increased from a small quantity than if full doses are given at once. Mercury should also be given, but no organic arsenical preparation should be used because of the danger of hepatic necrosis occurring as a result of its action on the already damaged liver cells.

HYDATID OF THE LIVER

Ætiology and Pathology.—Hydatid disease is produced by swallowing the ova of the echinococcus or hydatid worm (see p. 314). Food may be contaminated by the fæces of infected dogs, or infection may occur directly if an individual touches the tongue or muzzle of a dog which has been soiled with eggs from the fæces or anus of another dog. The frequency of the disease thus depends upon the number of infected dogs in a district. It is most common in Iceland and in parts of Australia and New Zealand; it also occurs in England, France and parts of Germany and Russia, but it is almost unknown in North America, except among foreigners.

When the eggs are swallowed, the embryos set free by digestion of the egg-shell pass through the walls of the stomach or small intestine into the radicles of the portal vein, by which they reach the liver, where they are generally arrested. The embryo now forms a small cyst, with an internal, nucleated, protoplasmic layer (the endocyst) and an external "cuticular membrane." The reaction in the surrounding tissues results in the formation of a fibrous capsule. After a time a dozen or more buds project from the endocyst, and develop into daughter cysts, identical in structure with the mother cyst; these soon separate from the endocyst of the mother cyst and become free.

The fluid in the cyst is clear or very slightly opalescent, with a specific gravity between 1·005 and 1·011. It contains chlorides, phosphates, traces of sulphates and succinates, and some unknown toxic substances, but only occasionally traces of albumin or sugar. Hooklets and less often hydatid heads may be found in the fluid.

The liver is involved in 60 per cent. of cases of hydatid diseases in man; a single cyst is generally present, but there are occasionally multiple cysts, or single ones may develop in more than one organ.

Symptoms.—The patient remains in good health until the weight of the cyst, its pressure on surrounding parts, or the occurrence of a complication, such as rupture or suppuration, causes symptoms. A hydatid cyst of the liver may remain latent and be discovered only after death or in the course of a routine examination of the abdomen in a patient without abdominal symptoms.

The increasing size of the liver may give rise to a sensation of weight and fullness in the right hypochondrium, and pain may be felt in the right shoulder. I have only once seen jaundice caused by pressure on the bile-

ducts and once œdema of the legs and scrotum by pressure on the inferior vena cava, but never ascites by pressure on the portal vein though this may occur in exceptional cases.

A small cyst may rupture into the biliary passages: intense jaundice results, and the patient generally develops suppurative cholangitis. A large cyst may burst into the general peritoneal cavity, especially after a blow on the abdomen. Symptoms of an allergic character may result, especially severe urticaria, erythema and pruritus. Less frequently there may be diarrhœa and vomiting, and dyspnœa, sometimes of an asthmatic character. In rare cases convulsions, collapse and cardiac failure may occur and end fatally. Rupture into the stomach or intestines may lead to spontaneous recovery.

The upper part of the right side of the abdomen and lower part of the thorax become prominent when the cyst is large. If the cyst reaches the front of the liver it becomes palpable in the hypogastrium. When it projects from the under surface, the liver is pushed forward and it may simulate a large gall-bladder or a renal tumour. A cyst near the convexity pushes the diaphragm upwards and may compress the lung and simulate a pleural effusion. In such cases the irregularity in the upper surface of the liver can be recognised with the X-rays. When deeply embedded in the liver, it produces a more general expansion and no local tumour is palpable. The tumour is generally tense and elastic. In rare cases, of which I have only seen two, percussion of the middle finger, when the left hand is placed flat over the cyst, produces a peculiar vibration—the hydatid thrill—which is almost pathognomonic. It does not, however, depend upon the presence of daughter cysts, as it has been observed in their absence and very exceptionally in other tense cysts.

Bacteria may invade the fibrous capsule and multiply between it and the cuticular membrane, with the result that the nutrition of the hydatid is impaired and the parasite dies. Its death results in a change in the cuticular membrane, which, when healthy, is impervious to bacteria and leucocytes, but now allows them to pass into the fluid, which acts as an excellent culture medium and gradually becomes filled with pus cells. Symptoms of hepatic abscess are now present, and the abscess may finally rupture into the general peritoneal cavity, stomach or intestines.

Diagnosis.—The discovery of a tumour of the liver should lead to a consideration of cancer, syphilis and hydatid cyst. The general health is greatly affected in the first, comparatively little or not at all in the second and third. In cancer and syphilis the tumour is likely to be irregular and multiple; in hydatid it is a uniform round swelling, and most frequently only one can be felt. The two former are hard and obviously solid, while the latter is elastic, and in rare cases the characteristic hydatid thrill can be felt. The Wassermann reaction is positive with a gumma and generally negative in the other diseases. Eosinophilia is frequent in hydatid, but in no other liver disease; it was known to have been present for eleven years when a patient, who proved to have a hydatid of the liver, first consulted me. The proportion of eosinophil cells may be enormous. In the case of a boy of 18, in whom the cyst had grown very rapidly, they amounted to 65 per cent. of 16,000 leucocytes per cubic millimetre; the total and differential counts fell to normal within 3 weeks of the removal of the cyst. I have

seen two cases of very large tumours of the right suprarenal, which produced a rounded protuberance on the anterior aspect of the displaced liver, closely simulating a hydatid cyst; the diagnosis was made more difficult by the presence of eosinophilia of 15 to 20 per cent. The intradermal injection of sterile hydatid fluid (Casoni's test) produces a positive cutaneous reaction in 90 per cent. of cases, and in one case of mine a pyrexial reaction lasting for three days. Once the skin has become sensitised it may remain so permanently in spite of removal of the cyst. The complement fixation and precipitin tests are less reliable.

Prognosis.—A cyst may continue to grow for as long as 20 years, but the possibility of suppuration or perforation is a constant danger. When it dies, the cuticular membrane folds on itself and may become calcified; its contents dry up and form a mass containing gritty material. It can then cause no further trouble.

Treatment.—PROPHYLACTIC.—In places where hydatid disease is common, the drinking water should be boiled, fruit and vegetables should be cooked or washed with boiled water, and care should be taken not to convey infection from dogs to food by the hands.

SURGICAL.—Hydatid cysts were formerly treated by tapping, but such methods have now been completely superseded by an open operation, in which the fluid is evacuated and as much of the cyst wall as possible is removed. In some cases the latter is very loosely attached and can be pulled out intact. The operation should be performed whenever a hydatid cyst is diagnosed, even if it causes no symptoms, as there is always a danger of serious complications.

CARCINOMA OF THE LIVER

Ætiology and Pathology.—(*a*) PRIMARY GROWTHS.—Primary carcinoma of the liver is found only about once in each thousand autopsies, and primary sarcoma is considerably rarer. Primary carcinoma may be derived from the liver-cells (hepatoma) or, much less frequently, from the bile-duct cells (cholangioma); 90 per cent. of the former and 50 per cent. of the latter occur in cirrhotic livers. Primary cancer occurs in about 7 per cent. of patients with cirrhosis, the incidence being fifty times as great as among patients free from cirrhosis. The incidence of primary carcinoma of the liver is very high in Dutch East Indies owing to the great frequency of non-alcoholic cirrhosis among the natives and to a special tendency of this form of cirrhosis to undergo malignant degeneration. Cirrhosis of the liver is a progressive lesion owing to the continuous action of the toxin, whereas in the fibrosis following subacute necrosis no further destruction of cells takes place after the original illness. Consequently the nodular hyperplasia of the latter never becomes malignant, whereas the progressive compensatory hyperplasia of the former may overstep the normal and take on the autonomous character of a new growth (*cirrhosis carcinomatosa*).

Primary cancer of the liver readily invades the portal vein, along which it spreads in both directions from the point of entry, forming a tree-like cast of the affected part of the portal system. On section the growth-distended vessels give the appearance of a tumour of multicentric origin, and dis-

semination to other parts of the liver often occurs through the portal system. In 40 per cent. of cases extrahepatic metastases are present. Spread by lymphatics may involve glands in the portal fissure, which press upon the portal vein and bile-ducts, as well as glands elsewhere in the abdomen and chest, and malignant emboli may pass by the hepatic veins to the lungs. After death the cirrhosis is found to be universal and of long standing, whereas the carcinoma appears to be of recent origin. The liver contains numerous nodules of carcinoma, which often reach the surface, but are never umbilicated. The symptoms may be indistinguishable from those of cirrhosis, the liver being normal in size or slightly enlarged. In the latter case, nodules can sometimes be felt on the surface. The spleen is often enlarged, and ascites is always present owing to portal obstruction. Pain in the right hypochondrium and jaundice are more common than in uncomplicated cirrhosis.

(*b*) SECONDARY GROWTHS.—Secondary carcinoma of the liver is about thirty times as common as primary carcinoma ; it is ten times as common as secondary sarcoma.

Secondary malignant disease occurs most frequently after the age of 50. It is more common in women than men because it frequently follows carcinoma of the breast and female genital organs, but it is rare in carcinoma of the lip, mouth and tongue, which are much more common in men than in women.

The most common seat of the primary disease is the stomach, and then in order the colon, œsophagus, pancreas and gall-bladder. It is a common sequel of cancer of the breast and uterus, and may occur when the primary disease is situated in any other organ. Cancer of the gall-bladder, extrahepatic bile-ducts and the stomach may invade the liver by direct continuity.

Symptoms.—The liver is almost always palpable, as it is enlarged and abnormally hard. It becomes progressively larger until it may be so enormous that it appears to fill the whole abdomen, the right lobe being generally most affected. The liver is irregular in shape, and individual nodules of growth are often umbilicated or depressed in the centre. Deposits of growth may be felt at the umbilicus and in the falciform ligament near the linea alba. A rub is sometimes heard over part of the liver as a result of perihepatitis.

Persistent pain is generally felt in the right hypochondrium and in the back ; it may pass to the right shoulder and occasionally down the arm. It is in part due to stretching of the capsule of the liver, especially when it grows rapidly, but the most severe pain is due to perihepatitis. Occasionally deep-seated growths, especially if primary, give rise to no pain throughout the illness.

Jaundice is present in 50 per cent. of cases owing to pressure on the main bile-ducts within the liver by the growth or on those in the portal fissure by glands. Jaundice is more frequent and more often severe in secondary than in primary growths, especially when the primary growth is in the stomach or gall-bladder, from which it has spread directly to the portal fissure. The fæces sometimes retain their colour, as the jaundice may be due to pressure on the intrahepatic bile-ducts, one or more of which escape. The jaundice is progressive and persistent, but it occasionally

develops acutely with vomiting and pain, the symptoms being indistinguishable from those of biliary colic due to gall-stones.

Ascites is present in 50 per cent. of cases. It is most commonly due to malignant peritonitis or to perihepatitis. It may also be caused by pressure on the capillaries when the liver is extensively infiltrated with growth and by portal thrombosis following invasion of the portal vein. The fluid is generally serous, and when jaundice is present it is bile-stained. Extravasation of blood into a superficial nodule may cause it to be hæmorrhagic. In rare cases it is chylous owing to obstruction of a main lymphatic, but more frequently it is chyliform. Perforation of the organ primarily involved or infection without perforation may cause it to become purulent. Œdema of the ankles is present in the late stages as a result of the toxæmia and cardiac weakness. More widespread dropsy may be caused by pressure upon or thrombosis of the inferior vena cava or some other large vein.

In the late stages the patient becomes rapidly weaker. The appetite is lost, and there is often a special distaste for meat. The body weight falls progressively, but occasionally the loss of weight due to the general emaciation is more than counterbalanced by the increase in weight of the liver and the accumulation of fluid in the abdomen. The skin is inelastic and sallow, and secondary anæmia develops. It is often possible to see the liver moving up and down with respiration through the wasted abdominal wall.

Fever is often present, especially in rapidly advancing cases, quite apart from the fever which may be caused by infection of the primary growth or of a necrotic secondary deposit. Suppurative cholangitis may be caused by the infection of ducts which have become dilated as a result of obstruction.

The large liver and the ascites may push the diaphragm up and compress the bases of the lungs, which are then likely to become congested, but the main enlargement is always downwards. The growth may spread through the diaphragm and cause hiccough and cough; pleurisy generally develops and often gives rise to a blood-stained effusion, but empyema is rare.

Finally the patient becomes somnolent and sometimes delirious. Coma is generally present during the last day or two of life; respiration becomes gradually more shallow, and death comes imperceptibly.

Diagnosis.—A painful and irregular enlargement of the liver is most frequently due to a growth, and the probability is increased if general symptoms of malignant disease are present. If there is evidence of a primary growth elsewhere or a growth has been removed by operation within the last five years, the diagnosis can be made with certainty.

The tumour produced by cancer of the liver must be distinguished from one produced by syphilis and hydatid of the liver. The shape of the liver often helps in the diagnosis, and umbilication of a nodule is conclusive evidence of cancer. The general health is much more impaired and the patient is generally older in cancer than in syphilis and hydatid disease. A history of syphilis or evidence of its effects in other parts of the body points to a gumma, and unless a primary growth is discovered the Wassermann reaction should always be tested. Whenever hydatid disease is possible, a differential blood count should be made, as eosinophilia is frequently present, but not in the other conditions. When there is much ascites it may be impossible to diagnose between cirrhosis and cancer, especially if the patient

is slightly jaundiced. The abdomen should be tapped so that the liver can be palpated; the irregularities of the cirrhotic liver are so much less marked than those in cancer that they are rarely recognisable through the abdominal wall. The spleen is generally large in cirrhosis but normal in size in cancer, and the liver is rarely very large in cirrhosis. Pain is generally more marked in cancer, and jaundice, when present, is more profound.

In secondary cancer of the liver the primary disease is often latent, especially when it is situated in the stomach, colon, tail of the pancreas, prostate and lung. But when a thorough investigation fails to reveal a primary growth elsewhere in the body, if jaundice and ascites are absent and emaciation is slight, a single, rapidly growing tumour of the liver is more likely to be primary than secondary.

Prognosis.—Cancer of the liver is always fatal. The course of primary cancer is very rapid, as it rarely lasts more than four months, and death may even occur within four weeks of the onset of symptoms. The duration of the illness in secondary carcinoma of the liver depends upon the primary disease, death being often due to the latter. If the primary disease has been removed by operation or is latent, death may not occur for a year or even longer after the disease of the liver is discovered; but most cases prove fatal within six months. The disease generally advances steadily, but it may remain almost stationary for a time and then rapidly progress to a fatal issue.

Treatment.—It is never justifiable to operate when it is known that a growth of the liver is present; but if during an operation for cancer of the stomach or gall-bladder the liver is found to be involved only in its immediate neighbourhood, an attempt should be made to remove the affected part. Moreover, the presence of one or more small nodules in the liver does not contra-indicate partial gastrectomy or colectomy for the primary growth, as the operation may be followed by a period of a year or more of complete freedom from symptoms.

The medical treatment of cancer of the liver is purely palliative, but by means of morphine the patient should be spared pain throughout the illness. An injection of morphine should be given whenever pain is felt, and the dose should be increased as the disease progresses and the patient becomes accustomed to the drug. There is no reason to fear giving very large doses several times in the day, as with their aid patients often feel perfectly happy and comfortable up to the end. The bowels should be kept regular by drugs, the dose of which generally requires to be increased as more morphine is given. The patient should be allowed to eat and drink exactly what he likes, and no restrictions should be made on account of the supposed indigestibility of certain articles of food, nor should large quantities of food be forced upon a patient who has no appetite. When the diagnosis has once been made with complete certainty, frequent examinations of the abdomen distress the patient without doing any good. If the distension produced by ascites gives rise to pain, the fluid should be removed.

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DISEASES OF THE PORTAL VEIN

NON-SUPPURATIVE PYLEPHLEBITIS AND PORTAL THROMBOSIS

Ætiology and Pathology.—The stagnation of blood caused by cirrhosis of the liver accounts for about 30 per cent. of cases of portal thrombosis, but the latter is so rare that it only occurs in about 1½ per cent. of cases of cirrhosis. Malignant disease of the liver, stomach or pancreas is the next most common cause; invasion of the veins of the affected organ leads to thrombosis, which spreads to the portal vein. Syphilitic changes in the walls of the portal vein and non-suppurative pylephlebitis caused by spread of infection from neighbouring parts may cause thrombosis.

Portal thrombosis may extend throughout the vein and its branches, but more frequently it is localised to the main trunk and one or more intrahepatic branches or extrahepatic tributaries.

Symptoms.—In the presence of cirrhosis of the liver or intra-abdominal growth, especially if ascites is present, there may be no indication that portal thrombosis has occurred. If, however, the patient is in comparatively good health, sudden occlusion of the portal vein may lead to the rapid development of ascites, hæmatemesis and melæna, and the spleen becomes enlarged. When the splenic vein is occluded, the splenic enlargement is rapid and considerable. When mesenteric veins are suddenly involved, hæmorrhagic infarction results and leads to intestinal paralysis with severe melæna and early death.

SUPPURATIVE PYLEPHLEBITIS

Ætiology.—Suppurative pylephlebitis is almost always secondary to some intra-abdominal inflammatory disease, generally associated with the presence of pus under pressure. Acute appendicitis accounts for nearly half of the cases.

Pathology.—The veins leading from the source of infection to the liver, together with the trunk and intrahepatic branches of the hepatic vein, may all be involved, but the disease is generally less extensive and may be confined by firm clots to a part of the portal vein or one of its branches. The affected veins contain pus and broken-down blood clots. Their walls are acutely inflamed and may give way, leading to the formation of abscesses. Thus a large abscess may develop in the mesentery or behind the pancreas. The liver is almost always involved by extension to the intrahepatic portal branches, or by secondary abscesses formed from infective emboli from the part of the vein primarily affected. Innumerable minute abscesses are present, many of which may coalesce to form a honey-combed appearance or large abscesses. Superficial abscesses may rupture and lead to general or local peritonitis, which may also result from the primary disease. The infection is generally caused by *B. coli*, streptococci or staphylococci, and very rarely *Bact. typhosum* or *dysenteriæ*.

Symptoms.—The onset is generally sudden, the symptoms due to the

primary disease being complicated by the occurrence of a rigor or pain and tenderness over the liver. The clinical picture is eventually a composite one of the symptoms of the primary disease, sepsis and liver disease, with the frequent addition before death of pneumonia, pulmonary abscesses or empyema, generally on the right side. Evidence of portal obstruction is rarely present. The patient looks anxious and ill. He is sallow and in about half the cases is jaundiced. The jaundice is generally slight, but may be severe from associated cholangitis. Fever is continuous, intermittent or remittent, leucocytosis is present, and the pulse and respiration are rapid. Rigors with profuse sweating are common, especially in the early stages. Uniform enlargement of the liver occurs in about 60 per cent. of cases. Pain and tenderness are generally present, and a rub may be heard over the liver. The spleen is only occasionally enlarged. Vomiting is common and diarrhœa may occur. Blood cultures are generally sterile.

Diagnosis.—The development of a septic state with rigors and enlargement and tenderness of the liver in a patient with appendicitis or other intra-abdominal disease is suggestive of suppurative pylephlebitis, but a correct diagnosis is rarely made. In amœbic abscess of the liver there is generally a history of dysentery, the progress of the disease is less rapid, and there may be signs of a single abscess instead of a uniform enlargement of the liver. A history of gall-stones is much more common in suppurative cholangitis than in pylephlebitis, and jaundice appears earlier and is deeper. The diagnosis from a sub-diaphragmatic abscess secondary to appendicitis may be impossible, and the two may be present together. Acute infective endocarditis with enlargement of the liver and spleen without cardiac murmurs closely simulates suppurative pylephlebitis.

Prognosis and Treatment.—The disease is always fatal, and no treatment is of any avail.

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DISEASES OF THE GALL-BLADDER AND BILE-DUCTS

CHOLECYSTITIS

Ætiology and Pathology.—Cholecystitis results from infection of the gall-bladder, most frequently with *B. coli*, but also with *Bact. typhosum* and *paratyphosus*, streptococci and staphylococci. The mere presence of bacteria in the bile does not necessarily lead to cholecystitis, just as bacilluria may occur without causing pyelitis. The *B. coli*, which normally inhabits the colon and lower part of the ileum, might theoretically gain access to the gall-bladder by four different channels.

(1) Typhoid bacilli pass from the intestines by the lacteals to the mesenteric glands, from which they are conveyed by the lymphatics to the thoracic duct and thence into the general circulation, a typhoid septicæmia being thus produced. The bacilli are excreted from the blood in the bile by the liver and in the urine by the kidneys probably in every case, but cholecystitis and pyelitis develop in only a comparatively small proportion. There is no

doubt that *B. coli* can pass through the healthy bowel wall, but under ordinary conditions it gets no farther than the lymphatic glands, which act as a very efficient filter, and there is no evidence that cholecystitis is ever preceded by a *B. coli* septicæmia. Even in ulcerative colitis, in which the inflamed and ulcerated mucous membrane of the colon might be expected to permit the easy passage of bacteria into the general circulation, neither septicæmia nor cholecystitis occurs.

(2) The portal vein would seem a likely channel for the passage of *B. coli* to the liver and thence in the bile to the gall-bladder without gaining access to the general circulation. But the portal blood is normally sterile and remains so even when the wall of the bowel is damaged, and bacteria injected into the portal vein of animals are not excreted in the bile.

(3) It has been suggested that cholecystitis is the result of infection with strains of streptococci having a special affinity for the gall-bladder, which are conveyed to it by the cystic artery from infected teeth, tonsils and other foci. But infection of the gall-bladder with streptococci is much less common than with *B. coli*, and later investigations have failed to confirm the experiments upon which this theory was based.

(4) Most cases of cholecystitis are probably due to an ascending infection from the duodenum. The duodenum is normally sterile, but in achlorhydria large numbers of *B. coli* and streptococci are often present. Achlorhydria is found in about 30 per cent. of cases of gall-stones. In the acute gastritis which occurs in food poisoning and influenza and other infections achlorhydria is generally present, although it is only likely to persist in association with chronic gastritis in individuals with constitutional hypochlorhydria. But observations after perforation of gastric and duodenal ulcers show that the stomach and duodenum are invaded by organisms ascending from the colon within a few hours of the appearance of the achlorhydria caused by sympathetic inhibition of secretion following the perforation. It is clear, therefore, that the duodenum may be infected during the temporary achlorhydria resulting from acute gastritis, and the infection may last sufficiently long for ascending infection of the gall-bladder to occur. It is in fact not uncommon for patients with chronic cholecystitis to date their symptoms from an attack of food poisoning or an acute infection, which may have been accompanied by achlorhydria, even if the gastric secretion when the patient comes under observation is normal. As acute gastritis is very common and few people pass through life without having one or more attacks, it is easy to understand why cholecystitis is such a common disorder.

Infection of the gall-bladder first leads to inflammation of the mucous membrane, the external appearance of the gall-bladder remaining normal. The inflammation subsequently spreads to the deeper tissues; the walls become thick and inelastic and the cystic lymphatic gland enlarged and inflamed.

Cholecystitis may be acute, subacute or chronic from the onset. Acute and subacute cases may become chronic, and suppuration or gangrene may occur in a chronically inflamed gall-bladder if a stone becomes impacted in the mouth of the cystic duct. The contents may become purulent in the course of an acute infection without gall-stones, but necrosis is very rare in their absence.

Acute Cholecystitis; Empyema of the Gall-Bladder

Ætiology and Pathogenesis. — Acute cholecystitis occurs in about 1 per cent. of cases of typhoid and paratyphoid fever. Apart from this it is rare unless the cystic duct is obstructed by an impacted gall-stone. Bile is generally present in the gall-bladder only if the contents are examined within a few days of the onset. The wall is thickened and obviously inflamed, and the cystic lymphatic gland is enlarged. When the cholecystitis is secondary to an impacted gall-stone suppuration or gangrene is likely to occur. Suppuration leads to empyema of the gall-bladder: if adhesions have previously formed as a result of chronic cholecystitis the empyema may rupture into the duodenum or colon; otherwise localised or generalised peritonitis results. Necrosis may be localised or general. When localised it is generally secondary to ulceration at the neck of the gall-bladder following impaction of a stone; rupture into the duodenum or the production of a local abscess commonly follows. The whole wall of the gall-bladder may become gangrenous as a result of over-distension from obstruction of the cystic duct or less commonly of the common bile-duct, especially in elderly people in whom the blood supply is deficient; unless cholecystectomy is promptly performed, general peritonitis is then certain to develop.

Symptoms.—Acute pain in the right hypochondrium is the most constant symptom. It often radiates to the angle of the right scapula and less frequently to the right shoulder. The gall-bladder may be felt as an extremely tender tumour, but more frequently the rigidity of the right rectus makes deep palpation impossible. Jaundice occurs only if there is a stone in the common bile-duct or the cholecystitis is part of a general infection of the biliary passages. Pyrexia with polymorphonuclear leucocytosis is always present.

The *défense musculaire* often involves the right dome of the diaphragm as well as the right rectus, signs of œdema and congestion of the base of the right lung being present.

In mild cases recovery takes place after a few days, but symptoms of chronic cholecystitis may develop at a later date. In suppurative or gangrenous cholecystitis fatal complications rapidly occur unless an early operation is performed.

Treatment.—Mild cases subside with the physiological rest provide by a lacto-vegetarian diet, the patient being kept warm in bed. In more severe cases, especially if there is a leucocytosis of more than 12,000 cells per c.mm., or if suppuration or gangrene is suspected, an operation should be performed without delay.

Chronic Cholecystitis

Symptoms.—Chronic cholecystitis is a common cause of chronic dyspepsia. The patient complains of intractable indigestion of an irregular character, in striking contrast with the clock-like regularity of the pain in duodenal ulcer. The time of onset and the severity of the pain vary greatly from meal to meal and from day to day; it sometimes begins immediately after food, and at other times it may not come until two or three hours after a meal, or it may only occur in the early part of the night. It is

unaffected or only incompletely relieved by taking food and by alkalis. In most cases the patient complains of what he calls flatulence, but this is really only a sensation of fullness, which is not associated with increased fermentation, and with eructation only when it gives rise to aerophagy by causing the patient to make repeated but futile efforts to belch in the hope of relieving his discomfort.

Nausea is common. It may occur on waking, when it is sometimes associated with vertigo, cold sweats or headaches, in which case migraine may be simulated, though the headache is not unilateral. It may be relieved by breakfast, unless eggs are eaten, when it is often aggravated. It is sometimes followed by vomiting, which gives much less complete relief than in ulcer.

Patients with ulcer generally lose all their pain in two or three days if put to bed on a strict diet, but improvement is less likely to follow in cholecystitis; the dyspepsia may, however, rapidly improve if yolk of egg and other fatty foods are prohibited. Constipation is generally present, but in some cases intermittent or continuous diarrhœa of a mild grade occurs, and in rare instances profuse, watery diarrhœa heralds the onset of an acute exacerbation.

If attacks of biliary colic, whether of the abortive or acute variety, occur in association with symptoms of cholecystitis, gall-stones are probably present.

The discomfort after meals is generally in the mid-epigastrium, but it often extends to the right and may be confined from its onset to the right hypochondrium. It is frequently associated with pain at the angle of the right scapula.

Tenderness of the gall-bladder is the most characteristic sign of cholecystitis. It is best elicited with the patient lying relaxed on his back; the fingers are then pressed beneath the right costal margin in the region of the gall-bladder. The pain is much increased when the fingers are brought into still more intimate contact with the gall-bladder by deep inspiration, which is then sharply arrested.[1] The pain produced in this way is in striking contrast with the absence of tenderness when deep pressure is exerted under the left costal margin or a short distance to the inner or outer side of the gall-bladder under the right costal margin, though it is not uncommon for a slighter degree of tenderness to be observed over the whole of the lower border of the liver, especially in the immediate neighbourhood of the gall-bladder. Pressure on the gall-bladder may also cause nausea.

The upper part of the right rectus abdominis muscle is often tender and rigid; tenderness and rigidity of the lowest intercostal muscles may cause impeded respiration and a stitch in the right side of the chest. Tenderness is also sometimes present over the third to the tenth dorsal spines, the muscles to their immediate right and the end of the eleventh rib.

In chronic cholecystitis there is generally no pyrexia, but occasionally the temperature rises to between 99° and 100° F. each evening or during exacerbations of the inflammation accompanied by more marked symptoms.

The healthy gall-bladder can be visualised with the X-rays by Graham's method (*cholecystography*). The patient is given a fat-free meal at 6 p.m. the evening before the examination, and at 9 p.m. he very slowly drinks a solution of phenoltetraiodophthalein in half a pint of water. During the following hour he sips water, but after that no further food or drink is allowed

[1] This sign was first described by Naunyn in 1892, but is often incorrectly ascribed to Murphy who described it ten years later.

until the first examination is made at the fifteenth hour. If the shadow is weak, another radiograph is taken at the eighteenth or twentieth hour. When a sufficiently clear picture has been obtained, a fatty meal, consisting chiefly of buttered eggs, is taken. If the gall-bladder has not filled at the eighteenth hour, an ordinary meal is given followed in six hours by a fat-free meal and a repetition of the whole procedure. Occasionally at the first examination the shadow of the gall-bladder is partially obscured by gas or undissolved dye in the colon; in such cases a normal saline enema should be given. The opaque dye is absorbed and excreted in the bile, in which it reaches the gall-bladder; as no further meals are taken it remains there, and as a result of absorption of water by the mucous membrane it becomes sufficiently concentrated to throw a shadow of the gall-bladder, which can be seen on the screen, and a cholecystograph can be taken. A normal gall-bladder gives a homogeneous shadow with a regular outline; it is not tender when directly palpated, and it is freely movable, being quite independent of the shadow of the duodenal bulb, which can be seen simultaneously by giving a small opaque meal. The normal gall-bladder is found to have contracted and evacuated the greater part of its contents an hour after the fatty meal. In simple cholecystitis the gall-bladder shadow is normal, but the visualised organ is found to be the seat of the tenderness previously discovered in the supposed position of the gall-bladder. Not infrequently the gall-bladder is found to be in an unusual position, and tenderness, which would not otherwise have been found, can then be elicited. If adhesions have formed, the outline may be deformed, remaining so even when contracted after a fatty meal, and it may be impossible to separate the shadow of the gall-bladder from that of the duodenal bulb. When the mucous membrane is severely damaged the shadow is either feeble or absent, though the latter is rare in the absence of gallstones, and when the muscular wall is involved both filling and emptying may be delayed.

Whenever cholecystitis is suspected, an attempt should be made to obtain some of the contents of the gall-bladder for pathological examination (*Meltzer-Lyon test*). A sterilised Einhorn tube is swallowed up to the 23-inch mark first thing in the morning before the patient has had anything to eat or drink. The stomach is emptied and washed out with sterile water. The tube is then slowly paid out up to the 28½-inch mark, which allows sufficient length for the duodenum to be reached. Samples are aspirated every quarter of an hour until the comparatively abundant, acid, turbid and colourless fluid present in the stomach is replaced by the very small quantity of neutral or alkaline, clear and generally bile-stained fluid present in the duodenum. The pylorus is generally passed in less than half an hour, but if delay occurs the sphincter can be made to relax by the introduction of magnesium sulphate. The duodenum is washed out with sterile water, and 25 c.c. of a 25 per cent. solution of magnesium sulphate are injected through the tube. This causes the gall-bladder and the bile-ducts to contract and the sphincter of the common bile-duct (Oddi's sphincter) to relax. An abundant flow of pure bile, first pale from the common bile duct and then dark from the gall-bladder, rapidly appears; this is aspirated, and the tube is withdrawn. In the absence of disease the gall-bladder bile never contains any pus cells, epithelial cells, pigment granules or cholesterol crystals, but often a little mucus; it is generally sterile, but a few bacteria may be present if the duo-

denum has not been sufficiently washed out, especially in cases of achlorhydria, in which the duodenal contents generally swarm with bacteria. In cholecystitis the quantity of mucus is greater than normal, and degenerated columnar epithelial cells, pigment granules and, less frequently, pus cells are present; the bile contains bacteria, most commonly an aberrant form of *B. coli* in pure culture, and rarely streptococci or staphylococci. In two cases of mine *Bact. typhosum* was isolated 23 and 10 years respectively after typhoid fever. The presence of a yellow liquid lipoid material in the gall-bladder contents suggests the presence of a strawberry gall-bladder. The combination of cholesterol crystals with pigment granules indicates the presence of gall-stones in 100 per cent. of cases. If large cholesterol crystals with the corners broken or rounded are found, gall-stones are almost certainly present, but small and perfect crystals are sometimes precipitated in the bile in the absence of stones.

Treatment.—The majority of early cases of cholecystitis can be cured by medical treatment, and great improvement often occurs in very chronic cases. Hexamine is excreted by the bile; whereas it acts as an antiseptic only in acid urine which sets free formalin from it, the presence of bile salts makes it active in bile in spite of its alkalinity (Knott). As a maximal concentration of the drug is required, alkalis should be given simultaneously in sufficient quantity to make the urine alkaline; by this means the production of formalin in the urine is prevented, and large doses can be given without irritating the bladder. A mixture containing 80 grains each of sodium bicarbonate and sodium citrate in 2 fl. oz. of water is given three times a day, the first dose after breakfast, the second after tea, and the third after a glass of water or milk on going to bed. When the urine, which is tested each time it is passed, has been constantly alkaline for 24 hours, 100 grains of hexamine are added to each dose of medicine. If the urine is not alkaline, the dose of alkali is increased. The patient should continue to take the 300 grains of hexamine a day for about 6 weeks. Hexamine can be given for further periods of 6 weeks if the symptoms recur. An autogenous vaccine prepared from the *B. coli* or other organism isolated from the bile may help to overcome the infection.

Stasis of bile in the gall-bladder aggravates the infection. It is fortunate therefore that thorough drainage can be assured by the oral administration of magnesium sulphate in concentrated solution when fasting an hour before breakfast. The largest quantity should be given which the patient can take without getting diarrhœa when no other aperient is used. This causes the gall-bladder and bile-ducts to empty their contents into the duodenum through the relaxed Oddi's sphincter. Olive oil in 240 minim doses should be taken three times a day half an hour before meals, as it has the same effect as magnesium sulphate on the gall-bladder.

If cholesterol crystals or liquid yellow lipoid material are found in the bile from the gall-bladder, a cholesterol-free diet should be given. No eggs and nothing made from the yolk of eggs should be allowed. Butter must be used sparingly; cream, cheese, kidney, liver, sweetbread, brain, duck, goose, suet and sausages are not allowed, and as little fat of meat as possible should be taken.

If achlorhydria is present, gastric lavage should be practised in the hope that normal secretion will be restored. If this fails, hydrochloric acid should

be given before breakfast and with lunch and dinner, but not during a course of treatment with hexamine, as it makes it difficult to keep the urine alkaline. If hyperchlorhydria is present, belladonna should be given in addition to the olive oil before meals.

If the appendix is diseased, it should be removed, and cholecystectomy should be performed at the same time, even if the external appearance of the gall-bladder is normal, as in many cases of chronic cholecystitis only the mucous membrane is obviously inflamed. Apart from this, the indication for surgery in chronic cholecystitis is the failure of medical treatment after it has been thoroughly carried out for an adequate time. If it is likely that gall-stones are present, it is generally useless to delay operation. In all cases cholecystectomy should be performed in preference to cholecystostomy.

GALL-STONES

Synonym.—Cholelithiasis.

Ætiology.—Clinically gall-stones occur about twice as frequently in women as in men, but they are found *post mortem* about five times more often in women than men. They are very rare before the age of 15; 75 per cent. of clinical cases occur between 30 and 60, 40 to 45 being the most common age. The incidence is greatest *post mortem* about 20 years later. Gall-stones occur in about 25 per cent. of all women and 7 per cent. of all men dying after the age of 25.

Pathology.—(*a*) *Infection.*—Infection of the gall-bladder leads to cholecystitis. The agglutinated bacteria, precipitated mucus and cellular debris may form the nucleus of gall-stones if excess of cholesterol or bile-pigment is present in the bile, especially if the flow from the gall-bladder is less free than it should be. The nature and the path of infection have been discussed in the description of cholecystitis (p. 722). Stones may form very rapidly: 25 faceted cholesterol stones, between $\frac{1}{8}$ and $\frac{1}{4}$ inch in diameter, were removed from a suppurating gall-bladder in a patient of mine 68 days from the onset of an attack of typhoid fever; *B. typhosus* was isolated in pure culture from the pus and from the centre of the stones.

When gall-stones have once formed, the infection frequently dies out, and the bile, stones and wall of the gall-bladder may be sterile, though the latter always shows signs of old inflammation. In other cases the organisms commonly found in cholecystitis are still present.

(*b*) *Excess of Cholesterol in the Blood and Bile.*—The majority of gall-stones contain a considerable proportion of cholesterol. Normal blood contains cholesterol, which comes from endogenous and exogenous sources. The endogenous cholesterol is produced by the constant activity of the cortex of the suprarenal glands, and by the periodic activity of the corpus luteum at each menstrual period. During pregnancy the corpus luteum produces a very large quantity of cholesterol, so that the percentage in the blood gradually increases to nearly double and that in the bile to four times the normal. The exogenous cholesterol comes from certain articles of diet; it is abundantly present in eggs and to a less extent in cream, and in liver, kidney, sweetbread and brain. The importance of hypercholesterolæmia in the pathogenesis of gall-stones has probably been exaggerated. Accurate post-mortem statistics show that the greater incidence of gall-stones in females

is not due to pregnancy, as the proportion of women with gall-stones who have borne children to those who have not is the same as the proportion among those who have no gall-stones. There is, however, no doubt that a biochemical factor must be present to explain the development of the large, solitary, pure cholesterol stones, which are occasionally found in perfectly healthy and sterile gall-bladders. Moreover, many patients with gall-stones have an instinctive distaste for eggs and animal fat of all kinds, which may date from childhood, and they know that such articles of diet are exceedingly likely to promote a "bilious attack." It is probable that some constitutional peculiarity in connection with cholesterol metabolism is an important predisposing cause of gall-stones; this would explain why only a certain proportion of individuals develop stones under apparently similar conditions.

(c) *Biliary Stasis.*—A stone is especially likely to form in the presence of infection and excess of cholesterol in the bile if biliary stasis is also present. In some cases there appears to be a congenital or acquired abnormality of the anatomical relations or of the neuro-muscular mechanism of the bile channels, which impedes the evacuation of the bile (*vide* p. 684). Deficient exercise also leads to biliary stasis.

By examining sections of gall-stones it is generally possible to get some idea of the history of their formation. Thus the centre of most is white and consists of pure cholesterol; only after the stone has reached a certain size is there as a rule any deposit of pigment and lime salts resulting from a period of infection. Then there may be a further layer of cholesterol caused by hypercholesterolæmia, possibly the result of pregnancy; then another stratum of pigment and lime salts may form, and so on. A pure cholesterol stone corresponds to a pure oxalic acid or uric acid stone in the kidney, and the presence of pigment and of lime salts corresponds to that of phosphates in a urinary stone. Pure pigment stones are always the result of infection, except in cases of acholuric jaundice, when they are secondary to excessive production of bile-pigment by hæmolysis.

Symptoms.—Gall-stones may be completely latent. More frequently their development is preceded and accompanied by continuous or intermittent dyspepsia. These "inaugural symptoms" are sometimes referred to as gall-stone dyspepsia: they are really due to cholecystitis (p. 724) and not to the presence of stones. Abortive attacks of biliary colic may occur independently of or associated with gall-bladder dyspepsia. Typical attacks of severe colic are less frequent and are uncommon in the absence of previous symptoms.

Many patients who suffer from gall-bladder dyspepsia and a few who have no such symptoms complain of short attacks of severe pain, which may occur at any time of the day or night without any obvious cause, such as an indiscretion in diet, although occasionally an attack is the direct sequel of a long railway journey, a drive in a motor-car on a bad road, or violent exercise. Attacks may occur daily or at long intervals, or there may be a series close together followed by a long spell of freedom. The patient may shiver during an attack, although his temperature never rises greatly and often does not rise at all. When the pain is acute, it is impossible to take a deep breath, the attempt producing a "catch" in the right side of the chest, which is very similar to that felt in pleurisy.

Attacks of biliary colic most frequently result from impaction of the stone in the neck of the gall-bladder close to or at its junction with the cystic duct. They often occur in the night. The attack begins with extremely sudden acute pain high in the epigastrium or in the region of the gall-bladder or both; it may pass through to the angle of the right scapula. The violent pain is accompanied by great restlessness, in marked contrast with the motionless state of a patient with a perforated ulcer, acute appendicitis or coronary thrombosis. Some relief may be obtained by pressing upon the abdomen. The patient feels cold, but sweats profusely. Slight inspiratory distress is common, but the presence of definite dyspnœa or faintness, when the pain is high in the epigastrium or still more so if it is substernal, should raise the suspicion of coronary thrombosis as an alternative diagnosis. Nausea almost always occurs; the presence of vomiting generally indicates that the stone has passed from the gall-bladder into the cystic or common bile duct. Aerophagy is generally present. The pain commonly disappears with absolute suddenness. The sudden onset and sudden cessation are specially characteristic of gall-stone obstruction in the cystic duct. The temperature may rise a degree or two during the attack, and there may be a slight temporary leucocytosis. Constipation is complete.

Jaundice occurs only when a stone reaches the common bile-duct. Repeated attacks without jaundice are generally caused by a stone of some size becoming impacted in the neck of the gall-bladder. Repeated attacks with jaundice, which may be very evanescent and sometimes completely latent and only recognisable by the temporary presence of a positive direct van den Bergh reaction, indicate the passage of small stones down the cystic and common bile ducts into the duodenum, numerous stones being generally still present in the gall-bladder. The slightest yellow tinge of the conjunctivæ or a trace of bile in the urine is strong evidence that an attack of pain of doubtful origin is due to gall-stones.

If a small stone, having traversed the cystic duct and passed down the common bile-duct to reach the ampulla of Vater, remains there owing to the smallness of the lumen of Oddi's sphincter, a special group of symptoms appears. In two-thirds of the cases one or more stones are still present in the gall-bladder. A stone in the ampulla acts as a ball-valve causing intermittent attacks of colic with incomplete jaundice. Pain is rarely absent; it is occasionally the only symptom. Vomiting is common in the attacks, which are accompanied by fever with chills or severe rigors in 50 per cent. of cases. The jaundice is rarely complete and persistent; it is occasionally absent, but in such cases van den Bergh's test generally gives a positive direct reaction showing that hyperbilirubinæmia is present; in rare cases it is unaccompanied by pain. In the intervals between attacks the patient may appear to be quite well, though a slight degree of jaundice or some residual pain in the gall-bladder region may be present. Sooner or later ascending cholangitis is likely to develop; there is then constant pyrexia with repeated rigors and polymorphonuclear leucocytosis.

Small gall-stones are rarely recognised in the stools and larger ones are very rarely passed. It is important to distinguish gall-stones from concretions produced by drugs or by the administration of large quantities of olive oil. The majority of gall-stones consist of cholesterol and can, therefore, be recognised by being very light and inflammable. The rarest form of stone to

be passed is a very small rounded one, which has probably traversed the normal passages during an attack of colic; as it may be the only one, a cure may result. More frequently faceted stones are passed; even if large numbers are found, it is very unlikely that all have left the gall-bladder. Lastly one, or less frequently two or three large stones, which may be formed by the agglomeration of several smaller ones, may be passed after traversing a fistulous communication between the gall-bladder and duodenum or colon. The fistula may develop very slowly without symptoms after chronic cholecystitis has led to the production of adhesions. More frequently the perforation appears to be sudden and takes place during or after an attack of colic. In other cases the fistula may be caused by the perforation of an empyema of the gall-bladder into the bowel. In rare cases a large stone may cause acute intestinal obstruction, generally near the end of the ileum. Occasionally the pain in the neighbourhood of the umbilicus or the right iliac fossa disappears spontaneously as the stone passes onwards; pain may be subsequently felt below the umbilicus and finally in the rectum, from which it may have to be dislodged by the finger. The complete passage may take from 1 to 8 days.

It is generally impossible to palpate the gall-bladder during an attack of acute pain owing to the rigidity of the abdominal muscles, but when the attack passes off the tenderness generally becomes localised to the gall-bladder itself. In some early cases the gall-bladder is found to be enlarged owing to distension with clear fluid, especially if the stone is impacted in the cystic duct. It gradually contracts on the stone or stones within it, probably after temporary dilatation, so that in long-standing cases it is rarely palpable. Even if a gall-stone passes into the common bile-duct, the gall-bladder does not often become enlarged; thus a large gall-bladder in a case of chronic jaundice generally indicates chronic pancreatitis or a growth of the head of the pancreas or of the common bile-duct.

Pure cholesterol gall-stones are never visible with the X-rays, but when much lime salts are present, especially in thin patients, they often throw a characteristic "ring" shadow. The shadow must be distinguised from that produced by a renal calculus, a calcified tuberculous focus in a kidney, a calcified tuberculous gland or a calcareous deposit in a costal cartilage. This can now be easily done by means of cholecystography. This method also makes it possible to photograph transparent stones, as they are often seen as pale areas surrounded by the dark shadow formed by the dye filling the rest of the gall-bladder. Failure to produce a cholecystograph on two successive occasions, especially in the presence of a good shadow of the liver, which proves that the dye has been absorbed from the intestines, indicates that the cystic duct is obstructed, probably by an impacted stone, that the lumen of the gall-bladder is entirely occupied by stones, or that its mucous membrane is so damaged that it is incapable of absorbing water and so producing the concentration of the bile necessary for the production of a shadow.

In doubtful cases valuable information can often be obtained by the Meltzer-Lyon method (p. 726). Failure to obtain dark bile on injecting magnesium sulphate into the duodenum would confirm a diagnosis of gall-stones suggested by absence of a gall-bladder shadow after cholecystography. The presence of large, broken cholesterol crystals with or without pigment granules is conclusive evidence of gall-stones, and other abnormal constituents may point to the presence of cholecystitis (p. 726).

Complications.—Cholecystitis is always present before gall-stones develop, except with the rare solitary sterile cholesterol stone. If the mouth of the cystic duct becomes obstructed suppuration or gangrenous cholecystitis may develop (p. 723). In some cases inflammation may spread up the hepatic ducts or down the common bile-duct; in the latter case the pancreatic ducts may become infected and chronic pancreatitis develops. In rare cases glycosuria or actual diabetes follows. Cancer of the gall-bladder or bile-ducts occurs in about 4 per cent. of people over 40 with multiple-faceted gall-stones compared with 0·4 per cent. of those with no gall-stones and with solitary cholesterol stones. The former are secondary to chronic cholecystitis, the latter to some metabolic disorder: the carcinoma is, therefore, presumably a result of the chronic cholecystitis, together perhaps with a direct chemical or mechanical carcinogenic action of the stones on the inflamed mucous membrane.

Treatment.—During an attack of biliary colic the pain should be controlled by the injection of morphine (gr. $\frac{1}{4}$) with atropine (gr. $\frac{1}{150}$). Slight attacks may be relieved by a tablet of glyceryl trinitrate (gr. $\frac{1}{100}$) placed under the tongue.

The early recognition and thorough treatment of cholecystitis can be regarded as a true method of prophylaxis of gall-stones.

Treatment of cholecystitis may also result in the solution or washing away of cholesterol deposited on the walls of the gall-bladder and of minute agglomerations of crystals—the basis of what might later become gall-stones. Moreover, even when definite stones are present it may cause the accompanying indigestion, the so-called gall-bladder dyspepsia, which is really due to the cholecystitis, to disappear. However, if the symptoms point definitely to the presence of gall-stones, and especially if repeated attacks of severe biliary colic have occurred, an operation should be advised, unless on account of obesity or renal or cardiac complications the patient is a bad subject for operation. Myocardial disease is not, however, a contra-indication, as the cardiac condition frequently improves after cholecystectomy, and patients with impaired hearts often stand the operation remarkably well. Fat patients should be strictly dieted for 2 or 3 months in order to bring their weight down before operation. Except in urgent cases a short preliminary course of treatment with hexamine (p. 727) is always advisable before operating, and the liability to complications or the recurrence of symptoms is greatly reduced by the regular use of magnesium sulphate to prevent stagnation of bile after the operation. Whenever feasible cholecystectomy should be performed in preference to cholecystostomy, and the common bile duct should always be explored for stones even if there has never been any jaundice.

BILIARY COLIC WITHOUT GALL-STONES

It occasionally happens, especially in otherwise healthy young adults of both sexes, that typical attacks of slight or severe biliary colic, generally unaccompanied by jaundice, occur in the absence of gall-stones. During an attack and for a short time afterwards the gall-bladder is tender. The bile obtained through a duodenal tube from the gall-bladder is normal in every

way. Cholecystography occasionally reveals some abnormality in the cystic duct in the form of acute angulation with or without dilatation of the proximal segment, and pressure upon the visualised gall-bladder, especially in a direction from its vertex towards its neck, causes pain; the gall-bladder is sometimes unusually large.

On abdominal exploration the gall-bladder looks healthy, but it may be tightly distended. Examination may show some abnormality in the anatomy of the cystic duct, or an accessory cystic artery may be present, which results in kinking when the gall-bladder is in certain positions. The condition is analogous to Dietl's renal crises. Cholecystectomy is generally followed by permanent cure, though neither macroscopical nor microscopical examination shows any abnormality in its walls or contents.

When no anatomical abnormality is discovered, the condition is probably identical with that which gives rise to attacks of biliary colic after cholecystectomy for gall-stones or cholecystitis, and which leads to the assumption that a stone has been left in the common bile-duct, though at operation no stone or other cause of organic obstruction is discovered. The attacks are, I believe, caused by a disturbance of the neuro-muscular mechanism of the biliary ducts and the sphincter of the common bile-duct—achalasia of Oddi's sphincter. When the gall-bladder has been removed, the common bile-duct often dilates to form a reservoir, which to some extent takes its place; this must be due to the resistance offered by the unrelaxed Oddi's sphincter to the flow of bile, corresponding with the dilatation of the œsophagus following achalasia of the cardia. It may take a long time for the neuro-muscular mechanism of the common duct and its sphincter to adapt itself to the conditions present after cholecystectomy, and during this period attacks of pain may result from temporary obstruction by the closed sphincter when the dilated common duct is attempting to empty itself.

Diagnosis. –This condition can be diagnosed when typical attacks of biliary colic are associated with definite tenderness of the gall-bladder, cholecystography shows that no stone is present, and the bile obtained from the gall-bladder is normal. Between attacks the tenderness over the gall-bladder gradually disappears, whereas in cholecystitis it rarely goes completely. When several attacks of colic occur after cholecystectomy has been performed and the common bile duct explored for gall-stones by a competent surgeon, crises of this kind are the most probable cause.

Treatment.—Regular contraction of the gall-bladder and ducts and relaxation of Oddi's sphincter can be promoted by giving Epsom salts with belladonna when fasting in the morning and olive oil half an hour before meals. Before resorting to morphia, an attempt to relieve attacks with one or two glyceryl trinitrate tablets (gr. $\frac{1}{100}$) placed under the tongue, failing this, the injection of a large dose (*e.g.* gr. $\frac{1}{50}$) of atropine should be tried. If attacks persist the gall-bladder should be removed if this has not already been done, the bile ducts explored, and Oddi's sphincter dilated.

CARCINOMA OF THE GALL-BLADDER

Carcinoma of the gall-bladder is a rare disease, which constituted only 0·5 per cent. of the gall-bladders removed at the Mayo Clinic. It is 3 times

more common among women than men, and few cases occur before the age of 50. Calculi are present in about 75 per cent. of cases (p. 732).

Symptoms.—In 70 per cent. of cases there is a long history of repeated gall-bladder attacks. This is followed by a short phase of constant pain, accompanied by progressive weakness, anorexia and loss of weight, but no anæmia. The pain is situated in the right hypochondrium and often radiates to the right scapular region. Flatulence, nausea and vomiting are common. A tumour can generally be felt; it may at first be smooth, but later becomes hard and irregular. It is generally not very tender, and there is less muscular rigidity over it than is commonly the case with an inflamed gall-bladder.

After a time secondary deposits lead to symptoms, and in some cases these are most prominent throughout, the primary disease remaining latent. Thus the liver is often large, hard and irregular from the presence of secondary deposits. Jaundice often occurs as a result of extension to the bile-ducts or compression by enlarged glands; it is occasionally remittent or intermittent, when it is generally due to cholangitis or a gall-stone in the common bile-duct.

Ascites is present in about a quarter of the cases as a result of malignant peritonitis or pressure of glands on the portal vein. Septic complications, such as suppurative cholecystitis or cholangitis, or local or general peritonitis, may occur. Death generally supervenes within six months of the development of definite symptoms apart from those due to the preceding cholecystitis or gall-stones.

Diagnosis.—The diagnosis is often exceedingly difficult, but the presence of a hard irregular tumour in the region of the gall-bladder with pain, anorexia and loss of weight in a middle-aged or elderly individual, especially if he has had symptoms pointing to cholecystitis or gall-stones, is suggestive of a growth of the gall-bladder.

Treatment.—It is rarely possible to remove a growth of the gall-bladder owing to the difficulty in making an early diagnosis. The operative mortality is high, and a very large proportion of cases recur within six months. The presence of early carcinoma is occasionally discovered on microscopical examination of a gall-bladder removed on account of chronic cholecystitis with or without gall-stones; permanent recovery may then follow.

CONGENITAL OBLITERATION OF THE BILE-DUCTS

Ætiology.—This rare disease occurs rather more frequently in male than female infants. It is occasionally familial and is not associated with congenital syphilis.

Pathology.—Some unknown toxin probably passes from the mother by the umbilical vein to the fœtus. Part of the toxin reaches the liver direct and causes multilobular cirrhosis. The rest passes into the general circulation and reaches the liver by the hepatic artery; it is excreted in the bile and gives rise to unilobular cirrhosis and inflammation of the small and large ducts and gall-bladder, which, being extremely small at birth, become more or less completely obliterated. The disease is thus a combination of portal and biliary cirrhosis with obstruction of the ducts.

Symptoms.—Jaundice is generally present at birth, but may not appear for two or more weeks. The meconium is normal, but the stools are free from bile from the first, and the urine is deeply bile-stained. The liver and spleen are large and hard. The infant is often remarkably well till the terminal stage, when purpura and hæmorrhages from the mucous membranes and umbilicus are common and convulsions may occur.

Diagnosis.—Deep jaundice in a new-born infant with a large liver and spleen and hæmorrhages without any early evidence of infection is generally due to this disease.

Prognosis.—Life may last from a few days to as much as 11 months.

Treatment.—No treatment is of any value.

CARCINOMA OF THE BILE-DUCTS

Ætiology.—The incidence of carcinoma of the bile-ducts is about half that of carcinoma of the gall-bladder. It is associated with gall-stones in about 50 per cent. of cases.

Pathology.—The growth arises most frequently in the ampulla of Vater, where a papillomatous projection into the duodenum develops. The common hepatic duct and the common duct are next most affected; a growth of either of the two hepatic ducts is very rare. Primary growths of the cystic duct can rarely be recognised, as at the time of death they are likely to have spread either to the gall-bladder or to the junction with the hepatic duct.

Symptoms.—The first symptom is generally jaundice, which develops gradually and is often intermittent; though the fæces are clay-coloured, they generally contain a little stercobilin. Apart from loss of weight and strength the symptoms are those of obstructive jaundice, but pain may be felt in the epigastrium or right hypochondrium, and attacks of colic may occur. In a case of mine the symptoms simulated those of duodenal ulcer and there was no jaundice, as ulceration of the growth had destroyed Oddi's sphincter. The condition was recognised with the X-rays by the presence of a filling defect on the inner aspect of the descending part of the duodenum associated with a diverticulum representing the ampulla of Vater. Occult blood is always present in the stools, and the patient may become extremely anæmic. The gall-bladder and less frequently the liver is enlarged. The primary tumour is never palpable. Ascites may occur as a result of secondary malignant peritonitis or of pressure of glands on the portal vein. The course of the disease is sometimes remarkably slow; in one case of mine the patient lived for over two years after the first attack of jaundice.

The diagnosis from carcinoma of the pancreas, chronic pancreatitis and a stone in the common bile-duct is discussed on p. 741.

Treatment.—Life may be rendered more bearable as well as being considerably prolonged by cholecystenterostomy if the obstruction is in the common bile-duct. Owing to the almost insuperable technical difficulties of the operation it is very rarely possible to excise a growth of the ampulla of Vater.

ARTHUR F. HURST.

DISEASES OF THE PANCREAS

THE INVESTIGATION OF DISEASES OF THE PANCREAS

The pancreas produces an external secretion—pancreatic juice, and an internal secretion—insulin. The two functions are entirely independent, and in the diseases affecting the former, which are alone considered in this section, glycosuria due to deficient insulin is rarely present and never severe.

The pancreatic juice reaches the duodenum by the large duct of Wirsung and the small duct of Santorini. The duct of Wirsung runs by the side of the common bile-duct for a short distance and then joins it to form the ampulla of Vater, a small cavity in the wall of the descending part of the duodenum, which opens in the biliary papilla, the end of the duct being kept closed by the tonic action of Oddi's sphincter. The duct of Santorini discharges through a small papilla a short distance nearer the pylorus, but in 30 per cent. of normal individuals it is not patent or is too small to perform the functions of the duct of Wirsung if the latter is obstructed. The common bile-duct is completely surrounded by the head of the pancreas in 62 per cent. of bodies; in the remainder it lies in a more or less deep groove in the gland. It is clear from these anatomical facts that deficient pancreatic digestion may occur owing to failure of the pancreatic juice to reach the intestine either as a result of diffuse disease of the pancreas, which inhibits the activity or actually destroys the secreting cells, or as a result of obstruction caused by a gall-stone in, or a growth of, the ampulla of Vater occuring in one of the 30 per cent. of people with an incompetent duct of Santorini. The effect on digestion will obviously be the same in each case. It is further clear that in 62 per cent. of cases of chronic inflammation or cancer of the head of the pancreas jaundice will result; but, if the duct of Santorini is incompetent, jaundice accompanied by deficient pancreatic digestion may be equally well due to obstruction of the ampulla of Vater without disease of the pancreas.

The stools in deficient pancreatic digestion.—The stools are bulky and pale owing to excess of fat, the proportion of which in the dried fæces may be increased to 60 to 80 per cent. from the normal of 15 to 25 per cent. The pallor is still more marked in the presence of jaundice, as stercobilin is then absent or reduced in quantity. The fat is present chiefly in its neutral form, whereas normally only about 10 per cent. is unsplit; in rare cases it separates as oil, which solidifies on cooling. Microscopically oil droplets are seen, together with crystals of fatty acids and soaps, which are formed by bacterial decomposition of the undigested fat, but the proportion of neutral fat to fatty acids and soaps remains high, in contrast with the excess of the latter and small proportion of the former in the fatty diarrhœa caused by deficient absorption (p. 626). Fragments of undigested meat can sometimes be recognised with the naked eye, especially if the presence of excess of fat is prevented by giving a fat-free diet; striated muscle fibres are always recognisable with the microscope, but there is often no excess of undigested starch. In severe diarrhœa associated with rapid passage through the small intestines the stools may contain some excess of undigested fat, meat and starch in the absence of pancreatic disease.

The irritating products of bacterial decomposition of undigested fat and meat may give rise to diarrhœa; in such cases excess of mucus is often present.

Pancreatic ferments in the duodenal contents, fæces and urine.—The duodenum normally contains trypsinogen, which is converted into active trypsin by the enterokinase of the intestinal juice amylopsin (diastase) and steapsin (lipase). Under the conditions already described, in which no pancreatic juice reaches the intestine, the ferments cannot be isolated from the duodenal contents obtained through an Einhorn tube; but it is impossible to recognise with certainty a simple reduction in the quantity present, owing to the great variations which normally occur and the technical difficulties in the quantitative estimation of the ferments. The same is true with regard to their presence in the stools, but a rough estimate of the quantity of pancreatic juice secreted can be made by measuring the tryptic activity of the fæces. On the other hand, the quantity of diastase present in the urine is fairly constant and not difficult to estimate. In destructive disease of the pancreas it is not reduced, as the ferment is apparently formed in the liver and simply excreted by the pancreatic juice. Consequently in acute pancreatic necrosis the diastase index is increased from the normal of between 6 and 30 units to 200 or more, and in many cases of subacute necrosis and of growth of the head of the pancreas, especially during exacerbations which manifest themselves by increase in pain, it is increased to a less extent, a unit being the number of cubic centimetres of 0·1 per cent. starch solution digested by 1 c.c. of urine. The index is low in renal disease owing to deficiency in the excreting power of the kidney.

Carbohydrate metabolism.—Although the secretion of insulin is rarely much affected in the disease of the pancreas considered in this section, a rise in the blood sugar with or without slight glycosuria is sometimes observed, and the glucose tolerance test may show some deficiency in carbohydrate metabolism. In doubtful cases this is a strong point in favour of pancreatic disease.

In very rare cases an adenoma or carcinoma develops from the cells of the islands of Langerhans and gives rise to hyperinsulinism with symptoms of hypoglycæmia, indistinguishable from those produced by an overdose of insulin.

ACUTE NECROSIS OF THE PANCREAS

Synonym.—Acute Hæmorrhagic Pancreatitis.

Ætiology.—The pressure under which bile is secreted is about 30 mm. to 100 mm. higher than the maximal pressure attained in Wirsung's duct after a meal, when pancreatic secretion is most active. Bile is not, however, forced into the pancreas, as the normal tone of Oddi's sphincter is overcome by a pressure of only 100 mm. But when the mouth of the common bile-duct is obstructed, the bile is forced into Wirsung's duct. The bile salts activate the pancreatic zymogens: the trypsin causes necrosis with secondary hæmorrhage of the pancreas, and the steapsin causes fat necrosis. If the bile is infected, but not otherwise, suppuration of the pancreas occurs simultaneously.

The obstruction is caused by a gall-stone in 50 per cent. of cases, and in

very rare instances by a pancreatic calculus or a round worm. When the lumen is free, the obstruction is probably caused by spasm of Oddi's sphincter secondary to acute gastro-duodenitis, which may be caused by acute corrosive poisoning. Necrosis of the pancreas may also follow a direct injury to the pancreas producing hæmorrhage.

Very rarely infection reaches the pancreas by way of the blood stream in pyæmia and infective endocarditis, and abscesses may result from retrograde thrombosis in suppurative pylephlebitis. Acute pancreatitis has been observed in influenza, typhoid fever and small-pox. It is a rare complication of mumps, but suppuration and necrosis never occur (*vide* p. 165).

Pathology.—Necrosis, hæmorrhages and suppuration are present in varying proportions in the pancreas. Opaque white areas of fat necrosis are found in the fat of the pancreas, the retroperitoneal tissue, omentum and mesentery, and also occasionally in that of more distant parts, such as the pericardium, to which the pancreatic lipase has been conveyed by lymphatics. Bacteria, especially *B. coli* and streptococci, can generally be isolated from the pancreas and often from the gall-bladder. The peritoneal cavity often contains bloodstained fluid, especially in the lesser sac; in the later stages this fluid is infected and suppurative peritonitis may be present.

Symptoms.—Without any warning a sudden very violent pain is felt in the epigastrium. It continues without intermission, but paroxysms of still more severe pain occur from time to time. Severe pain across the back is often present. After a short time vomiting begins and is repeated at frequent intervals; the gastric contents are first ejected, and after a time the vomit contains bile. Flatus may be passed, but the bowels are not opened, and no sounds indicating gastro-intestinal activity can be heard on auscultation. The abdomen soon becomes distended; it is very tender on palpation, but the muscles are often not correspondingly rigid. The tenderness and rigidity begin in the epigastrium, but before long become general. In rare cases the enlarged pancreas can be felt, but the rigidity of the abdomen generally makes this impossible. Slight jaundice is occasionally present as a result of pressure of the swollen pancreas on the common bile-duct. The patient soon becomes collapsed with a weak and rapid pulse and slight cyanosis; he appears more severely ill in the first few hours than is generally the case in acute peritonitis. The temperature is not greatly raised and may be subnormal, and leucocytosis is generally absent. Dyspnœa is occasionally observed. Glycosuria is rare, probably because death occurs too rapidly, as the diabetes produced in animals by the removal of the pancreas often does not develop until some days have elapsed. The diastase index of the urine is always raised above 100 and generally above 200.

Diagnosis.—The possibility of acute pancreatic necrosis should be considered in all cases of acute symptoms in the upper part of the abdomen in adults, especially if the patient is an elderly obese, alcoholic individual, who has previously suffered from symptoms which might have been due to gall-stones or gastro-duodenal catarrh. A carefully taken history may reveal the fact that the patient has previously had one or more similar, but much slighter attacks, probably due to acute but localised necrosis from which complete recovery took place. The symptoms may closely resemble those following perforation of a gastric or duodenal ulcer, but in the latter there is generally a history pointing to the presence of an ulcer before the onset of

acute symptoms; vomiting is continuous in pancreatitis, but occurs only at the onset or not at all in perforation, and the hepatic dullness does not alter in pancreatitis, but often disappears owing to the escape of gas through a perforated ulcer; and the abdominal muscles are generally less rigid in pancreatitis than in perforation. In other cases acute intestinal obstruction is simulated, but flatus generally continues to be passed, the abdomen is less distended, and intestinal sounds disappear at once instead of being unusually loud at first. A rise in the diastase index to 100 or more is conclusive evidence in favour of acute pancreatitis. At the operation the discovery of fat necrosis at once makes the diagnosis clear.

Prognosis.—The most acute cases are always rapidly fatal unless an operation is performed. Some cases run a subacute course, especially if one or more localised abscesses form; the illness may then continue for a week or lead to chronic pancreatitis.

Treatment.—An operation should at once be performed in all cases of acute pancreatic necrosis, except in those complicating mumps, the pancreas being drained at the site of greatest damage. If gall-stones or cholecystitis are present the gall-bladder should also be drained. The earlier the operation is performed, the greater is the prospect of recovery, but permanent deficiency of pancreatic secretion may follow.

SUBACUTE NECROSIS OF THE PANCREAS

Pathology and Symptoms.—Necrosis may occur in very small areas of the pancreas as well as in the generalised form just described. This condition is most frequently associated with gall-stones and with penetrating gastric or duodenal ulcer. It gives rise to recurrent attacks of mid- or left-sided epigastric pain, which tends to radiate round the left costal margin or to bore through to the muscles immediately to the left of the lower dorsal spine, when it may simulate renal colic. It may spread upwards to the left shoulder and downwards to the left iliac fossa and even to the left thigh and leg. The attacks generally occur two or three hours after food, when the functional activity of the pancreas is at its height. The pain may be associated with deep tenderness, but there is little or no rigidity, and the abdomen is often much distended. The patient may be perfectly well in the intervals between attacks. As in acute pancreatic necrosis, the attacks are often associated with cyanosis and a weak, though not specially rapid, pulse.

The stools are generally normal, and there is no constant glycosuria, but there may be temporary hyperglycæmia and glycosuria during the attacks.

Diagnosis.—Attacks of left-sided pain occurring in cholelithiasis and after cholecystectomy are generally caused by subacute pancreatic necrosis, which may also account for pain boring through to the back in gastric and duodenal ulcer, though I have seen very severe pain of this kind in which the ulcer was found at operation to be free from adhesions and the pancreas healthy. The sudden violent abdominal pain, with tenderness, rigidity and leucocytosis, which may occur in an attack of diabetic coma, is probably of similar origin.

Treatment.—The recurrence of attacks may be prevented if a diet is given which affords as complete rest as possible to the pancreas. The patient should be starved for 3 days and then given carbohydrates alone for 3 days. After that a more liberal diet is allowed, but fats and meat should be given very sparingly in spite of the fact that the stools show no evidence of pancreatic insufficiency.

In severe attacks the question of operation requires consideration: gall-stones, if present, should be removed and the gall-bladder drained but not excised.

CHRONIC PANCREATITIS

Ætiology and Pathology.—Chronic pancreatitis is generally due to infection spreading up Wirsung's duct. This is most likely to occur if the pancreatic secretion stagnates owing to obstruction of the duct, especially in an individual in whom the duct of Santorini is insufficiently developed to drain the gland. A small gall-stone impacted in the ampulla of Vater obstructs the mouth of Wirsung's duct and generally leads to chronic pancreatitis; if impacted in the terminal part of the common bile-duct, this complication may also occur, especially in an individual in whom the duct is completely surrounded by the head of the pancreas.

In rare cases the duct is obstructed by a pancreatic calculus, but this is probably itself a result of catarrh of the pancreatic ducts. Cancer of the head of the pancreas, and obstruction of the mouth of the common bile-duct by cancer of the ampulla of Vater or of the duodenum, are generally complicated by chronic pancreatitis, as the flow of pancreatic juice is obstructed.

When no obvious obstruction is found to account for chronic pancreatitis, the disease may be due to a gall-stone which has been passed, but the infection can also ascend from the duodenum, or descend from the upper biliary passages, as non-calculous cholecystitis is sometimes present. The cases which occur in alcoholic individuals are probably secondary to gastro-duodenal catarrh, and a typhoidal infection of the bile passages probably accounts for the occurrence of chronic pancreatitis as a sequel of typhoid fever. When a chronic gastric or duodenal ulcer erodes the pancreas, the neighbouring part of the gland becomes chronically inflamed.

In chronic pancreatitis the inflammation and the fibrosis to which it gives rise are mainly interlobular, coarse bands of connective tissue, often visible to the naked eye, separating the lobules of the gland from each other. The head of the pancreas is generally most affected; it is hard and somewhat enlarged.

Symptoms.—In chronic pancreatitis the normal functions of the pancreas must be more or less disturbed, but in the majority of cases it is entirely latent, as it is rare for the inflammation to be sufficiently severe and widespread to interfere seriously with pancreatic digestion. It is generally found accidentally during an operation for gall-stones, or at autopsy if the primary disease proves fatal. In an individual in whom the pancreas completely surrounds the common bile-duct jaundice is likely to develop. It is generally the only symptom, and chronic painless obstructive jaundice, developing insidiously without any of the initial symptoms characteristic

of catarrhal jaundice, is more often due to chronic pancreatitis than to carcinoma. The gall-bladder is dilated unless chronic cholecystitis has made relaxation of the walls impossible, but it is generally difficult to recognise by palpation, and the liver is often enlarged and abnormally hard, but not tender. In the rare cases in which pancreatic indigestion is present, the stools contain excess of fat and undigested meat (p. 623) and diarrhœa may result; the deficient digestion causes very gradual emaciation with increasing weakness. In exceptional cases diarrhœa is severe, emaciation is rapid and extreme, and there is complete anorexia.

Diabetes rarely results from chronic pancreatitis, but it may occur in very chronic cases if the inflammation spreads into the lobules and invades the islands of Langerhans.

Though chronic pancreatitis itself does not give rise to pain, severe attacks of colic are occasionally observed as a result of attacks of subacute necrosis even in the absence of gall-stones. The pain tends to radiate along the left costal margin, and to bore through to the muscles immediately to the left of the lower dorsal spine and to the angle of the scapula. Left-sided pain of this kind in gall-bladder disease should suggest the possibility that the pancreas is involved, and in chronic gastric and duodenal ulcer that penetration into the pancreas has occurred.

Diagnosis.—It is rarely possible to determine with certainty whether chronic pancreatitis is present as a complication of gall-stones or of the other conditions with which it may be associated. If hyperglycæmia with or without glycosuria develops in such a case, it is extremely probable that the pancreas is becoming affected. The changes in the fæces, which result from the absence of pancreatic digestion, do not prove that the pancreas is affected in a case of chronic jaundice, as in individuals in whom the duct of Santorini does not function obstruction of the ampulla of Vater may prevent the pancreatic juice as well as the bile from reaching the duodenum, although the pancreas is healthy.

The possibility of chronic pancreatitis should be considered in all cases of chronic jaundice in which the cause is doubtful. If the jaundice is preceded by symptoms of acute febrile gastro-duodenitis, catarrhal jaundice is the most likely diagnosis. Attacks of pain, even in the absence of a characteristic history, make the presence of gall-stones probable. In the absence of such attacks, especially if the gall-bladder be enlarged, either chronic pancreatitis or a growth is probably present. A growth is much more commonly associated with chronic pain, and emaciation and weakness develop more rapidly than with chronic pancreatitis. It is often impossible, however, even at an operation, to distinguish between a growth of the head of the pancreas and chronic pancreatitis; only when a patient recovers completely and permanently is it possible to be certain that the condition was inflammatory.

Prognosis.—The prognosis depends upon that of the primary condition in secondary cases, and the presence of chronic pancreatitis does not alter the outlook in operations for gall-stones. In cases of apparently primary pancreatitis complete recovery has taken place after an exploratory operation in which nothing was done. Chronic pancreatitis causes death only in the presence of complications. In one case death followed peritonitis secondary to rupture of the distended gall-bladder the day before an operation was to

be performed. In another the patient, who had suffered from painless jaundice for six months, refused operation, and death resulted from gastro-intestinal hæmorrhage, the exact source of which could not be found at the autopsy; it was apparently secondary to subacute necrosis of the liver, which had resulted from the long-continued biliary stasis.

Treatment.—It is only necessary to consider the treatment of those cases which appear to be primary, as when the pancreatitis is secondary no treatment beyond what is necessary for the primary disease is required. If the jaundice does not abate within three months, or a shorter period if the patient rapidly loses weight and strength or the lævulose test shows that the functional efficiency of the liver is becoming impaired, an operation should be performed. A cholecystenterostomy will cure the jaundice, remove one source of irritation of the pancreas by draining the infected bile, and prevent the development of secondary inflammation and necrosis in the liver.

SYPHILIS OF THE PANCREAS

The pancreas is affected in 20 per cent. of cases of congenital syphilis in the newborn; in most cases the liver is simultaneously affected, and somewhat less frequently the spleen, bones, lungs and other organs. The gland is enlarged and hard owing to proliferation of the interlobular connective tissue; the gland-cells atrophy, but the islands of Langerhans escape.

Syphilis in adults occasionally gives rise to chronic pancreatitis, and much less frequently to gummata of the pancreas.

Symptoms.—The symptoms are those of chronic pancreatitis or carcinoma of the pancreas. The tumour may be palpable, and it may lead to obstruction at the pylorus or duodeno-jejunal flexure with persistent vomiting. The occurrence of diabetes in a syphilitic patient should suggest that the pancreas may be affected. The Wassermann reaction should always be tested in cases of suspected chronic pancreatitis and carcinoma of the pancreas, whether the diagnosis is made clinically or at an operation, and in diabetes, and anti-syphilitic treatment instituted if it is positive.

PANCREATIC CALCULI

Pathology.—Between five and ten calculi are generally found, but in rare cases one only or as many as 300 may be present. They are white, yellow or brown, and vary in size from mere sand to smooth or irregularly shaped masses, an inch or more in length. Although pancreatic juice contains no calcium carbonate, this is the chief constituent of the calculi, which consequently throw much more definite shadows than gall-stones with the X-rays. Calculi never form in a healthy pancreas; they result from infection of the ducts and stagnation of the secretion. The ducts behind the calculi are dilated, and chronic pancreatitis is present, but suppuration is very rare. The condition may be associated with gall-stones.

Symptoms and Treatment.—Pancreatic calculi are very rare. I have seen two cases, which correspond with the two clinical types recorded in the literature, both of which may be associated with diabetes. (1) A woman

of 55 had had fatty diarrhœa for five years and her weight had fallen from 10 to 7 stone. Excess of neutral fat and striated muscle fibres were present in her stools. She had recently had an aching pain under both costal margins, especially the left. The X-rays showed multiple opacities in the region of the pancreas. She was given a fat-free diet and large doses of hydrochloric acid, as the pancreatic disorder was associated with achlorhydria. She gradually improved during the following year, and for the last ten years has been completely free from symptoms. Presumably the hydrochloric acid led to the formation of secretin, which stimulated the secretion of pancreatic juice sufficient to break down and dislodge the very friable calculi. (2) A man of 31 had attacks of severe pain in the right hypochondrium exactly simulating biliary colic; they had begun ten years earlier and recently two or more occurred daily. Nothing short of morphine gave relief. There was no jaundice. The X-rays showed a normal gall-bladder but shadows of pancreatic calculi. There was no diarrhœa, but the stools contained excess of neutral fat and striated muscle fibres and very little trypsin. At operation the pancreas was very large and hard. As the stones could not be found, an attempt was made to crush them by squeezing the pancreas. After temporary improvement the attacks recurred, severe diabetes developed, and the patient died within a year from acute pulmonary tuberculosis.

PANCREATIC CYSTS

Ætiology and Pathology.—Simple obstruction of the pancreatic duct leads to atrophy of the secreting tubules and not to the formation of cysts. When chronic pancreatitis is also present retention cysts may develop.

Hydatid cysts may develop in the pancreas, and congenital cystic disease, generally associated with cystic disease of the kidneys, may occur.

A single large pancreatic cyst may contain as much as 14 pints of fluid. Multiple cysts of various sizes, often quite small, may occur. The contents are generally turbid and dark reddish-brown or yellow. The fluid is alkaline, slightly viscid and albuminous, and may contain altered blood; microscopically degenerated epithelial cells, leucocytes, and occasionally crystals of cholesterol and rarely of leucin and tyrosin are found. The pancreatic ferments are often absent, especially in old cysts.

A large proportion of so-called pancreatic cysts are really pseudo-pancreatic cysts, being collections of fluid in the lesser sac of the peritoneum, the foramen of Winslow having been occluded by peritonitis. About a quarter of these cases follow an injury to the pancreas, which causes the escape of blood and pancreatic juice into the lesser sac with secondary peritonitis. In the remaining cases serous fluid collects slowly as a result of local peritonitis secondary to pancreatitis, the condition being analogous to a pleural effusion following pneumonia.

Symptoms.—There are often no symptoms when the tumour is accidentally discovered. In other cases symptoms due to the disease which gave rise to the cyst may precede its discovery. When the cyst has reached a considerable size there may still be no symptoms, but sometimes attacks of epigastric pain, which may radiate to the left shoulder, occur; they are

sometimes accompanied by vomiting, wasting and jaundice. Diabetes rarely develops.

The tumour is generally in the centre of the upper part of the abdomen, but it often extends farther to the left than the right. It does not move on deep respiration and is only very slightly movable in each direction. As it grows it extends farther down and may finally appear to fill the entire abdomen. It is smooth, rounded and elastic; a thrill is often produced on striking it.

Its relation to the stomach and colon can be readily determined by means of the X-rays after a barium meal and enema. It is first behind the stomach, but as it enlarges it generally reaches the anterior abdominal wall between the stomach above and the transverse colon below. Less frequently it comes forward above the stomach or below the transverse colon between the leaves of the mesocolon. It generally grows very slowly, but sudden enlargement may result from hæmorrhage into it.

Diagnosis.—There ought to be no difficulty in diagnosing a pancreatic cyst from ascites and from a hydronephrosis, enlarged gall-bladder, ovarian cyst or distended bladder. It is impossible to distinguish a true pancreatic cyst from a pseudo-pancreatic cyst clinically; even at an operation the distinction may be impossible. Mesenteric cysts are generally more movable than pancreatic cysts.

Treatment.—The cyst should be emptied and drained by operation. It is never wise to attempt to remove it owing to the dense adhesions which often fix it to its surroundings. The immediate results of operation are very satisfactory, but a recurrence is not uncommon.

CARCINOMA OF THE PANCREAS

Ætiology.—Primary carcinoma of the pancreas is a fairly common disease. The pancreas may also be invaded by direct spread of a growth of the stomach; less frequently a small secondary deposit is found when the primary disease is situated in some distant situation. Cancer of the pancreas occurs three times as frequently in males as in females.

Pathology.—The head of the pancreas is involved in 75 per cent. of cases. Cancer of the head of the pancreas obstructs the duct, which becomes dilated and occasionally forms retention cysts. The stasis of the pancreatic secretion frequently leads to chronic pancreatitis and very rarely a pancreatic calculus. Secondary deposits are often found in the neighbouring lymphatic glands, the liver and peritoneum, and less often in more distant organs.

Symptoms.—When the head of the pancreas is involved, jaundice is generally present owing to pressure on the common bile-duct, but the latter may escape if it is not embedded in the gland. The jaundice increases until it is very intense, bile being then completely absent from the fæces. The gall-bladder is almost always distended and is generally palpable; the liver is also generally large and hard. When the growth is confined to the body or tail of the pancreas there is no jaundice unless the duct is compressed by a secondary deposit, and neither the gall-bladder nor liver is enlarged. The patient complains of a dull, growing, aching pain deeply

situated in the upper abdomen and extending to the back. It is constantly present, and unrelated to meals and the bowels. In some cases it is paroxysmal. It is generally bilateral, but occasionally confined to the left, and tends to be worst at night. The pain may simulate that produced by a spinal tumour and is probably caused by involvement of the cœliac plexus. Wasting is rapid in almost all cases, and the patient becomes progressively weaker. If the head of the pancreas is involved, the stools may have the characteristic described on page 736, and diarrhœa is likely to occur, but a growth of the body or tail does not interfere with digestion. Severe constipation is common.

A tumour of the head of the pancreas is not often palpable, as it is deep-seated and likely to be hidden by the enlarged liver and the ascites, which is present in a third of the cases as a result of malignant peritonitis or pressure on the portal vein. A tumour of the body or tail of the pancreas is more often palpable, especially shortly before death when emaciation is extreme. It forms a hard, fixed mass extending across the abdomen on a level with the umbilicus, especially to the left, and is generally not tender. A tumour of the pancreas can be visualised by radiography in the lateral position by inflating with 500 c.c. of air a rubber balloon fixed to the end of a Ryle tube introduced into the stomach.

Insomnia, depression, anxiety and restlessness may be so prominent and so out of proportion to the abdominal pain, which may even be absent, that a primary neurosis may be diagnosed.

Diagnosis.—Chronic jaundice due to carcinoma of the head of the pancreas must be diagnosed from chronic pancreatitis, a gall-stone in the ampulla of Vater, and carcinoma of the ampulla of Vater. Pain is absent in chronic pancreatitis and the general health is very little impaired, whereas in carcinoma pain radiating to the back or in the back alone is often present, and there is a steady deterioration in health. A gall-stone rarely reaches the ampulla of Vater without a preceding attack of colic, whereas jaundice is generally the first symptom in carcinoma of the head of the pancreas; the jaundice in the former is often incomplete and intermittent instead of complete and permanent, pyrexia is common, and rigors may occur owing to infection of the bile passages. In carcinoma of the ampulla of Vater the jaundice, which is accompanied as in carcinoma of the pancreas by dilatation of the gall-bladder, is less complete and more intermittent than might be expected; it can sometimes be recognised with the X-rays by the characteristic filling defect it produces in the duodenum, and it always leads to the presence of occult blood in the stools.

In the absence of jaundice the possibility of a growth of the tail of the pancreas should be considered in a patient whose general condition suggests that he is suffering from cancer, but in whom no evidence of disease can be found in the organs most commonly affected. The possibility is converted to a probability if he complains of severe pain boring through to the left side of the back or a fixed tumour becomes palpable. A normal diastase index and stools showing no deficiency in fat or meat digestion do not militate against the diagnosis.

Prognosis.—Death generally occurs within six months of the onset of symptoms and is rarely delayed beyond a year.

Treatment.—If there is the smallest doubt about the diagnosis in a case of chronic obstructive jaundice, an exploratory laparotomy should be

advised. If a growth of the pancreas is found, a cholecystenterostomy should be performed in order to relieve the jaundice and thus save the patient from one of the most distressing of his symptoms. Moreover, in numerous instances permanent recovery has followed this operation when performed for a supposed growth of the pancreas, the surgeon having mistaken chronic pancreatitis for a growth. No operation can be of any use in the absence of jaundice, even in the rare cases in which a correct diagnosis is made.

ARTHUR F. HURST.

VISCEROPTOSIS

Ætiology and Pathology.—Visceroptosis is most frequently due to a fall in intra-abdominal pressure, caused by weakness of the abdominal and pelvic muscles, the normal tone of which maintains the viscera in position. The tone of the abdominal muscles is often impaired by the stretching which they undergo during pregnancy. After parturition the sudden diminution in the volume of the abdominal contents is so great that a considerable fall in intra-abdominal pressure occurs, as the stretched muscles are at first very lax. If the patient remains in bed for a sufficient period, they gradually regain their tone, and the separated recti come together again, but otherwise they become permanently weakened. Weakness of the abdominal muscles is common among people who take too little exercise.

The pelvic floor consists of a muscular diaphragm, which is formed by the levator ani and other muscles. These are often damaged in difficult labour.

When the intra-abdominal pressure is abnormally low, the viscera drop directly gravity comes into play, but at first they regain their normal position as soon as the individual lies down. At a later stage, when the daily descent of the viscera has continued for a considerable time, the displacement persists in the horizontal position.

The degree of ptosis of the different organs depends upon their weight and upon the length and elasticity of their peritoneal attachments, which, in the absence of their natural support, act as true ligaments.

True visceroptosis must be distinguished from the "hyposthenic habitus," a constitutional condition common in women, but comparatively rare in men, which is characterised by a long narrow chest and a small epigastric angle. In this the viscera are congenitally lower than in the average individual, owing to the relatively small capacity of the upper part of the abdominal cavity.

Symptoms.—Most of the symptoms of visceroptosis occur only when the erect position is assumed. They consequently disappear on lying down and are absent at night. They are temporarily relieved when the lower part of the abdomen is compressed by means of the hand, and in women they frequently show a steady improvement as pregnancy advances owing to the rise in intra-abdominal pressure and the support given to the viscera by the growing uterus. They are often worse in the later part of the day than in the morning owing to the progressive relaxation of the abdominal muscles resulting from fatigue.

The symptoms have been ascribed in turn to the kidneys, stomach, intestines and uterus, according to which happened to be the special object of study. It is certain, however, that the general effects are commonly of much more importance than those due to ptosis of individual organs.

GASTROPTOSIS.—Gastroptosis is uncommon, and even when present it is rarely the cause of symptoms. The normal stomach varies greatly in length. In the erect position it swings between the œsophagus, where it passes through the diaphragm, and the junction between the movable duodenal bulb and the descending retro-peritoneal portion of the duodenum. In a stomach of average length the umbilicus (or inter-iliac line) is about half-way between the lesser and greater curvatures. The greater curvature of the short hypersthenic stomach does not reach the umbilicus. On the other hand, in the long stomach, which is particularly common in individuals with a hyposthenic habitus, the lesser as well as the greater curvature is below the umbilicus, and the latter may reach the true pelvis. This condition has generally been called gastroptosis, but, as it is congenital and the stomach has never occupied a higher position, the name is quite inappropriate. Moreover, the long stomach is just as competent as a short one or one of average length.

When the abdominal muscles become weak, a long stomach is likely to be more affected than one of ordinary length, and a short one does not drop at all. But the gastroptosis caused in this way does not lead to kinking of the pylorus, as the pyloric end of the stomach together with the first part of the duodenum is surrounded by peritoneum and is freely movable. It may, however, give rise to a kink where the first part of the duodenum joins the second or descending part, as the latter is situated behind the peritoneum and is less mobile. Discomfort may then occur, which begins during the meal and reaches its greatest intensity as soon as all the food has been taken. It depends more upon the quantity than the quality of the food, milk producing just as much disturbance as an equal weight of solid food. Much more commonly, however, the duodenum drops with the stomach, so that a considerable degree of gastroptosis may be present with little or no gastric disturbance. It is thus always necessary to note the position of the duodenum as well as that of the stomach during an X-ray examination: if the upper extremity of the duodenum is not at least an inch above the umbilicus, duodenal ptosis is present.

After having found the position of the stomach and duodenum in the erect and horizontal positions, it must next be determined whether the stomach evacuates its contents in a normal manner. If the duodenum drops with the stomach, the passage of food out of the stomach and through the duodenum is generally normal in rate. This is also sometimes the case even if the duodenum has not dropped, but more frequently, especially if the ptosis is well marked, it can be seen with the X-rays that, although the food may pass without difficulty from the stomach into the first part of the duodenum, there is delay in the passage beyond this point.

A second examination should be made 6 hours after the opaque meal, no food having been taken in the interval. The patient should not lie down, but should follow his ordinary occupation. Gastric stasis is present if the stomach still contains food at this second examination. In order to decide whether this is due to the ptosis, a second opaque meal should be given on another day, and the patient should lie on his right side in the interval between

the two examinations. If the ptosis is the sole cause of the stasis, the stomach will be empty in 6 hours, and if an intermediate examination is made it will probably be found to be already empty in 2 or 3 hours. If there is no delay in the evacuation of the stomach in the erect position, the indigestion is not due to the gastroptosis.

It is important to observe whether voluntary contraction of the abdominal muscles in the erect posture is sufficient to raise the stomach to its normal position, as if this is the case the prognosis is good, and abdominal exercises together with the temporary use of a support will probably result in a cure. If the stomach cannot be raised to the normal position in this way, the back should be supported by the left hand whilst the lower part of the abdomen is pressed inwards and upwards with the right. In most cases this results in raising the stomach to the normal position, which indicates that an abdominal support is likely to give relief, though it will not by itself cure the condition.

ENTEROPTOSIS (COLOPTOSIS).—Ever since Glénard drew attention to the condition he called "enteroptosis," which has also been named Glénard's disease, this has been erroneously supposed to produce kinks of the intestines, especially at the flexures of the colon, and to give rise to obstruction to the onward passage of fæces. I have seen a pelvic cæcum in almost as large a proportion of strong healthy individuals, especially females, with perfect digestion and no constipation as of constipated patients. The colon, like the stomach, varies greatly in length. When the ascending colon is unusually long the cæcum is situated in the pelvis even on lying down. The lowest part of the transverse colon of normal people is almost always situated well below the umbilicus in the erect position. When it is longer than the average, as it is in most people with a long stomach, it reaches the true pelvis. Under these conditions neither a pelvic cæcum nor a pelvic transverse colon can be regarded as a result of ptosis. The position of the colon varies greatly in the course of the day: it is lowest when full and highest when empty just after defæcation; it is depressed by a full stomach; and a pelvic cæcum and transverse colon are raised out of the pelvis by a full bladder. In normal individuals examined with the X-rays the hepatic and splenic flexures often appear to be acutely kinked. This is the result of the shadow being cast in a single plane, as the limbs of the flexures belonging to the transverse colon are in front of those of the ascending and descending colon respectively, and the flexures appear to be acute, although they form a wide angle when looked at from the side.

The constipation, which is often associated with visceroptosis, is generally due to interference with the voluntary part of the act of defæcation caused by the weakness of the abdominal and pelvic muscles, and the ptosis of the diaphragm. Ptosis of the transverse colon never leads to kinking at the hepatic flexure, as the cæcum and ascending colon drop with it. A true kink is occasionally produced at the splenic flexure, as the phrenico-colic ligament is stronger than any other of the intestinal attachments. A dragging pain together with a sense of distension may then be felt in the left hypochondrium, but no serious obstruction to the passage of fæces ever occurs.

The characteristic bulging of the lower part of the abdomen and retraction of the epigastrium seen on standing are due mainly to ptosis of the small intestine, but are of no clinical importance.

HEPATOPTOSIS.—When the liver drops it rotates towards the right, or less frequently it falls forward so that its upper surface bulges in the epigastrium. The condition can be recognised by palpation and percussion, the upper border of the hepatic dullness being abnormally low. A palpable liver is thus not necessarily an enlarged one, but may simply be displaced. It gives rise to no special symptoms except occasionally a vague discomfort in the right hypochondrium which may radiate towards the shoulder; it is increased by jumping, walking and coughing, and disappears on lying down.

A *dropped spleen* can be distinguished from a large spleen by the fact that it can be manipulated into its normal position, where it is no longer palpable; it generally gives rise to no symptoms, but in very rare instances great pain is produced by twisting of its pedicle.

For *nephroptosis*, see p. 1346.

When the pelvic floor is weak, it allows the *pelvic viscera* to drop, and retroflexion of the uterus generally occurs simultaneously; it may also result in actual prolapse of the uterus and rectum.

Downward displacement of the *diaphragm* results in dyspnœa, as, being constantly in the position of extreme inspiration, it is no longer possible for its normal respiratory excursions to occur. This is particularly noticeable in patients with weak hearts, whose abdominal muscles have been stretched by an accumulation of ascitic fluid which has since been absorbed or tapped. The downward displacement of the diaphragm is accompanied by a similar displacement of the heart, which gives rise to no special symptoms.

Under normal conditions the abdominal wall and pelvic floor are the only support of the viscera; the peritoneal folds help to maintain them in position, but they do not support their weight. If, as a result of weakness of the muscles of the abdominal wall and of the pelvic floor, the viscera drop when the individual is erect, a pull is exerted on the peritoneal folds, which become true suspensory ligaments. Their sensory nerves are constantly stimulated, the patient often complaining of vague abdominal discomfort, which is generally described as a weight or pressure or as being of a dragging nature; it is relieved by lying down and by pressure upon the lower part of the abdomen. The discomfort is most marked in neurasthenic individuals owing to the irritability of their nervous system; if the nervous system is healthy it may be completely absent. It is increased by exercise and physical fatigue and to a less extent by mental fatigue.

Visceroptosis leads to an alteration in the centre of gravity of the body. In order to maintain the upright position certain muscles of the spine which are ordinarily little used are brought into action; this is a frequent cause of chronic backache.

The maintenance of the circulation when the erect position is assumed depends to a considerable extent upon the tonic contraction of the abdominal muscles. When this is deficient, as it is in visceroptosis, the abdominal veins dilate and the pulse becomes abnormally accelerated on standing; giddiness and syncope may also occur.

Treatment.—Much can be done to prevent visceroptosis in women by proper management of the puerperium. The patient should remain in bed for the first 12 or 14 days after parturition, in order that the most active period of involution of the pelvic organs should be completed before the uterine supports are subjected to strain. But when much bruising has

occurred, especially in the case of primiparæ, or when the mother is much debilitated by frequent child-bearing, this period should be extended to 3 or 4 weeks. During the whole of this time exercises for the abdominal and perineal muscles should be regularly practised under expert supervision. Most of the time during the first few days after getting up should be spent on a couch, and a return to full physical activity should be permitted only after 6 weeks.

The first indication in the treatment of visceroptosis is to raise the intra-abdominal pressure. In order to do this the condition of the abdominal and pelvic muscles must be improved. Exercise out of doors and special remedial exercises are of great value. It is essential to prevent the over-stretching of the muscles, which occurs whenever the erect position is assumed, as it is impossible for them to regain their normal postural tone so long as they have to bear the weight of the viscera for the greater part of the day. In many cases, therefore, a support is required for a time, but it should be discarded as soon as the abdominal muscles have regained their normal postural tone. An abdominal support should fit closely to the symphysis pubis and Poupart's ligaments below; it should not extend above beyond the umbilicus. It should be so made that it presses the abdominal contents upwards, backwards and inwards. In mild cases of visceroptosis in women all that is necessary is a special straight-fronted corset, which does not constrict the waist, but supports the lower part of the abdomen. In most cases, however, a light support, hinged in the middle line and fixed in position by steel springs, which pass over the hips to end in pads applied to the sacrum, is required. The abdominal support should always be put on when the patient is lying down with the pelvis raised so that the organs are held in proper position, and it should be worn all day. Not infrequently the X-rays show that the stomach and colon drop on standing almost or quite as far when the support is worn as without it. This is particularly likely to occur in cases in which an organ falls into the true pelvis, as the support does not then reach low enough, and in thin patients upon whom it is impossible to exert sufficient pressure. Such a patient, however, often derives benefit from wearing a support, although it does not hold the colon or stomach up. It acts by increasing the intra-abdominal pressure, symptoms ascribed to kinks being really the result of the low intra-abdominal pressure interfering with the circulation and with the proper performance of defæcation.

When visceroptosis is due in part to weakness of the pelvic floor, this may require treatment by pessaries and local operations, which have the object of restoring the injured parts to a more normal condition, but an exercise for the levator ani muscles is often of great value in such cases. The patient is instructed to perform the movement she would make were she attempting to overcome an urgent desire to defæcate. The exercise should be repeated about thirty times twice a day while in the recumbent position. I have often seen a tendency to prolapse of the rectum and of the uterus overcome in this way, the associated dyschezia being cured at the same time.

Gastroptosis requires treatment only in the exceptional cases in which it has led to definite gastric stasis. In slight cases the patient should lie down after meals, but in severe cases, in which there is much emaciation or the abdominal muscles are greatly atrophied, it is best for her to remain in bed for some weeks, as by this means the intra-abdominal pressure is reduced

to a minimum, and all tension is removed from the abdominal and pelvic muscles. The foot of the bed should be raised as high as possible, as this helps the organs to return to their proper position, which is often maintained after the patient gets up again, especially if she gains weight during the rest. She should lie on her right side during and for an hour after meals. She can get up to open her bowels and to wash when her stomach is empty before breakfast. Small meals should be given at frequent intervals, and food should be chosen which contains a maximum of nourishment in a minimum of bulk. Upward massage is useful, especially if the stomach or colon is low in the horizontal as well as in the vertical position; it is most effective if the masseuse gives her first treatment under the X-ray screen, so that she can see what manipulations are required to bring the stomach and colon back to their normal position. After the period of complete rest the patient should at first lie for an hour on her right side after meals.

In no circumstances should any operation be performed for raising dropped viscera. I have never seen the slightest benefit follow, and the anxious mental condition of many of the patients makes surgical interference of any kind most undesirable.

GASTRO-INTESTINAL ALLERGY

When paroxysmal attacks of abdominal pain are not obviously the result of biliary or renal colic, the possibility of abdominal allergic attacks should be considered. The pain may occur in any part of the abdomen, and its situation generally varies in different attacks. The onset is sudden, and the attack terminates abruptly after a period lasting for a few minutes to 24 or 48 hours. The patient has no abdominal symptoms of any kind in the intervals between the attacks, which may occur almost every day or not more than once or twice a year. Nothing abnormal is found on examining the abdomen between the attacks, and during the attacks there is little or no rigidity and generally little or no tenderness. The pain may be extremely severe and only partly relieved by morphine. It is often associated with vomiting and, when the pain is in the lower part of the abdomen, watery diarrhœa with or without mucus, but without blood, is generally present. The mucus may form membranes (muco-membranous colic) and in rare cases the mucus contains eosinophil cells. In some cases vomiting and diarrhœa occurs with little or no pain.

The patient often gives a family history of asthma, hay fever, skin disease or migraine, and he is often himself a sufferer from one or other of these conditions. In some cases the vomiting or diarrhœa is often or always preceded by rhinorrhœa. The abdominal attacks generally occur, however, during periods of complete freedom from other allergic manifestations, so that the frequent presence of slight eosinophilia is an important help in diagnosis. Still more characteristic is the complete relief obtained by injecting 3 to 5 minims of adrenaline (1 in 1000), as this drug has no effect on any other form of abdominal pain.

Cutaneous reactions may show that the patient is sensitive to certain articles of food, especially wheat, milk and eggs in the case of children, and pork or other pig food, cabbage, potatoes and chocolate in adults, but the

absence of such reactions does not exclude an allergic origin of the symptoms, nor does their presence prove with certainty that the articles consumed must be excluded from the diet. Sensitiveness to foods frequently consumed is rarely recognised by the patient, who is, however, generally aware of an idiosyncrasy to such articles of diet as strawberries, tomatoes, onions, spinach, cucumber, melon, shell-fish and turtle. Gastro-intestinal allergy occurs at all ages, but is most common in infants and children. In rare cases attacks are brought on by foreign proteins absorbed by the nasal mucous membrane. I have seen a typical case caused by the emanation of cats. In one patient severe attacks of abdominal pain, with vomiting and diarrhœa, were always preceded by rhinorrhœa and sometimes by swelling of the eyelids and tinnitus. The skin gave a strongly positive reaction to cat but to no foods, and it was found that the attacks occurred only at the patient's house and only during the past two years, during which she had had a cat in her room.

Treatment.—The patient should avoid any articles of food which he has found give rise to attacks, and also any which give a positive cutaneous reaction. If attacks continue to be frequent, the effect of ½ grain of ephedrine hydrochloride three times a day before meals should be tried. Nocturnal or early morning attacks may be prevented by taking 1 to 2 grains of phenobarbitone and an additional dose of ephedrine on going to bed. The patient should learn to give himself adrenaline, and at the first sign of an attack he should inject the smallest dose which experience shows prevents an attack: generally 3 to 5 minims are sufficient. The injection can be repeated at intervals if the attack does not at once completely disappear.

ARTHUR F. HURST.

DISEASES OF THE PERITONEUM

ACUTE PERITONITIS

Definition.—Peritonitis is the disease which results from infection of the peritoneum with bacteria. Owing to the large area of the peritoneum and its great powers of absorption the results are very severe, and because of its intimate relationship to the alimentary canal the risk of such an infection occurring is considerable.

Ætiology.—Infection may reach the peritoneum (1) from without; (2) by the blood stream; and (3) from the contained organs.

1. Infection from without is possible in the case of wounds, but is of infrequent occurrence. In most instances severe abdominal wounds injure the contained viscera also, and the consequent peritonitis is usually the result of this.

2. Infection by the blood stream is an occasional though uncommon mode of infection. In streptococcal and staphylococcal septicæmia peritonitis may occur as a terminal event; it frequently gives rise to so few symptoms, however, that its existence is unrecognised during life. When pneumococcal peritonitis complicates pneumococcal lesions elsewhere the infection is undoubtedly blood borne.

3. Infection from contained or neighbouring organs is by far the commonest cause of peritonitis. The majority of cases depend more or less directly on the passage of bacteria from within the alimentary canal owing to changes in its walls. The appendix is the most frequent seat of the primary condition. When there is no actual breach of continuity in the organ, bacteria escaping through its damaged walls generally lead to the formation of peritoneal adhesions and possibly to a local abscess. When, however, the infection is particularly virulent or the patient's resistance unusually poor, a sufficient local reaction does not take place, and spreading diffuse peritonitis results. This is commoner in children than adults, and may occasionally occur, even when the local reaction has been good, through manipulation or ill-judged surgery separating the adhesions and allowing the infection to spread. Diverticulitis and acute cholecystitis are occasional causes of this type of acute peritonitis, but more usually result in local adhesive changes. Peritonitis complicating typhoid fever in the absence of perforation, and pneumococcal peritonitis when associated with pneumococcal enteritis, have a similar origin.

In intestinal obstruction and strangulated hernia the changes which occur in the bowel wall speedily permit the passage of organisms through it to the peritoneum. This takes place first in the neighbourhood of the obstruction, but as paralysis and distension spread along the bowel, organisms can make their way through, and consequently most cases of this type are widely generalised. The infection, however, is gradual, and the reactive forces of the peritoneum have time to respond. By far the commonest organism in these cases is the *B. coli communis*, usually preceded by or accompanied by the *Staphylococcus epidermidis albus*.

Perforation of a hollow viscus into the peritoneal cavity is responsible for some of the most virulent and widespread cases of peritonitis; the lower the perforation in the bowel, the more virulent the resulting infection will be. The appendix is the commonest source, gangrene or a perforating ulcer leading to a sudden peritoneal infection before any gradual passage of organisms has had time to produce a local peritoneal reaction. Perforating ulcers of the stomach and duodenum come next in order of frequency; less common causes are perforating ulcers of the ileum, the most important of which is the typhoid ulcer, rupture of the gall-bladder, bile-ducts or ureters, and perforating wounds of any of the hollow organs, or leakage from surgical anastomoses. Abscesses of the liver, appendix, gall-bladder or Fallopian tubes occasionally burst into the general peritoneal cavity. Infection of the peritoneum may also result by direct spread from neighbouring parts. This type of case is particularly common in women, spread taking place either directly through the Fallopian tubes, or by lymphatic permeation of the uterine walls. Peritonitis is a very rare sequel to infections of the lung and pleura, although the reverse is far from unusual. In the infant an infection of the thrombosed umbilical vein may lead to peritonitis by direct spread.

Symptoms.—As acute peritonitis is almost invariably a secondary condition, its symptoms and course are subject to very considerable variations, depending not only on the nature of the primary lesion from which it arises and on the nature and virulence of the infecting organism, but also on the general condition of the patient.

1. *Acute generalised peritonitis.*—This is usually associated with the

perforation of a hollow organ or the sudden bursting of an abscess into the peritoneum, and owes its chief characters to the fact that in such cases the peritoneum is suddenly flooded with infection without any preliminary preparation. The patient may have been free from any symptoms of ill-health, and is suddenly seized with very acute abdominal pain, accompanied sometimes by a sensation of something having given way. The pain may at first be localised in position, and thus help in the diagnosis of the actual lesion; but it speedily spreads to the whole abdomen, and is followed almost at once by a feeling of syncope or collapse. Within a few minutes the patient becomes cold and pale; his features are pinched and betray the most intense anxiety; beads of sweat stand out upon the skin, and the pulse may be almost imperceptible. He complains of nausea, but does not often vomit, and his respirations are shallow and quickened. In a short time a certain amount of improvement takes place; the pulse, though rapid, is of better volume, and the pain may take on an intermittent colicky character. The abdomen is absolutely rigid, and is usually retracted, though it may be distended; it is very tender on pressure. The liver dullness is usually absent; but this is only important if an abdominal examination made at the onset of the attack revealed a normal area of dullness. These symptoms are caused by the perforation or other primary cause and the resultant flooding of the peritoneum with infective material. Occasionally they may be sufficiently severe to lead to death by themselves: but more usually they gradually merge into the symptoms of the consequent acute peritonitis itself. The latter are reactive in nature, and are due to nature's attempts to limit the process.

The patient becomes extremely restless, this being one of the most characteristic and distressing features of nearly all forms of peritonitis. Owing to the loss of fluid by sweating, vomiting and exudation, the subcutaneous tissues become shrunken and give the patient the so-called "facies Hippocratica." The tongue is dry and furred, and the teeth become covered with sordes. The pulse increases in rate and becomes thready and later running in character, and the temperature, which at first may be subnormal, rises. The abdomen is of a uniformly board-like rigidity and extremely tender. It is held immovable, respiration being entirely thoracic, and the patient lies with his knees drawn up to relieve the abdominal tension. There is usually absolute constipation, and the intestinal sounds are absent. Gradually the paralytic intestine becomes dilated, and the abdomen distended. Vomiting is early and frequent. The vomited matter is usually only small in quantity; it speedily becomes exceedingly foul, though it is rarely fæcal, and the breath is extremely offensive. The urine is scanty and may contain traces of albumin, and its passage may produce a paroxysm of pain. It usually contains a large amount of indican.

Throughout the whole course of the disease the outstanding feature is the pain. This may at first be intermittent and colicky; but as the peritonitis develops it becomes constant and agonising, being increased by the smallest movement. In spite of this the restlessness persists, the patient being unable to resist the desire to move his limbs. The pain and restlessness, with the persistent vomiting, the intense thirst, which is hardly relieved by drinking, combine to make the patient's misery extreme. The pulse increases in rapidity until it can scarcely be counted, the extremities become

cold, the eyes grow more sunken, and the features more pinched. As death approaches, the skin takes on a cyanotic hue; the persistent restlessness, the increasing voicelessness, and the remorselessly unimpaired consciousness bring death as a merciful release, even though the pain may be somewhat relieved towards the end.

The foregoing description applies to an acute fulminant case of peritonitis, running its course to death in from 24 to 48 hours; its outstanding features are a condition of profound shock and toxæmia, giving a measure of the high grade of peritoneal absorption. In the aged, and in patients with tabes or Bright's disease, the symptoms may be very atypical; pain may be but little marked, and vomiting and tenderness may be absent, while the bowels may act freely throughout. The striking restlessness, the condition of the tongue, the pulse and the ultimate meteorism will, however, usually indicate the true nature of the condition.

2. *Acute spreading peritonitis.*—This variety differs from the preceding in that the peritoneum is not suddenly flooded with infective material, but is prepared for infection by the more or less gradual spread of the condition. It accompanies many cases of appendicitis, and is a sequel of intestinal obstruction if unrelieved for a sufficiently long period. The peritoneal reaction is intense, and the coils of intestine become glued together with a sticky exudate, while pockets of pus form between them. The pain is at first localised to the region of origin; but as the infection spreads it extends until it may become generalised over the whole abdomen. It is, however, never so intense as in the preceding variety, and may be distinctly spasmodic in character. The general abdominal symptoms are also less severe, the tenderness, rigidity, meteorism and constipation being of varying grade. The aspect of the patient betokens a profound septic infection, the tongue is furred and dry, the pulse rapid, and the temperature of the hectic type. Rigors and sweats are not uncommon, and if left alone the case may terminate with fatal septicæmia, suppurative pylephlebitis, or in rare cases the pus may accumulate and burst either externally in the region of the umbilicus or into one of the hollow viscera.

3. *Pneumococcal peritonitis.*—This presents certain fairly characteristic features, which in many cases enable the nature of the infection to be correctly diagnosed from the clinical picture alone. It is far more frequent in children than in adults, and in girls than boys in the proportion of nearly 7 to 3. It occurs in a diffuse and an encysted form, depending probably on the resistance of the patient. In many cases there exists a definite pneumococcal enteritis, the organisms penetrating the wall of the bowel and so infecting the peritoneum. The predominance of the disease in girls is probably due to the female genitals being a source of infection, as the pneumococcus has been cultivated from the vagina in some instances. In the majority of cases, however, the peritonitis is part of a pneumococcal septicæmia; thus, when it is secondary to pneumococcal disease of the middle ear, local pneumococcal abscesses or pneumococcal arthritis, the blood stream appears to be the source of infection, and it probably is so also in those cases which follow pneumonia or empyema, since the physics of the upper abdomen renders a direct spread through the diaphragm unlikely.

There is a striking resemblance between the symptoms of most forms

of pneumococcal infection, a resemblance which strongly supports the view of their origin in a septicæmia. The onset is usually sudden, often accompanied by a chill and a high temperature, the pain is violent and persistent, and the prostration severe. The patient has the characteristic flush, the respiratory rate is raised, and the accessory muscles of respiration are called into play. Vomiting is frequent, and tenderness and rigidity are marked; but in place of the usual absolute constipation there is frequently profuse diarrhœa, which, associated with the other symptoms of acute peritonitis, is often almost diagnostic. In the diffuse form, unless operation is undertaken, death takes place early; but if the patient lives long enough there may be a sudden fall of temperature about the seventh day, as in pneumococcal pneumonia.

The encysted and more common variety of pneumococcal peritonitis is less severe, and shows a remarkable tendency for pus to collect in the lower abdomen. There is the same acute onset as in the diffuse variety; but the patient then appears to improve for a few days. Later, however, he gets gradually worse, the abdomen becomes distended, the diarrhœa changes to obstinate constipation, and an abscess forms in the lower abdomen and finally bursts at the umbilicus. The exudate in these cases is a greenish, odourless pus, which is sufficiently characteristic to enable the infection to be diagnosed when it is discovered at operation.

4. *Gonococcal peritonitis.*— Gonococcal peritonitis is rare; it occurs both as an acute diffuse affection of the peritoneum and as a localised pelvic inflammation. It is commoner in females than in males, owing to the ready channel for infection through the Fallopian tubes, and when it occurs in males it is usually secondary to epididymitis. The infection is generally a mixed one, the more fragile gonococcus being readily overgrown, and some cases of unexplained peritonitis, which on culture show only *B. coli*, are possibly gonococcal in origin. The symptoms do not differ in the diffuse cases from those of other forms of acute peritonitis, although the primary focus usually gives rise to symptoms. The prognosis is, however, good, and the majority of cases, even those presenting severe symptoms, recover without operation.

5. *Streptococcal peritonitis.*—Peritonitis due to the *Streptococcus* is occasionally secondary to lesions of the alimentary canal; but much more frequently it is a sequel of puerperal infections. It occurs commonly after a first delivery, and is frequently associated with retained products. Infection takes place along the lymphatics of the damaged uterus or through the Fallopian tubes, and may be localised in the pelvis; but it often gives rise to generalised peritonitis. The symptoms are characteristic, and are associated with evidence of a marked septicæmia. The abdominal walls, being already greatly stretched, do not show the usual rigidity, and extreme distension occurs rapidly. Diarrhœa is commoner than constipation, and a high temperature with rigors is usual. The uterine discharges are offensive, the milk secretion is suppressed, and the cases frequently progress to death within the first week. This type of infection is more fulminant than any other, except certain cases of perforative peritonitis.

Diagnosis.—The diagnosis of acute peritonitis is not usually difficult, except in cases where the severity of the causal condition is so great that it masks the peritoneal response, or where the peritonitis occurs in a patient

already so severely ill that no response is possible. It is often extremely difficult to make a correct diagnosis of the lesion to which the peritonitis is secondary, and in many cases this is only possible after laparotomy. The most valuable signs of acute peritonitis are the severe pain and tenderness, the rigid abdomen, the small, rapid, and thready pulse, the dry tongue, the restlessness, vomiting, and constipation, and the absence of sounds of gurgling on auscultation. Any of these symptoms may, however, be absent, and a diagnosis must be based on their occurrence in combination. In post-operative cases there is sometimes a remarkable absence of both pain and rigidity, and the all-important early recognition of the condition in these patients is often one of much difficulty.

Peritonitis is most likely to be mistaken for lead colic or acute intestinal obstruction. From the former it can be distinguished by the fact that the abdomen in peritonitis is usually extremely tender, while in colic pressure often, though not invariably, relieves the pain; in colic a blue line is present, and the red corpuscles show punctate basophilia, the pain is intermittent, and there is usually no vomiting and less extreme rigidity. From acute intestinal obstruction the diagnosis is often far more difficult, particularly since the two conditions frequently coexist. In the early stages of obstruction, before peritonitis has developed, the intermittent nature of the pain, the absence of great tenderness or rigidity, the copious nature of the vomit, and the evidence of increased peristalsis from inspection or auscultation should help to distinguish the two conditions.

In acute pancreatitis the pain is more definitely hypogastric, the patient is usually over middle age, and collapse is extreme. The menstrual history, the typical pallor, and the results of vaginal examination usually serve to indicate a ruptured tubal pregnancy, and in other acutely painful abdominal conditions the localised nature of the pain and the absence of any extreme general tenderness help to distinguish the condition from peritonitis.

The gastric crises of tabes are seldom likely to be a source of error; but the comparative absence of severe symptoms in tabetics, the subjects of peritonitis, is very apt to lead to a mistaken diagnosis.

Basal pneumonia and diaphragmatic pleurisy may lead to acute abdominal symptoms. The temperature and pulse, the raised respiration rate, and a routine examination of the chest in all cases should prevent a mistake being made.

Prognosis.—The prognosis of acute peritonitis is always grave, even with early surgical treatment. Without operation no case of acute perforative peritonitis can be expected to recover; such exceptions as have been recorded must be regarded as medical curiosities. Usually death takes place within 48 hours, though it may be delayed a week or even longer when the perforation is high in the bowel and the latter is empty at the time.

In diffuse spreading peritonitis and streptococcal puerperal infections death is almost as invariable, unless operation is undertaken; but the process is less rapid, and a small proportion of cases undoubtedly recover without surgical aid. These cases occasionally merge into a form of chronic fibro-purulent peritonitis, characterised by the progressive formation of collections of pus between neighbouring viscera, and by repeated outbursts of symptoms as other parts of the peritoneum become successively involved. This con-

dition usually terminates in fatal septicæmia, with infections in the pleura, pericardium or endocardium. The prognosis in pneumococcal cases is considerably better, as even without operation, a fair proportion recover, either with or without the formation of a hypogastric purulent collection, which may discharge at the umbilicus. In the rare gonococcal cases recovery is the rule, and the fatal cases recorded have almost invariably followed operation.

In forming a prognosis the chief importance must be placed on the degree of toxæmia and the severity of the intestinal paralysis, and to a less extent on the degree of meteorism and the frequency of the vomiting. Spontaneous bowel actions or their induction by enemata make the prognosis relatively more favourable.

The rate of rise of the pulse and its ratio to the temperature are also of importance; cases with a subnormal temperature throughout are almost always rapidly fatal.

Treatment.—The principles that must underlie the successful treatment of acute peritonitis are, firstly, the removal or limitation of the process to which the peritonitis is secondary by a thorough and speedy exploration of the abdomen, followed by closure of a perforation, removal of an appendix, or such other measures as the pathology present may indicate; secondly, drainage and relief of tension in the peritoneal cavity; thirdly, the encouragement of the normal peritoneal response and the least possible damage to its protective agencies; and, fourthly, the combating of the shock and toxæmia.

By the adoption of the Fowler position, in which the patient is propped up in bed in a sitting position, not only is infective material removed from the dangerous diaphragmatic area and brought into contact with the much more highly resistant pelvic peritoneum, but at the same time the diaphragm is relieved from the pressure of the dilated stomach and intestines.

A further important adjunct to surgical treatment is the intravenous injection of saline by the continuous drip method. This raises the blood pressure and redresses the chloride and fluid loss which has taken place, and being excreted by the peritoneum, it reverses to a certain extent the lymphatic circulation, and consequently largely prevents the absorption of toxic material as well as dilutes that already present. Gas-gangrene antitoxin is often of value in combating the toxæmia arising from the paralysed bowel.

Until a definite diagnosis has been made and operation advised and agreed to, the administration of opium in any form is definitely contra-indicated. It masks the symptoms, and by bringing to the patient and his advisers a false sense of security may lead to a fatal delay in undertaking the operation. When, however, a diagnosis has been made, and operation is agreed to, morphine is beneficial in reducing both the mental and physical symptoms while the necessary preparations are being made. Morphine as a method of treatment has been adopted more and more of recent years, the morphine being given deliberately and in doses sufficient to affect the respiration rate with the object of diminishing the activity of peristalsis, as well as of combating the shock, pain and restlessness, which help so largely to exhaust the patient's powers of resistance. It is very doubtful whether it ever prevents the response of the bowels to enemata in cases in which they would otherwise respond. If vomiting is a prominent symptom, lavage of the stomach is of value. It should, if possible, always be done before opera-

tion, as post-anæsthetic vomiting of fæcal material is a fruitful cause of fatal broncho-pneumonia. The introduction of an in-dwelling Ryle's tube through the nose, into the stomach, or even the duodenum, with frequent suction by syringe, is a valuable method of keeping the stomach and upper intestine empty.

In pneumococcal cases there is not quite the same urgency for operation, and in some cases recovery follows the use of sulphapyridine (M. & B. 693) and serum, if the pneumococcus can be typed, as it can be in some cases, from the urine. In gonococcal peritonitis, if a diagnosis can be made, conservative treatment should be followed; but if there is doubt, as there often must be, of the nature of the infection, or if the patient shows any increase of symptoms, laparotomy is the only safe course to follow.

E. G. SLESINGER.

CHRONIC PERITONITIS

Chronic peritonitis is a condition in which widespread and progressive chronic inflammation of the peritoneum occurs independently of tuberculous or malignant peritonitis.

Ætiology.—Chronic peritonitis may be associated with chronic inflammatory changes in the thorax. Effusion may occur from all the serous membranes (polyserositis); this condition is probably in most cases tuberculous. In other cases chronic peritonitis is associated with chronic mediastinitis and adherent pericardium (Pick's disease, p. 961). The peritoneum covering the liver (perihepatitis) and spleen (perisplenitis) is generally most severely involved.

Pathology.—The liver may be covered with a thick, hard and white coating of fibrous tissue, which can be peeled off to expose the smooth peritoneal surface. Perihepatitis is almost always associated with a similar thickening of the capsule of the spleen and with thickening of other parts of the peritoneum.

Symptoms.—The only important symptom is ascites. Its onset is generally gradual, but it may be acute. Frequent tapping is required, and the intervals between the performance of paracentesis tend to diminish and may finally be as short as a fortnight, when as much as a pint of fluid may be poured into the peritoneal cavity in a day.

Œdema, especially of the feet, is frequent in the late stages; it is generally cardiac or renal in origin, but may also be caused by pressure of the ascitic fluid on the inferior vena cava.

Course.—The course of the disease is very slow, death generally occurring from some intercurrent disease. The general health may remain good for a long time.

For the diagnosis and treatment, see Ascites (pp. 765, 766).

TUBERCULOUS PERITONITIS

Ætiology.—The peritoneum is involved in 15 per cent. of fatal cases of tuberculosis. Tuberculous peritonitis is rare in infants and uncommon

after 30; the majority of cases occur between the ages of 3 and 20. Boys and girls are equally liable to the disease; it is found much more frequently in women than men at operations, but more frequently in men than in women after death.

Primary tuberculous peritonitis is uncommon in children and rare in adults. It is probably due to infection conveyed by the intestines, which do not themselves become infected. More often, especially in children, the mesenteric glands become tuberculous, generally without any lesion developing in the intestines, and the peritoneum is infected from the glands. In males the primary focus may be the prostate, vesiculæ seminales or testes, and in females the disease frequently begins in the Fallopian tubes; but the latter may also be infected from the peritoneum. Although tuberculous ulcers are found in 75 per cent. of fatal cases of pulmonary tuberculosis, the peritoneum is affected in only 4 per cent. of cases. The peritoneum, the pleura and occasionally the pericardium may be involved together in the absence of any other tuberculous focus.

Pathology.—Tuberculous peritonitis may occur in three forms—the ascitic, loculated and obliterative.

1. In the ascitic form, which may be acute, subacute or chronic, miliary tubercles are scattered over the whole peritoneum, which is free or nearly free from adhesions. In chronic cases the tubercles are larger and more fibrotic than in the acute; the peritoneum is thickened and the mesentery is shortened so that the intestines are tethered to the posterior abdominal wall. This form may closely resemble malignant peritonitis.

2. In loculated tuberculous peritonitis the fluid may be clear, the condition being then intermediate between the ascitic and obliterative forms, or it may be turbid or purulent. In the latter case masses of tuberculous material separated from each other by adherent coils of intestine have broken down to form suppurating foci, which may erode the intestine or open at the umbilicus or even into the vagina.

3. Chronic obliterative, adhesive or fibrous tuberculous peritonitis may occur after absorption of fluid in the ascitic form or may develop primarily. No effusion is present, but universal adhesions obliterate the lumen of the peritoneum, all the viscera being inextricably bound together and to the parietal peritoneum.

In each form of tuberculous peritonitis the mesenteric glands are generally caseous ("tabes mesenterica") and may break down in the centre; the mediastinal glands may also become tuberculous. The omentum is often rolled into a solid mass, which sometimes contains caseous nodules.

Symptoms.—Tuberculous peritonitis is sometimes completely latent, and may be discovered accidentally during an operation for some independent disease or for a hernia, when the sac may be the only part involved.

The onset of abdominal symptoms is generally preceded by a period of ill-health; the patient loses weight and strength, his appetite is poor, and his temperature may rise slightly at night. After a time he complains of general abdominal discomfort. Constipation is common, especially in the obliterative form. In other cases diarrhœa may occur owing to tuberculous ulceration of the intestines, fistulous communications between adjacent coils of intestines or simple entero-colitis. The stools are occasionally bulky owing to deficient absorption of fat caused by obstruction of the lacteals by caseous

mesenteric glands (*vide* p. 626). The spleen and less often the liver may be enlarged. The skin, especially over the abdomen, is dry, inelastic and sometimes so pigmented that Addison's disease is simulated. In chronic cases there is sometimes no pyrexia; more often the temperature is intermittently slightly raised. In acute and suppurative cases the temperature is generally high and irregular, and the pulse is rapid. Traces of albumin may be present owing to the pressure on the renal veins caused by the large accumulation of fluid in the abdomen or to the effect of the toxæmia on the renal cells. A moderate degree of anæmia is often present, and leucocytosis develops if suppuration occurs.

In the ascitic form the abdomen gradually becomes distended. At first it is tympanitic, but after a time evidence of the presence of free fluid is obtained, but the quantity is not often very great. Less frequently a large amount of fluid collects with great rapidity; the sudden stretching of the abdominal muscles is likely to cause a considerable amount of pain. Moderate tenderness of the whole abdomen is generally present. A large accumulation of fluid may compress the inferior vena cava and give rise to œdema of the legs. The diaphragm is pushed upwards and respiration becomes shallow and thoracic. The skin over the abdomen is shiny and the veins are enlarged. The ascitic fluid is generally clear; it contains a large proportion of lymphocytes and often coagulates on standing; less frequently it is turbid or blood-stained. Tubercle bacilli are rarely found in the effusion, although they must be present, as the fluid may produce tuberculosis when injected into guinea-pigs.

In the loculated form with suppuration the abdominal pain is generally greater; attacks of colic are common, especially after exercise. The abdomen is distended and doughy; on percussion, irregular tympanitic and dull areas are found. Large caseous glands and collections of pus between adherent coils of intestines may form palpable masses, which are immobile, tender and dull on percussion. The omentum can often be recognised as a thick cord stretching across the upper part of the abdomen; the transverse colon generally forms a resonant band immediately above it, which helps to distinguish it from the lower edge of an irregularly enlarged liver. The ease with which the masses are felt varies from time to time with the amount of flatulent distension of the intestines. When an abscess is about to point at the umbilicus, the latter becomes indurated, red and tender; a similar condition is occasionally observed in pneumococcal peritonitis and in pelvic peritonitis in women. On rectal and vaginal examination thickened Fallopian tubes, enlarged glands or collections of pus may be felt.

The signs of obliterative tuberculous peritonitis are ill-defined; the abdomen gives a characteristic rubbery resistance on palpation and is generally somewhat distended. Irregular masses may be felt in it, and the peristaltic waves of the small intestines are often visible, especially in children. This does not necessarily indicate that partial obstruction is present, as it may be simply a result of the abnormal thinness of the abdominal wall.

Symptoms of tuberculous disease of other organs, especially of the lungs, pleura and intestines are often present. Generalised tuberculosis may develop at any time, especially in children. Vomiting and constipation, which suggest intestinal obstruction, may be the first symptoms of tuberculous meningitis.

In rare cases acute peritonitis may develop as a result of rupture of a softened caseous gland or perforation of a tuberculous ulcer.

When a patient recovers from tuberculous peritonitis, the tubercles and adhesions may completely disappear. More frequently localised adhesions remain, and calcified tuberculous mesenteric glands are often found with the X-rays, at operations and after death. They may give rise to confusion when the abdomen is X-rayed on account of suspected renal calculi. They do not, however, move with the shadow of the kidney with changes in posture, and the diagnosis can always be settled by pyelography. The bands, which may form from localised adhesions, occasionally cause acute intestinal obstruction, sometimes not until many years after the active disease has disappeared.

Diagnosis.—In the presence of tuberculous disease of the lungs or other organs, abdominal distension, especially if associated with ascites or irregular abdominal masses, generally indicates that tuberculous peritonitis is present. The discovery of tubercle bacilli in the sputum, and their much less common discovery in the fæces or vaginal discharge, is very strong confirmatory evidence. Ascites in children, and in females with symptoms pointing to tuberculous salpingitis, is generally due to tuberculous peritonitis.

Acute cases may at first closely simulate pneumococcal peritonitis or even appendicitis; but in non-tuberculous inflammatory exudates of the peritoneum most of the cells are polymorphonuclear leucocytes instead of lymphocytes. Ascites due to cirrhosis of the liver in children is almost always mistaken for tuberculous peritonitis; on the other hand, the ascitic form of tuberculous peritonitis in middle-aged alcoholic individuals is likely to be mistaken for ascites due to cirrhosis. When cirrhosis is undoubtedly present, ascites may still be due in part to tuberculous peritonitis; a large proportion of lymphocytes in the fluid is very strong evidence in favour of this, as the ascitic fluid in uncomplicated cirrhosis contains few except endothelial cells. In simple chronic peritonitis there is no fever and little or no pain, and the ascitic fluid contains few if any lymphocytes. The presence of irregular masses together with fluid in the abdomen generally indicates tuberculous peritonitis in children; but it is more frequently due to malignant disease in adults, especially in males. The history of the case and any evidence of tuberculous or of malignant disease in other parts of the body help to settle the diagnosis.

Fever, inflammation of the umbilicus, and the presence of lymphocytes in the ascitic fluid point to tuberculosis, whilst nodular infiltration without inflammation of the umbilicus, hard and enlarged glands in the groin or neck, and the presence of large, multinuclear cells or groups of cells in the effusion point to cancer.

Prognosis.—Recovery takes place in a large proportion of cases of the ascitic form of tuberculous peritonitis. When localised abscesses develop complete recovery is rare, and when a fæcal fistula forms death almost always follows. Prolonged fever, rapid emaciation and intractable diarrhœa are the most serious symptoms. The prognosis also depends on the severity of any tuberculous disease of the lungs or other organs which may be present. Apparent recovery is sometimes followed by a relapse, generally owing to reinfection from an unhealed primary focus, such as a tuberculous gland, appendix or Fallopian tube.

Treatment.—The patient should be kept in bed completely at rest so long as the temperature is raised. He should be in the open air all day and night when the weather permits, and if indoors an abundant supply of fresh air is essential. Heliotherapy or artificial sunlight should be employed, but care must be taken to avoid over-exposure. The mercurial ointment, which is sometimes applied on a binder to the abdomen, is probably quite valueless. Diarrhœa should be treated by a non-irritating diet, and in intractable cases by opium preparations. If fatty diarrhœa is present, fat must be excluded from the diet. With this exception, the food should be as abundant and nourishing as possible. Tuberculin has been much employed, but I am not convinced that it is of any use.

When the abdominal distension in ascitic cases gives rise to discomfort paracentesis should be performed. Nothing is gained by laparotomy. The occurrence of intestinal obstruction is an indication for operation, though it is rarely possible to do anything useful owing to the extensive adhesions present and the danger of tearing the intestines.

CANCER OF THE PERITONEUM; MALIGNANT PERITONITIS

Ætiology.—Cancer of the peritoneum is almost always secondary. The primary disease is generally in the abdomen, especially the stomach and the ovary, the peritoneum becoming involved by spread along lymphatics or blood vessels, by direct contact, or most commonly by malignant cells being set free and scattered widely over the peritoneum. The disease may also spread from cancer of the breast by the deep lymphatics of the chest and abdominal wall, and by lymphatics from malignant disease of the testis.

Pathology.—Malignant deposits may form minute tubercles, larger white non-caseating nodules or even very large masses. The parts most generally involved are the omentum, mesentery and pelvis. Chronic fibrotic changes frequently occur, and result in the omentum being rolled up and the mesentery shortened as in tuberculous peritonitis. The diaphragm is often invaded with growth, which spreads to one or both pleuræ. Acute or subacute peritonitis may occur.

Symptoms.—The symptoms are caused in part by the primary disease and in part by the secondary malignant peritonitis. As the former is generally situated in the abdomen, it is impossible to distinguish between the symptoms due to the two causes. Malignant peritonitis generally results in ascites; the fluid is clear or turbid, hæmorrhagic, chyliform, or less frequently chylous owing to obstruction and subsequent rupture of lacteals. The umbilicus is often infiltrated with growth, and nodules may be felt along the falciform ligament. Tumours are often felt in the abdomen or on rectal examination; they are sometimes too small to be palpable, and in other cases they can only be felt after the fluid has been removed. The rolled-up omentum can often be recognised as a thick transverse cord above the umbilicus. The malignant masses or peritoneal adhesions may give rise to obstructive symptoms.

Diagnosis.—The development of new abdominal tumours or ascites in a patient who is known to have cancer of the stomach or other organ is conclusive evidence that the peritoneum is involved. When there is no clear

evidence pointing to the presence of a primary malignant or tuberculous focus, it may be difficult to distinguish between tuberculous and malignant peritonitis (see p. 763). When ascites is present and no tumour is palpable, cirrhosis, simple chronic peritonitis or portal thrombosis may be simulated; the abdomen should be tapped, when a tumour often becomes palpable if malignant disease is present.

Prognosis and Treatment.—It is rare for the patient to survive for more than six months after the peritoneum becomes involved. Treatment is purely palliative. Considerable relief may follow paracentesis.

ASCITES

Definition.— Ascites is the accumulation of free fluid in the peritoneal cavity.

Ætiology.— Ascites is a constant symptom of simple, tuberculous and malignant chronic peritonitis. It occurs when there is a rise of pressure in the portal circulation; it is always present in portal thrombosis and when the portal vein is obstructed by a growth or an aneurysm, and portal obstruction is in part responsible for its presence in cirrhosis of the liver. Ascites is very common in heart failure, in which it is almost always associated with œdema of the feet. It is in part due to the same causes as the œdema, but it is also in part caused by portal congestion, and by obstruction to the lymph flow from the thoracic duct owing to the rise of venous pressure. Lastly, ascites accompanies the dropsy of Bright's disease and severe anæmias.

Symptoms.—The abdomen becomes gradually enlarged, at first in an antero-posterior direction, the costal margin being pushed forward, but at a later stage the bulging occurs in the flanks also. The stretching of the abdominal wall gives rise to a tight sensation, which may amount to actual pain if the fluid collects rapidly. It causes the muscles to atrophy and lineæ atrophicæ develop in the skin. The umbilicus becomes everted and may form a thin-walled bladder.

The rise in intra-abdominal pressure caused by the accumulation of ascitic fluid obstructs the inferior vena cava; œdema of the legs may occur, and the obstruction to the renal circulation may cause albumin to appear in the urine, the quantity of which is reduced owing to the loss of water in the ascitic fluid. Compensatory dilatation of other venous channels results: the dilatation of the veins passing between the abdominal wall and those in the falciform ligament is manifested by the development of large and prominent subcutaneous veins around and above the umbilicus; others pass from the superficial and deep epigastric veins in the middle of the groin towards the costal arch, where they join the superficial epigastric and long thoracic veins. When paracentesis is performed, the dilated veins disappear if they have developed as a result of pressure on the inferior vena cava, but not if obstruction of portal veins is the primary condition.

The diaphragm is pushed up; its excursions on respiration are reduced and dyspnœa may result. The impulse of the heart may be felt in the third intercostal space; the twisting of the heart may temporarily produce a pulmonary systolic murmur. Cardiac irregularity, palpitation and attacks of faintness may follow. The upper border of hepatic dullness may reach

the fourth, third or even second intercostal space in front; the right base is dull behind owing to the liver being pushed up and the lung compressed. A pleural effusion may be suspected, but the upper limit of dullness is altered on taking a deep breath if it is due to the liver being pushed up, and the increased dullness diminishes or disappears when the patient lies on his face; in pleural effusion the dullness is higher in the axilla than behind, but this is not the case if it is due to an abnormally high position of the liver.

The pelvis and renal regions hold a considerable amount of fluid, so that no accumulation occurs in the flanks until at least a litre is present in the abdomen. As more fluid collects, the resonant note in the flanks is replaced by dullness, but the change may be delayed if there is much gas in the colon. The level of dullness now gradually rises and spreads over the pubes towards the umbilicus. On turning from one side to the other the most dependent part remains dull. This is not, however, absolutely pathognomonic of ascites, as similar movable dullness may occur in chronic obstruction of the small intestines.

In chronic peritonitis the mesentery may be so shortened that the intestines are unable to float on the fluid; the fluid then accumulates in front of the intestines, and the highest part of the abdomen is dull.

A characteristic fluid thrill is felt when one side of the abdomen is sharply flicked by the fingers of one hand, whilst the other hand is placed flat upon the opposite side of the abdomen. When the patient is very fat or the abdominal wall is œdematous, a similar but less marked sensation may be produced; in doubtful cases the hand of an assistant should therefore be pressed perpendicularly over the middle line of the abdomen, as this prevents the transmission of the impulse through the abdominal wall, but not through the fluid contents of the abdomen.

When the liver or spleen is enlarged and hard, or when an abdominal tumour is present, the sensation produced by dipping the tips of the fingers suddenly through the fluid on to the solid organ, which jumps away from them, is most characteristic.

Diagnosis of Ascites.—Confusion has often occurred between ascites and a large ovarian tumour. The history of the development of the abdominal swelling may help the diagnosis. In many cases the outline of an ovarian tumour can be definitely felt, and its pelvic attachments can be recognised by vaginal examination. The antero-posterior enlargement is greater than the lateral bulging, whereas the reverse is the case in ascites; the maximal girth is below the umbilicus instead of at the umbilicus or above; the umbilicus, which is normally and in ascites an inch nearer the pubes than the ensiform cartilage, is proportionately farther from the pubes; and the distension on one side is often greater than the other instead of being uniform.

Diagnosis of Cause of Ascites.—In cirrhosis of the liver the fluid collects rapidly and the patient is obviously ill; in chronic peritonitis the accumulation on the first occasion is generally very gradual and the patient may be otherwise well. An enlarged spleen or the occurrence of hæmatemesis points to cirrhosis, evidence of chronic interstitial nephritis to chronic peritonitis. A patient with ascites due to cirrhosis alone rarely survives the performance of paracentesis more than two or three times, as his general health has already greatly deteriorated by the time that ascites develops. If tapping is frequently performed, chronic peritonitis is therefore probably

present, even if other evidence indicates that the patient is also suffering from cirrhosis. Tuberculous peritonitis is rare in adults, except as a complication of cirrhosis of the liver and when secondary to tuberculous Fallopian tubes. Evidence of tuberculous disease in other parts of the body, solid masses palpable in the abdomen or on rectal examination, pain and tenderness in the abdomen except over the liver, and induration and redness of the umbilicus point to tuberculous peritonitis; the fluid is generally turbid, the specific gravity is above instead of below 1015, and lymphocytes are present.

In malignant peritonitis there is generally evidence of the primary disease in some other organ, and nodules may be felt in the abdomen, in the neighbourhood of the umbilicus, or in the middle line above it, and enlarged glands may be present. The spleen is not enlarged, emaciation is generally greater than in cirrhosis, and, except when the primary disease is in the stomach, there is no hæmatemesis. A rectal and vaginal examination are particularly important, as ascites, which may recur very frequently, sometimes results from ovarian tumours. In a doubtful case the diagnosis may become clear after paracentesis, when the large hard liver and spleen may be felt in cirrhosis, and an irregular enlargement of the liver, but no splenomegaly, in cancer of the liver. In malignant disease the fluid may contain cancer cells; it is more often hæmorrhagic than in tuberculous peritonitis or cirrhosis.

Rapid development of ascites with enlargement of the spleen and sometimes hæmatemesis suggests portal thrombosis; if symptoms pointing to cirrhosis are already present, it is probably secondary to this, and even in their absence it may be secondary to latent cirrhosis.

An examination of the circulatory system and the urine should prevent confusion between ascites due to cirrhosis and that due to heart failure or kidney disease; but these conditions may be associated together.

Treatment.—Paracentesis should be performed as soon as the accumulation of fluid causes discomfort or seriously interferes with the digestion, circulation or respiration. Hæmatemesis is a further indication, as paracentesis reduces venous engorgement. The trocar should be inserted in the middle line between the umbilicus and pubes, or in the flank. Care must be taken to avoid the liver and spleen. A trocar and tube of moderate bore should be used, as the very fine Southey's tube formerly employed tends to become blocked and the discomfort caused by the paracentesis is needlessly prolonged.

A salt-free diet should be given, as ascitic fluid never contains less than 8 grm. of sodium chloride in each litre; if the quantity of salt taken in the day is reduced to 0·8 grm., less than 100 c.c. of ascitic fluid can collect during the same period, as the urine always contains some salt, and the percentage in the body fluids never falls greatly below the normal. The quantity of salt and water retained can be still further reduced by giving 30 grains of calcium chloride three times a day.

Organic mercurial diuretics, such as mersalyl, which diminish absorption of water by the renal tubules, so increase the urinary output that the accumulation of fluid in the abdomen is much retarded. They are most effective if the patient is already on a salt-free diet and is taking calcium chloride, and if a diuretic, such as theophylline (theocin), which stimulates glomerular secretion, is given simultaneously. Ampoules containing 1 or 2 c.c. of a 10 per cent. solution of mersalyl with 5 per cent. theophylline (injection of

mersalyl, B.P.) are used. Initial doses of 0·5 c.c., 1 c.c., 2 c.c., and 3 c.c. are given intramuscularly on alternate days, after which 2 c.c. are injected weekly as long as necessary.

Diuretics are more valuable as preventatives when the fluid first appears or after it has been removed than as curatives when a large quantity is present, as the pressure on the renal veins makes the kidneys less active, and an enormous quantity of fluid has to be excreted by them before the accumulation can disappear, whereas comparatively little urine need be passed to prevent re-accumulation of ascitic fluid after tapping.

Operations devised with the object of increasing collateral circulation between the portal and the general venous system are so rarely successful and are so often followed rapidly by death that they should never be performed.

The bowels should be kept well open, but severe purging weakens the patient and is likely to aggravate the catarrh of the alimentary canal which is often already present. Epsom salts, which also promotes biliary drainage, is the most suitable aperient.

ARTHUR F. HURST.

SECTION X

DISEASES OF THE BLOOD

THE blood is sometimes regarded as the mixed secretion or product of the blood-forming organs. For the purposes of description and for the better understanding of the changes in disease, it is more convenient to think of the blood and blood-forming organs as composed of three distinct systems or tissues: (1) the red cells and their precursors, sometimes known as the erythron; (2) the white cells and the immature cells from which they arise; (3) the platelets and the megakaryocytes. These three systems of cells exist side by side in the plasma and bone-marrow, and are often affected simultaneously by disease, but they are to a large extent independent of each other. Before discussing separately the three systems of cells and their diseases, it will be convenient to say a few words about the total volume of the blood.

THE BLOOD VOLUME

The total volume of the blood is about 90 c.c. per kilogram of body weight, *i.e.* some 6000 c.c. in an average individual, or about one-eleventh of the body weight. Of this volume the cells constitute about 42 per cent., the remainder being plasma. The blood volume is moderately diminished in anæmia; it is moderately increased in the splenomegalies, in leukæmia and in erythrocytosis, and greatly increased, even to two or three times the normal, in erythræmia. There is a slight increase in œdema, due to an associated œdema of the blood, but no change in arterial hypertension. The blood volume is moderately increased in pregnancy, in order to allow for the fœtal circulation. Of great importance in practice are the conditions in which the volume of circulating blood is suddenly and considerably diminished. The chief causes are hæmorrhage and shock. In acute anæmia from hæmorrhage or blood destruction there is extreme exhaustion, faintness or syncope, air-hunger, sweating and thirst. The degree of shock depends largely on the rate of bleeding. A sudden hæmorrhage of 1500 to 2000 c.c. may be fatal, while as much as 60 per cent. of the total amount of blood may be lost without death if the hæmorrhage is prolonged over 24 hours or more. The blood count is of limited value in determining the patient's condition, inasmuch as the concentration of the blood may be unaffected in the early stages. In alimentary hæmorrhage the blood urea may be raised, owing to absorption of the effused blood, and the height of the rise is a fair measure of the severity of the bleeding. In all forms of hæmorrhage a systolic pressure below 80 mm. of mercury, a progressive increase in pulse-rate and the development of crepitations in the lungs are all serious signs.

Examples of the shock syndrome are trauma, anaphylaxis, burns, dehydration and toxæmia such as are met with in alkalosis, diabetic coma, cholera and severe infections. The patient becomes collapsed, complains of thirst, the skin is pale, cold and moist, the breathing quick and shallow, the pulse rapid and almost imperceptible, and the blood pressure low. The kidneys are inadequately supplied with blood and the output of urine may almost cease. The symptoms are often mistaken for heart failure, but there is no orthopnœa, venous engorgement, or œdema, and the symptoms are really due to loss of fluid from the circulation and stasis of blood in the capillaries.

The logical treatment in all forms of shock is to increase the blood volume and the venous return to the heart in any way possible. The foot of the patient's bed may be elevated, the legs bandaged from the ankles to the mid-thigh and the intake of fluid by the mouth increased, unless these measures are otherwise contra-indicated. The patient should be kept warm, and inhalation of oxygen or oxygen plus carbon dioxide may be helpful. Apart from sedatives for pain, drugs are of little value. Various types of infusion have been used at different times with the object of restoring the blood volume to normal and it has thus been discovered that whole blood and plasma are the ideal fluids. Solutions of saline or dextrose produce only transient improvement and, moreover, both these solutions and also gum acacia often have undesirable side effects. In shock due to hæmorrhage a transfusion of 500 c.c. of blood should be administered at once and this may be followed, if necessary, by the continuous transfusion of blood at a rate of 90 to 150 c.c. an hour until the hæmoglobin has been raised to 70 per cent. or over. In shock not due to hæmorrhage there is no reduction in the oxygen-carrying power of the blood—indeed, the concentration of hæmoglobin is usually higher than normal. In such cases it is better to give plasma or human serum rather than whole blood, as they restore the volume and normal concentration of the blood and resist diffusion from the capillaries. The amount required may vary between 200 and 1000 c.c.

THE RED BLOOD CELLS

The red blood cells are biconcave discs with a mean diameter of 7·20 microns (6·7 to 7·7 μ), a mean volume of 85 cubic microns (75 to 95 $\mu\mu$), and a mean corpuscular hæmoglobin content of 29 micromicrograms [1] (26·5 to 31·5 $\gamma\gamma$). Their size and shape are adapted to the carriage of hæmoglobin and the supply of oxygen to the tissues. The blood of a healthy young male contains about 5·5 millions of red cells per c.mm. and 16 g. of hæmoglobin per 100 c.c.; of a healthy female about 4·75 millions of red cells per c.mm. and 14 g. of hæmoglobin per 100 c.c. The normal range of variation of the erythrocyte count is from a million above to a million below the average male value, *i.e.* any figure between 4·5 and 6·3 million red cells per c.mm. may be considered normal, and there is naturally a corresponding fluctuation in the hæmoglobin percentage. A hæmoglobin percentage below 85 per cent. is always abnormal and evidence of anæmia, though symptoms rarely appear until the hæmoglobin falls below 75 per

[1] A micromicrogram is the millionth of a millionth part of a gram ($1 \text{ g.} \times 10^{-12}$), and is abbreviated by the Greek letters gamma ($\gamma\gamma$).

cent. Erythrocytes and hæmoglobin are subject to much less diurnal variation than the white cells, but significant changes may occur after exertion. For purposes of calculation the normal red cell count is taken as 5 million cells per c.mm., and the corresponding amount of hæmoglobin (14·5 g. per 100 c.c. of blood) is taken as 100 per cent. hæmoglobin. The *colour index* measures the average amount of hæmoglobin contained in the red corpuscles of a sample of blood, and is calculated from the formula

$$\text{Colour index} = \frac{\text{Hæmoglobin per cent.}}{\text{Number of red cells per cent. of the normal.}}$$

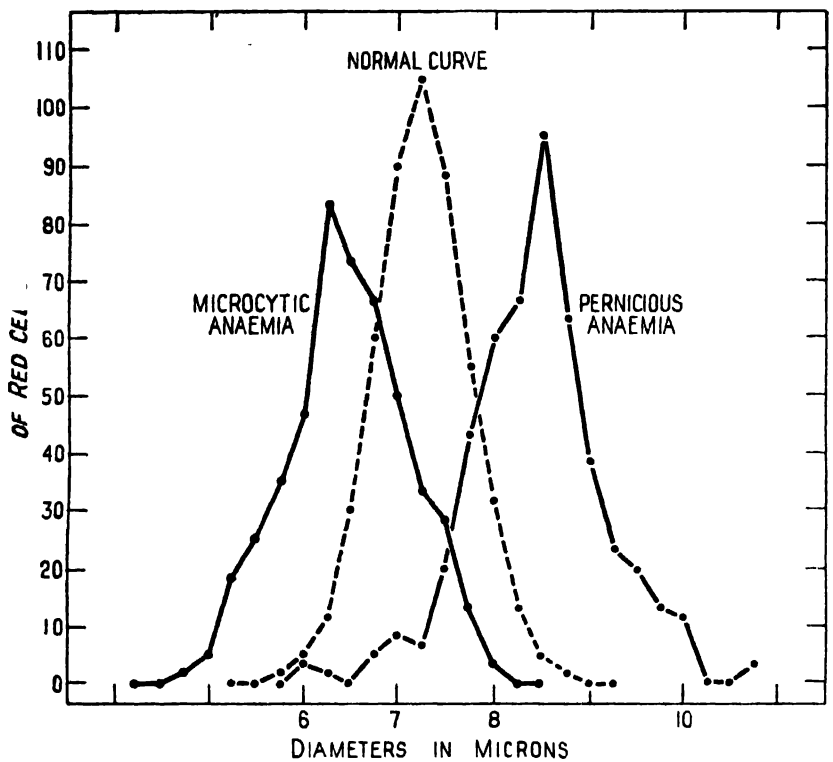


FIG. 18.—Frequency distribution curves of red cell diameters in health and disease (Price-Jones curves).

The red cells in any sample of blood are never absolutely equal, but show a certain amount of variability in size, or *anisocytosis*. The degree of variability, or anisocytosis, is often increased in anæmia and may be of diagnostic significance. The mean diameter of the red cells and their variability is determined by measuring the diameter of 500 successive red cells under the microscope on a stained thin smear. The results are then plotted on squared paper, with the number of cells counted as ordinates and the

diameter of the cells as abscissæ, to obtain what is known as a red cell diameter distribution curve, or Price-Jones curve (Fig. 18). Abnormal variability in the size of the cells will be shown by a widening of the base of the curve. Cells which are larger than normal and fall to the right of the limits determined on healthy individuals are called *megalocytes*. Small cells which fall to the left of the limits of health are called *microcytes*. A cell of normal diameter is a *normocyte*. The cell volume is obtained by centrifuging a sample of blood under standard conditions; the mean cell volume is calculated from the height of the column of red cells and the total red cell count. As the red cells age, they become malformed and finally broken into fragments which are engulfed by the phagocytic cells of the liver, the spleen and other tissues. These malformed red cells are called *poikilocytes*. In all forms of anæmia the cells put into circulation are less perfect than in health, and poikilocytosis more rapidly develops.

Blood Groups.—In the year 1900 Landsteiner and his pupils made the surprising discovery that the red cells of mankind are not immunologically identical, and that the sera of many people contain antibodies which agglutinate and destroy the red cells of others. There are, in fact, four main blood groups, which are determined by the presence or absence of two agglutinogens, A and B, of which either may be present separately (groups A and B), neither may be present (group O), or both may be present together (group AB). Corresponding to these two agglutinogens are their homologous antibodies or agglutinins—anti-A (or α) and anti-B (or β)—which are present in the serum in reciprocal relationship to the agglutinogens of the cells. The following table illustrates the Landsteiner classification of blood groups and the distribution among the population in England.

Blood Group.	Agglutinin.	Agglutinogen.	Per Cent.
AB	None (0)	A and B	3
A	β	A	42
B	α	B	9
O	α and β	None (0)	46

It can be seen that the serum of group AB will not agglutinate the red cells of any other group, and for this reason group AB has been called "universal recipient." For similar reasons members of group O are called "universal donors," because their red cells contain no agglutinogen; but blood from group O should only be transfused into members of other groups in extreme emergency, as the agglutinins in the serum of the donor may destroy the red cells of the recipient. If we wish to administer human plasma or serum, we must use either the same group or group AB. The supply of donors belonging to group AB is unfortunately small, but recently it has been suggested that plasma of this group may be prepared artificially by mixing equal parts of blood of groups A and B. By this procedure the agglutinins are absorbed on the corresponding red cells and a plasma free of agglutinins is obtained. It has been shown by a number of observers that

the blood groups have sub-groups, and interaction may occur between members of the same group. The existence of agglutinogens A_1 and A_2 is now generally accepted. For this reason the compatibility of donor and recipient must always be confirmed by direct cross-matching of the cells of the donor and the serum of the recipient. Two further agglutinogens, M and N, are recognised, but as there are no naturally occurring antibodies to these substances, they have no clinical significance and are estimated only for medico-legal or anthropological evidence.

Nomenclature.—The red cells are formed in the bone-marrow, probably within the lumen of capillary vessels which connect the sinuses to each other. The nucleated precursors are known by the generic name of *erythroblasts*. In normal marrow the erythroblasts are *normoblasts*, which subsequently develop into normocytes, but in certain diseases larger forms with more primitive nuclei are found, the *megaloblasts*, which give rise to megalocytes. The nucleated red cells lose their nuclei by extrusion or solution, but for a time they still contain remnants of the original basophil cytoplasm, which gives the red cell a bluish tinge in ordinary stained smears (*diffuse basophilia* or *polychromasia*). Certain dyes, such as brilliant cresyl blue, when brought in contact with the fresh-drawn blood, precipitate this basophil cytoplasm in a network or reticulum, and on this account these immature red cells are called *reticulocytes*. Polychromasia and reticulocytosis are identical conditions revealed by different stains. The normal reticulocyte count is ½ to 2 per cent. A similar precipitation may occur *in vivo* when poisons, such as lead, circulate in the blood stream and the reticulum becomes visible in ordinary preparations (*punctate basophilia*).

As we learn more about the so-called blood diseases, we find it increasingly difficult to classify them in a simple way, as they may be due to causes originating outside the blood stream and the bone marrow. On this account we refer to many of them by names which merely describe the type of reaction or blood picture. Thus, anæmias may be described as hæmorrhagic, hæmolytic, or aplastic in type. According as the colour index is high, normal, or low, they are described as *hyperchromic*, *orthochromic* or *hypochromic*. They can also be classified by the size of the red cells into *megalocytic*, *normocytic* and *microcytic* anæmias. These two sets of terms correspond roughly with each other, but they are not absolutely interchangeable, and each should be used strictly according to definition. As the colour index is always determined, whilst the size of the red cells is not often measured, the former set is more commonly employed.

THE SYMPTOMATIC ANÆMIAS

Synonym.—Secondary Hypochromic Anæmia.

Definition.—A symptomatic anæmia is one which arises in the course of some other well-defined disease. The colour index is usually low and hardly ever above unity. In the rare cases in which the colour index rises above unity, the disturbance of the erythropoietic tissues is usually so profound that for practical purposes all the megalocytic anæmias can be regarded as definite diseases of the erythropoietic tissues.

Ætiology.—The most obvious cause of anæmia is hæmorrhage: acute hæmorrhage occurs most commonly from trauma, bleeding from the alimentary tract, and the accidents of child-birth; chronic hæmorrhage is often due to hæmorrhoids, menorrhagia, and in tropical countries hookworm disease. Hæmolysis is a rare event, but it may be induced by chemical poisons, such as sulphanilamide and arseniuretted hydrogen, or by infection by hæmolytic organisms, such as the *Streptococcus hæmolyticus* or the *Bacillus welchii*, or by malaria. Acute infections rarely produce much anæmia, but severe anæmia may develop in protracted septic infection, acute rheumatism, rheumatoid arthritis, and other subacute or chronic infections, such as typhoid fever. In my experience focal sepsis is seldom responsible for an anæmia. Tuberculosis causes little anæmia until the later stages, when hæmorrhage, suppuration or intestinal ulceration has occurred. Syphilis also is rarely the cause of anæmia, except in the more florid stages, or from involvement of the liver, or from paroxysmal hæmoglobinuria. Malaria has already been mentioned. Of the toxæmias responsible for anæmia, nephritis and lead poisoning are the most important. Malignant disease is one of the commonest causes of anæmia; it may act in various ways—hæmorrhage from a malignant ulcer, cancerous cachexia, and invasion of the bone-marrow. Anæmia which is due to mechanical limitation of the bone-marrow by tumours or tumour-like conditions, such as leukæmia, Hodgkin's disease, infective granulomata and kala-azar, is sometimes described as myelophthisic anæmia, but this is an incorrect and unnecessary use of a word which is one of the synonyms for aplastic anæmia.

Pathology.—Two factors can be distinguished in these symptomatic anæmias. The first is loss of blood by hæmorrhage or hæmolysis. This leads to hyperplasia of the bone-marrow, and an outpouring of new red cells to repair the deficiency. The colour index is low, because hæmoglobin regeneration lags behind the restoration of a normal cell count, and the reticulocyte count is increased to 5 or 10 per cent., or higher. Chronic and repeated hæmorrhage may so exhaust the hæmatinic reserves that the body cannot repair the hæmoglobin deficiency, the anæmia remains torpid, and the reticulocyte count is low; rapid recovery occurs on the exhibition of large doses of iron. The second factor in the symptomatic anæmias is depression of the erythropoietic tissues by toxæmia. Hæmopoiesis may be inhibited without much structural alteration in the marrow, but in other cases the marrow becomes hypoplastic and may even degenerate completely. The output of new red cells is diminished, the reticulocyte count is low and the colour index a little below unity. Usually increased blood destruction and diminished blood formation are present in varying degree, and the blood picture is modified accordingly. The white cells and platelets are normal or increased in number, unless the marrow is greatly depressed. The other tissues generally show anæmia, œdema, and fatty change.

Symptoms.—The symptoms, other than those of the primary malady, depend on the speed with which the anæmia develops, and in acute anæmia from hæmorrhage or blood destruction there may be actual shock. In chronic anæmia, on the other hand, it is surprising how well the patient may feel. No complaint may be made with a hæmoglobin of 40 per cent., and only of undue fatiguability with a hæmoglobin of 20 per cent. Inquiry elicits such

symptoms as dyspnœa, palpitations, anginal pain, fainting attacks and œdema of the extremities. The pallor is best seen in the conjunctivæ or the palate; the skin is a bad guide, for it is often pale when there is no anæmia, and sunburnt and deceptively healthy when anæmia is severe. The pulse is rapid and the heart dilated, and systolic murmurs may be audible over the præcordium.

Diagnosis.—The cause of a symptomatic anæmia may be obvious, but on the other hand it may demand the most searching overhaul of the patient with all the resources of a modern hospital. Attention should be particularly focussed on the alimentary tract, as conditions such as diaphragmatic hernia, peptic ulcer, carcinoma of the stomach or bowel, polypi and hæmorrhoids may exist with no other symptom than anæmia.

Prognosis and Treatment.—The prognosis and treatment are those of the primary disease. In acute anæmia the patient should be transfused if his condition is critical. In chronic hæmorrhagic anæmia iron is of great value. In the majority of the symptomatic anæmias it is possible to produce a normal blood picture for a time by iron, liver and repeated transfusions, and so bring the patient into condition for operation or similar treatment. Apart from such emergencies, it is doubtful whether the transient benefit of a transfusion is commensurate with its risks in patients suffering from toxæmia, while iron and liver may have little effect if the cause of the anæmia is not removed. The treatment of anæmia is discussed in detail at the end of this section.

THE DEFICIENCY DYSHÆMOPOIETIC ANÆMIAS

An important group of anæmias is due to a defective supply of raw materials for blood formation. As these anæmias are the result of a disturbance in the growth of the red cells, they are called *dyshæmopoietic*. Absence of the factor which protects against pernicious anæmia (P.A. factor) gives rise to a megaloblastic reaction in the marrow and a megalocytic anæmia. The erythropoietic tissue hypertrophies and red marrow encroaches on the shaft of the long bones, but few of the cells mature or are delivered into the blood stream. Iron and traces of copper are needed for the manufacture of hæmoglobin, and when these minerals are lacking, the normoblasts do not mature and only a subnormal number of small pale cells is produced—a microcytic hypochromic anæmia. Vitamin C and thyroxine are also essential for blood formation. In their absence there is a general decline of hæmatopoiesis, rather than a specific variation from the normal. Both the latter conditions are frequently complicated by hæmorrhage and iron deficiency, but if this does not happen, hypothyroidism may produce a megalocytic anæmia which closely mimics pernicious anæmia. The dyshæmopoietic anæmias are frequently associated with glossitis, gastro-intestinal disorders and degeneration of the nervous system. The reticulocyte count is low, and the white cells and platelets are normal or diminished. Remission of the disease is attended by an outpouring of reticulocytes in numbers directly proportional to the extent of the hyperplasia of the bone-marrow. This is called the *reticulocyte crisis*.

1. NUTRITIONAL ANÆMIA OF INFANTS

Synonym.—Anæmia of Prematurity.

Anæmia of moderate degree is present in practically all infants, whether fed by the breast or artificially. It may become very severe, especially in twins and premature babies, who come into the world with a small store of iron, or after intercurrent infection, or when suckling is protracted beyond the normal period. It disappears spontaneously on the adoption of a mixed diet, and it appears to be a pure mineral deficiency, resultant from the low iron and mineral content of the milk, and reparable by inorganic salts of iron. In severe cases the hæmoglobin is reduced to 30 per cent. or less. The colour index is low. Death may occur, especially when the anæmia is exacerbated by intercurrent infection. Repair of the anæmia is followed by increased resistance to infection. Treatment is by iron and ammonium citrate, in a dosage of 4½ to 9 grs. daily. It is essential to accustom the infant to the iron slowly, as the sudden administration of the full dose may cause colic and diarrhœa. For this reason administration is started very gradually, particularly in young infants. In bottle-fed babies the solution of iron and ammonium citrate is added to the milk, or proprietary foods containing iron are used. The mother should be warned that the stools will be dark. There are few babies, whether breast-fed or bottle-fed, who are not improved by the prescription of iron.

2. IDIOPATHIC HYPOCHROMIC ANÆMIA

Synonyms.—Chlorosis and Late Chlorosis; Achylic Chloranæmia; Simple Achlorhydric Anæmia; Chronic Microcytic Anæmia of Women; Anæmia of Iron Deficiency.

Definition.—A chronic anæmia of low colour index occurring almost exclusively in women and associated frequently with glossitis and achlorhydria.

Ætiology.—This is the commonest of all the idiopathic anæmias, occurring typically in women between the ages of 20 and 50. It was formerly most prevalent in adolescent females and was known as chlorosis, or green sickness. Juvenile cases have now become rare, as a result probably of improvement in the diet, dress and environmental conditions of young females, and the incidence of idiopathic hypochromic anæmia has shifted to the later years of the reproductive epoch. A few cases are met in both sexes in childhood and in old age. It is more common in hospital than in private practice, probably because of the higher birth-rate and the poorer nutrition. The anæmia is the result of a deficient supply of iron to the blood-forming organs, which may be brought about in three ways: firstly, a diet poor in iron; secondly, impaired absorption of iron owing to achlorhydria or hypochlorhydria; thirdly, loss of iron in menstruation or pregnancy. There is no doubt that the last factor is the most important, as is shown by the facts that the complete syndrome of idiopathic hypochromic anæmia with glossitis, koilonychia, splenomegaly and microcytosis seldom occurs in the male, and that in the female the disease disappears spontaneously after the menopause. Moreover, women tend to eat less iron-containing

food than men, although they require more iron. The absorption of iron is promoted by the solvent action of the hydrochloric acid of the gastric juice and is therefore impaired in achlorhydria. An important group of cases of idiopathic hypochromic anæmia is the result of gastro-enterostomy and similar operations which neutralise or abolish the gastric secretion. The occasional appearance of idiopathic hypochromic anæmia and pernicious anæmia in different members of the same family is usually associated with a hereditary tendency to achlorhydria. Although achlorhydria may predispose to anæmia, epithelial symptoms, such as glossitis, angular stomatitis, achlorhydria and koilonychia, may be the result of iron deficiency and may occur in the absence of anæmia.

Pathology.—The bone-marrow is moderately hyperplastic, and microscopic examination shows an increased number of normoblasts. The spleen is moderately enlarged by a simple hyperplasia. The epithelium of the tongue and pharynx may show a leucoplakial degeneration. In patients with achlorhydria there is a diffuse chronic gastritis which eventually leads to atrophy of the mucous membrane of the stomach. The other organs exhibit the effects of a simple anæmia.

Symptoms.—Symptoms may first be complained of after a pregnancy, or an influenzal attack, but careful inquiry often elicits the information that the patients were always pale, or that they have previously come under medical care for anæmia. Symptoms fall into two categories. First there are those due to anæmia: general weakness, headaches, palpitation and dyspnœa; præcordial pain on exertion is common and may be of anginal severity; slight œdema of the ankles occurs, but anasarca or ascites is unusual. The second category of symptoms is composed of those due to dyspepsia, probably the result of the achlorhydria: lack of appetite, epigastric pain and distress, retching and vomiting after meals, flatulence and bilious attacks; constipation is frequent, but diarrhœa is unusual.

The facies is often pathognomonic, the sallow, wrinkled face and prematurely grey hair contrasting with the smooth, white and transparent body skin. The nails are frequently brittle and painful, and occasionally they are hollow and depressed like a spoon (koilonychia); on cure of the anæmia the new nail exhibits the normal contour and consistence. Glossitis is present in about half the cases. It is often painless and unknown to the patient, but on the other hand it may be the chief complaint. In the active stages the tongue is reddened and excoriated, and vesicles may appear and break down to form shallow ulcers. In the chronic and quiescent stages the filiform papillæ are destroyed, leaving a smooth bald tongue. The inflammation may spread to the buccal mucosa and to the corners of the mouth and lips, conditions known as angular stomatitis, perlèche or cheilosis. Passing backwards to the pharynx, the affection produces huskiness and a most troublesome dysphagia, which may be the presenting symptom (the Plummer-Vinson syndrome, see p. 546). Idiopathic hypochromic anæmia is, in my experience, much the commonest cause of the Plummer-Vinson syndrome. The spleen is palpable in less than 10 per cent. of cases of idiopathic hypochromic anæmia and is rarely greatly enlarged. The other signs are those of anæmia. There are no changes in the spinal cord, but functional nervous disorders, nervous breakdowns, aphonia, and pruritus frequently occur. The menses are more often scanty than heavy; owing to relaxation of the anæmic uterus these women

are, however, prone to postpartum hæmorrhage and to menorrhagia about the menopause.

Achlorhydria or extreme hypochlorhydria is found in about 70 per cent. of cases with the Rehfuss test meal, but stimulation with histamine shows that only about half have absolute achlorhydria. The gastric ferments are still present, although often reduced in amount. The achlorhydria is usually a permanent abnormality, preceding the anæmia and remaining when it is cured. The anæmia is of low colour index, and the red cells are usually smaller than normal. It is essentially a hæmoglobin deficiency, and often the red cell count is little below normal. The white cells and platelets are normal; an occasional normoblast may be present. Reticulocytes are within normal limits, and van den Bergh's reaction is negative. A typical count is: red cells, 3,500,000 per c.mm.; hæmoglobin, 35 per cent.; colour index, 0·5; white cells, 7000; differential count normal. In exceptional cases the red cells may fall nearly to a million and the hæmoglobin to 15 per cent. On treatment with iron there is a reticulocyte crisis, most marked in the most anæmic cases, but seldom exceeding 15 per cent., the red cells are rapidly restored to the normal number, and the hæmoglobin is more slowly regenerated. There may be a transient erythrocytosis during the recovery phase.

Complications and Sequelæ.—The Plummer-Vinson syndrome is the most important complication, occurring in about 15 per cent. of cases. The changes in the epithelium of the tongue and pharynx predispose to malignant disease, and epithelioma of the tongue and carcinoma of the hypopharynx develop in a few instances. There is a risk of transition into pernicious anæmia, most marked in women with a family history of that disease, but in my experience the risk is not great. Thrombosis is a rare complication.

Diagnosis.—Many cases are overlooked, or diagnosed as debility or functional nervous disorder, on account of the vagueness of the symptoms. Such mistakes are only to be avoided by examining the blood. Care should be taken to exclude other causes of anæmia, more especially malignant disease, and it is wise to remember that idiopathic hypochromic anæmia is very uncommon in females past the menopause, and in males of any age. The symptoms may suggest pernicious anæmia, but the low colour index and negative van den Bergh reaction are incompatible with this diagnosis, as also is the failure to respond to treatment by liver or stomach. In the rare disease aplastic anæmia the colour index is high, white cells and platelets are diminished, necrotic ulcerations occur, and there is no response to iron. If the spleen is enlarged the differentiation from splenic anæmia may present much difficulty. In splenic anæmia the spleen is greatly enlarged, there is often a history of jaundice or hæmatemesis, the skin may be pigmented and the fingers clubbed, and there are signs of liver damage, such as enlarged veins, positive van den Bergh reaction and impaired lævulose tolerance. In the absence of such symptoms the patient should first be treated with large doses of iron, when both the anæmia and the splenic enlargement will disappear if the correct diagnosis is idiopathic hypochromic anæmia.

Course and Prognosis.—The disease is chronic, and the average duration of symptoms before treatment is 5 years. It is rarely fatal, but in the

absence of proper treatment many patients remain invalids for years. There is a strong tendency to relapse, which can only be avoided by re-examination at intervals or by persisting with a small dose of iron.

Treatment.—Treatment is by large doses of iron by the mouth. Liver and stomach extracts are of no value in this disease. Transfusion is seldom necessary, and should be reserved for patients *in extremis*. Septic foci should be removed, especially from the mouth and pharynx. Factors likely to aggravate the anæmia, such as hæmorrhoids, should be dealt with appropriately. Hydrochloric acid relieves the dyspepsia, but has no action on the anæmia. Glossitis and dysphagia commonly improve when the anæmia is repaired; a simple mouth-wash may be prescribed, and Hurst's mercury tube may be passed for the dysphagia. Menorrhagia may be very troublesome; with rest in bed at the periods, large doses of calcium salts by mouth, and, if necessary, injections of cotarnine hydrochloride or hydrastinine hydrochloride, in younger subjects the condition usually subsides after a few months. After age 40 this complication is more intractable, and if it persists then, it is advisable to induce an artificial menopause by means of X-rays or operation.

3. PERNICIOUS ANÆMIA

Symptom.—Addison's Anæmia.

Definition.—A disease characterised by megalocytic anæmia, achylia, and a tendency to degeneration of the spinal cord, which pursues a remittent course, and which is invariably fatal unless appropriate treatment is instituted.

Ætiology.—The disease is most common between the ages of 40 and 60, though analysis shows that it becomes relatively more frequent in each decade. True pernicious anæmia has been observed in children, but it is very rare before the third decade. It is found in all civilised countries, though it is not very common in Jews, and it affects males and females equally. There is a hereditary proclivity, and achlorhydria without symptoms, achlorhydric dyspepsia, simple achlorhydric anæmia, pernicious anæmia and subacute combined degeneration of the spinal cord are sometimes observed in different members of the same family.

The disease is due to absence of an *intrinsic factor*, which is secreted by the pyloric segment of the stomach, the duodenum, and in diminishing degree possibly by the remainder of the intestine. It is generally held that the intrinsic factor is a ferment, which reacts with an *extrinsic factor* in the food to produce the principle which prevents pernicious anæmia (P.A. factor). Intrinsic factor is quite distinct from pepsin and rennin. The nature of the extrinsic factor is not known, but it is present in any well-balanced diet. P.A. factor is absorbed from the small intestine and stored in the liver and, to a less extent, in other organs, such as the kidney and the central nervous system. P.A. factor is essential for normal blood formation and the nutrition of the spinal cord. In its absence the bone-marrow undergoes megaloblastic degeneration, and the circulating red cells probably break down more rapidly than normal. The lesion which abolishes the secretion of intrinsic factor by the pyloro-duodenal segment practically always suppresses the secretion of hydrochloric acid and pepsin by the body of the

stomach. Achylia is therefore a cardinal symptom of pernicious anæmia; but it is important to remember that the achylia is coincidental with and not causative of the anæmia, and that owing to the secretion of intrinsic factor by the duodenum, resection of the stomach is not necessarily followed by pernicious anæmia. We do not know the nature of the lesion in pernicious anæmia which affects the rather widely distributed system of cells which secrete intrinsic factor, but probably it is often a degenerative change associated with advancing years and favoured by hereditary vulnerability. Gastro-enteritis, dysentery and similar infections, and operations on the stomach appear to be important predisposing agencies. The occasional occurrence of pernicious anæmia during pregnancy and as a result of hyperthyroidism and pituitary disease suggests that endocrine factors are sometimes at work and probably dietetic errors also are occasionally responsible.

Megalocytic anæmia similar to pernicious anæmia occurs in a number of other conditions in which nutrition or digestion is impaired. These anæmias may be classified in the following three categories: first, megalocytic anæmia due to a defective diet; second, megalocytic anæmia due to defective absorption of anti-anæmic factors when the intestines are diseased; and third, megalocytic anæmia due to defective storage or metabolism of anti-anæmic factors, as when the liver is extensively damaged. The gastric juice may be perfectly normal in such conditions, and for some unexplained reason subacute combined degeneration of the spinal cord is much less frequent than in pernicious anæmia. In all these anæmias the red cells show anisocytosis and megalocytosis, and the bone-marrow shows megaloblastic degeneration comparable with the findings in Addison's anæmia. Recent research has nevertheless indicated that there are a number of subtle differences in the blood pictures and in the response to treatment, and though the whole group responds to the injection of crude liver extract, some of them are refractory to treatment by the more highly purified liver extracts now available. It is possible that liver contains a number of related hæmopoietic principles, rather than a single P.A. factor.

(*a*) *Nutritional macrocytic anæmia.*—Megalocytic anæmia due to defective diet is uncommon in temperate zones except in fanatical vegetarians, but very common in tropical and subtropical countries where large populations subsist on famine diets. The attack is usually precipitated by an extra factor, such as pregnancy or malaria, and hæmolysis may be much more evident than in pernicious anæmia.

(*b*) *Stenosis, resection or ulceration of the small intestine.*—These conditions probably act by interfering with the absorption of the P.A. factor.

(*c*) *Intestinal parasites.*—The most important is Bothriocephalus latus. The mode of action is unknown, but is probably an interference with absorption.

(*d*) *Sprue.*—Megalocytic anæmia is almost the rule in sprue. It is in part due to the intestinal disease, but in the majority of cases the gastric secretion is also impaired.

(*e*) *Fatty diarrhœa.*—In fatty diarrhœa, such as occurs in cœliac disease, idiopathic steatorrhœa, pancreatic disease, gastro-colic fistula and extensive operations on the alimentary tract, megalocytic anæmia from interference with absorption of P.A. factor is occasionally observed, though not so constantly as in sprue.

(*f*) *Disease of liver.*—Megalocytic anæmia with normal gastric secretion is occasionally observed in cirrhosis and other diffuse diseases of the liver. It is attributed to inability to store pernicious anæmia factor in the liver, but it may be noted that the anæmia of hepatic cirrhosis rarely responds to treatment in the same satisfactory way as other deficiency dyshæmopoietic anæmias.

Pathology.—The remainder of this section deals with true pernicious anæmia, though similar changes are observed in the other megalocytic anæmias just mentioned. The body may not be wasted, the fat is a peculiar yellowish colour and the muscles reddish-brown. All the tissues are anæmic, and the heart muscle shows fatty degeneration. Free iron is present in the liver, the kidneys and other tissues. The bone-marrow is hyperplastic, like red currant jelly, but usually there are some areas of aplasia; microscopic examination shows many megaloblasts, and in addition endothelial cells containing phagocyted red cells and their débris. Degeneration of the postero-lateral columns of the spinal cord is present in about 80 per cent. of cases. The stomach shows a diffuse atrophic gastritis.

Symptoms.—Patients with pernicious anæmia are not infrequently well built, with broad faces, short deep chests and wide sub-costal angles; the hair is often prematurely grey, and the skin may be pigmented. Its incidence in persons of this type was first noted by Addison, whose description of the symptoms remains unsurpassed. "The disease makes its approach in so slow and insidious a manner that the patient can hardly fix a date to his earliest feeling of that languor which is shortly to become so extreme. The countenance gets pale, the whites of the eyes become pearly, the general frame flabby rather than wasted; the pulse perhaps large, but remarkably soft and compressible, and occasionally with a slight jerk, especially under the slightest excitement; there is an increasing indisposition to exertion, with an uncomfortable feeling of faintness or breathlessness on attempting it; the heart is readily made to palpitate; the whole surface of the body presents a blanched, smooth and waxy appearance; the lips, gums and tongue seem bloodless; the flabbiness of the solids increases; the appetite fails; extreme languor and faintness supervene, breathlessness and palpitations being produced by the most trifling exertion or emotion; some slight œdema is probably perceived about the ankles; the debility becomes extreme, the patient can no longer rise from his bed, the mind occasionally wanders, he falls into a prostrate and half-torpid state, and at length expires; nevertheless, to the very last and after a sickness of perhaps several months' duration, the bulkiness of the general frame and the amount of obesity often present a most striking contrast to the failure and exhaustion observable in every other respect."

A lemon-yellow colour of the skin was common in the days before liver therapy was introduced, but now that patients come under effective treatment early it is rarely seen. The same is true of splenomegaly, which requires considerable time for its development and is now found in only about 5 per cent. of untreated patients. The temperature may be slightly raised. Angina may occur from impoverishment of the blood supplied to the heart. The liver may be enlarged. The urine contains much urobilin and often a trace of albumin. Alimentary symptoms constitute an important chapter of the disease. Glossitis of the type described in idiopathic hypochromic anæmia occurs in

over 50 per cent. of cases, but curiously enough there is no tendency to involvement of the pharynx, or to dysphagia. It may precede the anæmia by some years. Achlorhydria is an invariable symptom, and pepsin is greatly reduced or absent. Achlorhydria has many times been demonstrated before the onset of the anæmia, and it persists when the blood has been repaired. Dyspepsia is frequently present, with flatulence, ill-defined generalised abdominal pain, soft bowel movements and recurrent attacks of diarrhœa. The dyspepsia is partly due to the achlorhydria, but it is greatly aggravated by the anæmia, and in the critical periods of the disease the pain and vomiting may be so troublesome as to prevent effective medication by mouth. If the trouble persists after repair of the anæmia, disease of the gall-bladder should be suspected. Nervous symptoms, due to subacute combined degeneration of the spinal cord, are an integral part of the disease, but for convenience they are described elsewhere (p. 1738). Mental symptoms appear in a small percentage of cases; they are usually delusions of persecution, and the patient swears that he is being poisoned by his relatives or his physician. Exceptionally such patients become stuporose and die in coma, even though their anæmia is not profound.

The cardinal feature of the blood picture is megalocytosis. By the time the patient seeks medical advice the red cells are often less than 2 millions per c.mm., and counts of the order of half a million have occasionally been obtained. Hæmoglobin is not reduced to the same extent as the red corpuscles and the colour index is above unity. Such complications as hæmorrhage may lower the colour index, but megalocytosis persists. The mean diameter of the red cells averages about 8·3 microns; there is much anisocytosis and poikilocytosis. Reticulocytes are within normal limits except during a remission, spontaneous or induced. Normoblasts and megaloblasts are often present, more especially in the agonal stages of the disease and also on the inception of very active treatment; they are rarely present in mild cases, and their diagnostic importance has been greatly overestimated. The serum is brownish-yellow, and the indirect van den Bergh reaction is positive. The white cells are reduced in number, an average count being about 4000; the decrease is chiefly due to diminution in the granulocytes and the monocytes. The neutrophil cells are of an old type, many having 5 or more lobes to their nucleus, and occasional giant neutrophils and myelocytes are present. Platelets are scanty.

Complications and Sequelæ.—Complications are infrequent, for subacute combined degeneration is one of the elements of the disease and not truly a complication. It is doubtful whether pernicious anæmia ever terminates in aplastic anæmia, and most reports of this sequel can be attributed to errors of diagnosis or to incomplete examination of the marrow after death; arsenic may have produced aplasia of the marrow in rare cases before liver was introduced into treatment. Gout and venous thrombosis occasionally occur, especially during intensive treatment. The gall bladder is diseased in about 25 per cent. of cases. It has been suggested that patients with pernicious anæmia are abnormally prone to carcinoma of the stomach, but the evidence is not statistically convincing. Intercurrent infection, whether from diminished resistance on account of the anæmia, or from the trophic or bladder lesions of spinal paralysis, is a very dangerous event.

Course.—In young subjects the disease may run an acute course, with

fever and purpura, and prove fatal after a short illness. Such a course is unusual, for remissions are one of the most constant features of the disease. The commonest number is two, but there may be five or six; their duration is about six months. The patient may feel perfectly well during a remission, but the blood rarely becomes quite normal. The untreated disease is usually fatal in one to three years, though exceptional cases may live much longer, as the result of an unusual remission. One of the patients at Guy's Hospital first came under treatment at age 30 for dyspepsia; at age 41 he was re-admitted for typical pernicious anæmia, with high colour index and megaloblasts, which responded to treatment by arsenic; he remained well till age 64, when he was readmitted to hospital for relapse of the pernicious anæmia of ten months' duration; he had complete achlorhydria; the anæmia responded to treatment with liver. The cause of the remissions is uncertain, but is probably a partial recovery of the secretion of intrinsic factor.

Diagnosis.—The disease is often suggested by the triad of symptoms, glossitis, anæmia and acroparæsthesia. It is confirmed by the blood picture, more especially the megalocytosis and anisocytosis, the absence of reticulocytosis, and the presence of hyperbilirubinæmia. In doubtful cases a test meal should be performed, for free hydrochloric acid in the gastric juice for all practical purposes rules out the diagnosis. Marrow obtained by sternal puncture or biopsy shows the pathognomonic megaloblastic degeneration. The megalocytic anæmias of nutritional and alimentary disease which closely resemble pernicious anæmia have already been discussed. An important differential diagnosis is from carcinoma of the stomach. In this disease the fæces contain occult blood, and the anæmia is usually of a hypochromic type. In a few cases the two diseases coexist, the pernicious anæmia being the result of a cancerous gastritis and achylia, or cancer developing in the stomach of a patient who already has pernicious anæmia. Aplastic anæmia may be mistaken for pernicious anæmia, but there is less anisocytosis and megalocytosis, van den Bergh's reaction is negative, free hydrochloric acid is frequently present in the gastric juice and liver treatment is unsuccessful. The rare diseases aleukæmic leukæmia and chronic hæmolytic anæmia can usually be differentiated by careful analysis of the symptoms and the blood. In the absence of complicating infection, anæmia which does not respond to liver treatment in effective dosage is very unlikely to be pernicious anæmia.

Prognosis.—The underlying deficiency is for all practical purposes incurable, but with thorough and persistent substitution therapy both the anæmia and the spinal symptoms can be completely arrested, and there is no reason why the patient should not live the normal span.

Treatment.—Treatment is by liver or stomach, as described at the end of the chapter (p. 821). I cannot too strongly emphasise the necessity of keeping the blood at a level of 5 million red cells per c.mm., and 100 per cent. of hæmoglobin if nervous and infectious complications are to be avoided. Many patients have a delusive sense of well-being with a blood count as low as 3 million red cells per c.mm., and 60 per cent. hæmoglobin, but at this level the degeneration of the nervous system may continue to advance. It is, therefore, essential to examine the blood at regular intervals. Even with a normal blood count, acroparæsthesia or increase of the nervous symptoms demands a larger dosage of effective substance. After all, it is

impossible to give an overdose. In patients who are profoundly anæmic transfusion may be necessary, but in view of its dangers it should, wherever possible, be withheld in favour of injections of liver extract. Hydrochloric acid may be advisable for the dyspeptic symptoms, but it is rarely necessary. Iron deficiency and hypothyroidism are occasional complications of pernicious anæmia. They should be suspected especially in patients in whom it is difficult to bring the blood completely back to normal, and they should be corrected by appropriate doses of iron or thyroid. Arsenic and intestinal antiseptics are to be avoided. Septic foci should be removed, though the operation should be postponed until the anæmia is under control.

On instituting successful treatment in a patient with pernicious anæmia there is a reticulocyte crisis, which reaches its maximum between the tenth and fourteenth days with oral therapy, and between the third and the seventh days with parenteral therapy. The peak is directly proportional to the severity of the anæmia, and values of 30 to 40 per cent. are by no means uncommon. The blood and the general condition of the patient are gradually restored to normal, glossitis becomes quiescent, and the surface of the tongue may be reclothed with filiform papillæ. The nervous symptoms improve more slowly, and gross spastic paralysis is unlikely to be repaired. Nevertheless the degree of improvement may be surprising. In more than one bedridden case I have felt I was doing the patient little service in curing his anæmia, but after months of careful treatment, massage and re-education, the patient has successively discarded his wheel-chair, his crutches and his sticks, and has returned to active employment.

LEUCO-ERYTHROBLASTIC ANÆMIA

Synonyms.—Osteosclerotic Anæmia; Myelophthisic Anæmia; Leukanæmia.

Leuco-erythroblastic anæmia is uncommon. It is found in association with certain diseases of the bones or bone-marrow, and is characterised by the presence in the peripheral blood of unusually immature red cells and a few immature white cells. It is described here rather than with the symptomatic anæmias because the disturbance of blood formation is so profound as to suggest an affinity with the dyshæmopoietic anæmias. The anæmia is characterised clinically not by its severity but by the number of cells in the peripheral blood that normally are confined to the marrow as precursors of the red and white cells of the blood. The colour index is commonly a little below unity and the mean diameter of the red cells usually within normal limits. Reticulocytes are constantly above normal and nucleated red cells are present, often in large numbers. The leucocyte count is commonly normal or only a little raised, but occasionally very high values may be observed, even above 100,000 per c.mm. There is always an excess of myelocytes and on many occasions myeloblasts are also present. The platelet count is usually low. The van den Bergh reaction is usually negative, unless complications are present. The spleen may be palpable, either as a result of myeloid metaplasia or more rarely from neoplastic infiltration. The anæmia is presumably due to irritation or disturbance in the maturation of the hæmopoietic tissues by the bony disease. It does not respond to iron or liver, and transfusion is the only effective treatment. Leuco-erythroblastic

anæmia has been observed in the following conditions, but in some of them it is the exception rather than the rule. In the adult, at any rate, malignant disease is much the most important cause of leuco-erythroblastic anæmia.

1. Erythroblastic Anæmia of Cooley [Thalassæmia or Mediterranean Anæmia].—This disease is practically confined to children of Mediterranean stock, and is characterised by numerous immature erythrocytes in the peripheral blood, mongoloid facies, splenomegaly and generalised bony changes due to hypertrophy of the marrow tissue. It is a hereditary condition which manifests itself soon after birth, and life is rarely prolonged past childhood. The bony dystrophy is similar to osteitis fibrosa, but pathological fractures are not common and symptoms come principally from the anæmia, which is severe and ultimately fatal. X-ray examination shows widening of the medullary portion of the bones, erosion and thinning of the cortex, and a peculiar fuzzy outline of the skull often compared to hair standing on end.

2. Marble-Bone Disease of Albers-Schonberg.—This is a congenital disease characterised by increased density of the bones, spontaneous fractures, splenomegaly, and anæmia which is often of the leuco-erythroblastic type. Symptoms usually begin in childhood with fractures following trivial injury and general backwardness. The anæmia is mainly due to narrowing of the marrow cavity from progressive broadening of the cortex and the X-ray appearances are pathognomonic.

3. Myelosclerosis.—In this bony dystrophy of unknown ætiology there is an excess of bone or fibrous tissue in the spongiosa and medullary cavity of the bones without any appreciable alterations in the corticalis or tendency to fracture. It is a disease of adult life. The only complaint is of the anæmia and there are no symptoms referable to the bones. The differential diagnosis from leukæmia may offer the greatest difficulty, though X-ray examination and biopsy of the skeleton may be of assistance.

4. Carcinomatosis of Bone.—As already emphasised, this is the most important cause of this type of anæmia. Symptoms of the primary growth may be elicited, and X-ray examination will usually reveal the metastases in the skeleton. It is often stated that growths of the thyroid and the prostate are especially liable to metastasise in the bones, but growths of the breast, stomach and lungs are more common causes of leuco-erythroblastic anæmia, owing presumably to their greater frequency.

5. Multiple Myeloma.—Only a small percentage of cases of multiple myeloma are accompanied by leuco-erythroblastic anæmia (p. 1390).

6. Leukæmia and Other Conditions.—In rare instances of leukæmia large numbers of reticulocytes and nucleated red cells may appear in the circulating blood as a result, presumably, of the leukæmic deposits in the bone-marrow. This phenomenon has sometimes been described as "mixed leukæmia" when myelocytes and erythroblasts appear in a case of lymphatic leukæmia, or as "leukanæmia" when the disturbance of erythropoiesis is prominent, but it is now believed to be a manifestation of the leuco-erythroblastic process. Numerous immature red and white blood cells may very rarely appear in the blood in the course of miliary tuberculosis, syphilis and Hodgkin's disease. The evidence suggests that in all such cases the bone marrow is involved and the blood disorder is of the leuco-erythroblastic type, but owing to their great rarity, their pathology has not yet been satisfactorily worked out.

APLASTIC ANÆMIA

Synonym.—Panmyelopathy.

Definition.—Aplastic anæmia is produced by aplasia of the bone-marrow, which results in reduction or total failure of blood regeneration. Usually all three elements in the bone-marrow—erythropoietic tissue, leucopoietic tissue and megakaryocytes—are simultaneously involved. Rare cases occur in which there is a pure lesion of one of these tissues, and not infrequently one of them is predominantly affected. The term *aplastic anæmia* is applied more particularly to cases in which the erythropoietic tissue is especially damaged. Aplasia of the leucopoietic tissues is described later under the title *agranulocytosis*, and aplasia of the megakaryocytes under the title *malignant thrombocytopenia*.

Ætiology.—The disease occurs at all ages and in both sexes. In a number of cases the aplasia of the bone-marrow is due to destruction by a well-recognised poison: 1. X-rays, radium and thorium; the latter two are most dangerous when they are taken into the body and produce persistent internal radiation. 2. Benzole and many of its derivatives, such as arseno-benzol, dinitrophenol, trinitrotoluene and the sulphonamides. 3. Mercury, silver and gold, the last of course being now widely used in the treatment of rheumatism and tuberculosis. 4. Acute infections, such as measles, scarlatina, diphtheria and typhoid; these causes are more potent in childhood. In a large proportion of cases no noxious agency can be traced and it is possible that many are due to an idiosyncrasy to substances not normally regarded as harmful, a phenomenon we have already learnt to recognise in amidopyrine agranulocytosis and sedormid purpura.

Pathology.—A variety of changes may be found in the marrow in refractory anæmias which have been regarded as aplastic during life. In the classical aplastic anæmia the marrow is hypocellular or acellular. An actual excess of erythropoietic tissue may be found in radium poisoning and in the rare *achrestic anæmia* which is believed to be due to inability of the marrow to utilise P.A. factor. In other cases the changes resemble leukæmia, Hodgkin's disease, or myelosclerosis, though no other organs are involved. Necrotic ulcers are commonly found in the mouth and more rarely in the bowel. The liver, spleen and lymph-glands show no gross change, but microscopically there is usually some hæmosiderosis of the liver and spleen, attributable both to the absorption of extravasated blood and to the breakdown of transfused red cells.

Symptoms.—It is possible to distinguish acute and chronic forms of aplastic anæmia, and it is clear that the degree of aplasia or hypoplasia of the marrow varies in different patients and probably at different times in the same patient. In one of my cases, which subsequently came to autopsy, the onset was abrupt, with jaundice and high fever. More common initial symptoms are hæmorrhage from the thrombocytopenia, and necrotic ulcerations from the leukopenia. Cases which begin acutely are liable to run a rapid course and terminate fatally in a few weeks or months. In chronic cases the presenting symptom is more likely to be anæmia and the disease may pursue a remittent course. Physical examination is commonly negative except for the anæmia and such complications as purpura and ulceration. There are

no specific alimentary or nervous symptoms, and the spleen and lymph glands do not enlarge. The blood picture is characterised by a decrease of all the cells, erythrocytes, leucocytes and platelets; the absence of immature white cells and nucleated red cells; and the lack of signs of reaction, such as hypochromia, anisocytosis and reticulocytosis. By the time a blood count is done the red cells have often fallen to about 1·5 million per c.mm. and the colour index is about unity. Van den Bergh's reaction is negative. The white cells are about 3000 or 4000 per c.mm., usually falling below 2000 before death; the diminution is chiefly due to the small number of polymorphonuclear cells. In chronic cases a very considerable degree of megalocytosis may develop, and so long as the colour index remains high and the leucocyte count low, the disease cannot be regarded as cured.

Diagnosis.—Acute cases are commonly mistaken for an infectious process and it should therefore be the rule to examine the blood in all cases of severe oral or faucial infection. Chronic cases are more often confused with pernicious anæmia, but do not respond to liver. Essential thrombocytopenia may be suggested by the low platelet count and the hæmorrhagic tendency, but is excluded by the leucopenia and the non-regeneratory character of the anæmia. Aleukæmic leukæmia offers most difficulty. The absence of enlargement of the lymph-glands, liver, or spleen, however, should differentiate aplastic anæmia from this disease. In doubtful cases a sternal marrow puncture or biopsy should be performed.

Prognosis and Treatment.—In all cases enquiry should be made for exposure to toxic substances. No very adequate statistics are available for prognosis, as aplastic anæmia has only recently been properly separated from other grave anæmias. It was formerly considered hopeless. Some patients recover outright and others continue without need of treatment for a number of years, but the seriousness of the illness should not be minimised. Probably the response to transfusion is the best guide. The blood should be brought approximately to normal by a rapid series of transfusions, or by a continuous transfusion of two or three litres of blood. If it is then possible to maintain a normal count by transfusions at intervals of two or three weeks, there is good hope that the bone-marrow may gradually regain its hæmopoietic function. But too often it is found that the transfused blood is lost by hæmorrhage or is quickly and mysteriously destroyed. However well the patient appears clinically, the prognosis should be guarded as long as the blood picture is abnormal, for such patients are always liable to sudden deterioration from infection or an acute hæmolytic reaction. Iron, liver and similar remedies are of little value.

THE HÆMOLYTIC ANÆMIAS

In discussing the symptomatic anæmias, I have mentioned the occasional development of anæmia from hæmolysis of the corpuscles by micro-organisms, bacterial toxins and other poisons. There is also evidence that excessive hæmolysis plays a part in the pathology of the megalocytic anæmias due to deficiency of hæmopoietic principles. There now remains for discussion a group of hæmolytic anæmias which are relatively uncommon and of which

the most important examples, acholuric jaundice, sickle-cell anæmia and the grave familial jaundice of infants, are due to congenital anomalies in the blood-forming organs. Before treating these diseases individually, it will be convenient to describe the characteristics which are common to all the hæmolytic anæmias. If a great many red cells are broken down in a short time, there are hæmoglobinuria and jaundice, but in chronic hæmolytic anæmia it is sometimes surprising how slight is the jaundice. The colour index varies according to the mode of reaction of the bone-marrow, but it is usually round about unity and there may be frank megalocytosis. Owing to the vigorous attempts of the bone-marrow to repair the anæmia, the reticulocyte count is high, and nucleated red cells and even megaloblasts appear in the peripheral blood. In chronic hæmolytic anæmia the white cells are unaffected or a little diminished. When hæmolysis is acute and rapid, there is a leucocytosis, during which very immature white cells may appear in the peripheral blood; the platelets first fall and later rise above their normal level. Apart from the hæmolysis, which gives rise to anæmia, enlargement of the liver, spleen, and occasionally the lymph-glands, hyperplasia of the bone-marrow and hæmosiderosis, there are no signs of systemic disease and the alimentary and nervous systems are normal.

1. ACHOLURIC JAUNDICE

Synonyms.—Spherocytosis; Congenital Hæmolytic Anæmia (type Chauffard-Minkowski).

This disease, which is due to congenital abnormality of the red corpuscles, and is characterised by increased fragility of the cells, a variable degree of jaundice and anæmia, splenomegaly, and a strong tendency to the formation of gall-stones, is described elsewhere (page 689).

2. SICKLE-CELLED ANÆMIA

Synonym.—Drepanocytosis.

Definition.—A severe anæmia, characterised by the appearance in the blood of a number of red blood corpuscles of a peculiar sickle shape.

Ætiology and Pathology.—Up to the present the disease has been observed only in the negro. It is hereditary and familial, behaving as a Mendelian dominant. In the affected families some members who have sickle cells in their blood do not suffer from anæmia. The disease usually dates from infancy. Of its essential cause, nothing is known. The post-mortem appearances do not throw any light upon the pathology.

Symptoms.—The patients are obviously anæmic, and the sclerotics exhibit a greenish-yellow tinge. The liver is bulky, but the spleen is not enlarged. The disease is characterised by intermittent paroxysms of fever, up to 103° or 104°, with severe stabbing pains in the muscles and joints, which last for two or three weeks. In the intervals the patients suffer but little, though they are listless and depressed. The red blood corpuscles in the intervals reach a number of about 3,000,000 per c.mm., but during the paroxysms they rapidly fall to less than half that number. The white cells are usually about 15,000 per c.mm., but may rise to as much as 40,000. The sickle-shaped corpuscles vary in numbers. They appear to increase in

number on a warm slide. The coagulation-time, the bleeding-time, the fragility of the corpuscles, and the numbers of platelets are all within normal limits.

Course and Prognosis.—The course of the disease is slow but progressive, and death usually occurs before the age of thirty.

Treatment.—Up to the present time, no treatment has appeared materially to influence the progress of the disease, and splenectomy is of no value.

3. OVALOCYTOSIS

In rare cases the red cells are elliptical, instead of being circular. This again is a familial abnormality, inherited as a Mendelian dominant, but it is not certain that it predisposes to anæmia.

4. FAMILIAL ICTERUS GRAVIS NEONATORUM

This is a familial disease in which successive infants in the same family become jaundiced within a few hours to a day after birth, though the first-born often escapes. The children become progressively anæmic, pass into a drowsy condition, and usually die in a few days or weeks. At its onset the disease resembles physiological jaundice. During intra-uterine life the red cells circulate in higher concentration than after birth, to compensate for the poor supply of oxygen from the placenta. It is probable that physiological jaundice results from the hæmolysis of superfluous corpuscles on the inception of pulmonary respiration, and that grave familial jaundice is a morbid exaggeration of this process. It is now recognised that grave familial jaundice is the most important manifestation of a pathological state known as *Erythroblastosis Foetalis*, which may affect several children of the same parents and appear in rather different guises. In *congenital hydrops* the child is still-born or dies a few hours after birth; the placenta is enlarged, the vernix caseosa is often a deep yellow colour, the body is dropsical and the blood anæmic. In *congenital anæmia of the newly-born*, on the other hand, the disease is less acute than in familial jaundice, there is little or no jaundice, but there is severe hyperchromic anæmia with numerous immature red cells in the blood, and enlargement of the liver and spleen. Post-mortem examination in all forms of erythroblastosis fœtalis usually shows much extra-medullary hæmopoiesis and considerable deposition of iron in the viscera. It is still not certain whether erythroblastosis foetalis is a hæmolytic anæmia, as suggested here, or whether it may not be a dyshæmopoietic anæmia due to a failure in the normal development of the red cells. The diagnosis is suggested by the family history, the large placenta and the golden vernix caseosa, and is confirmed by the discovery of an abnormal number of nucleated red cells in the blood smear. Treatment must be prompt, owing to the rapid progress of the anæmia and the deleterious effect of the jaundice which at this early age may produce degenerative changes in the central nervous system. Either 30 to 50 c.c. of blood should be given by transfusion, or 5 to 10 c.c. of the mother's serum should be injected intramuscularly daily. If given in time this treatment arrests hæmolysis and a complete and lasting recovery takes place.

5. ACUTE HÆMOLYTIC ANÆMIA OF LEDERER

Synonym.—Acute Febrile Anæmia.

Lederer's anæmia occurs most commonly in the first two decades of life, though cases have been observed at every age. The onset is acute, with fever, slight rigor, headache, lassitude and vomiting. Jaundice of more or less intensity appears early, though as a rule the patient is more anæmic than icteric. In the most acute cases there is hæmoglobinuria. A variety of symptoms may occur as a result of thromboses or infarcts in various organs. The red count may fall in a few days to a million cells per c.mm.; the red cells are usually normal in size and resistance, and the colour index is about unity. There is a reticulocytosis, often with many nucleated red cells. The white count is usually raised and occasionally there is a remarkable leucocytosis, with an outpouring of myelocytes and even myeloblasts in the circulating blood. The cause of the sudden breakdown of the red cells is unknown; it is not due to any recognised infection. The disease ends in death, or recovery within a period usually of two to six weeks. The differential diagnosis is from other forms of hæmoglobinuria (see p. 1292), from infections such as septicæmia, and from acute leukæmia. The mortality of the untreated disease is high. Treatment is by transfusion, repeated if necessary until the hæmolytic process appears to have been arrested. The results of such treatment are good and recovery once established is permanent.

6. HÆMOLYTIC ANÆMIA WITH RECURRENT HÆMOGLOBINURIA

Synonyms.—Nocturnal Hæmoglobinuria; Hæmosiderinuria; Chronic Hæmolytic Anæmia (type Marchiafava-Micheli).

A rare chronic disease characterised by paroxysms of hæmoglobinuria, which commonly occur at night, and persistent hæmolytic anæmia. It is a disease of adult life and affects both sexes. The spleen is usually enlarged though not to the same degree as in acholuric jaundice. The disease is differentiated from acholuric jaundice by the normal size, shape and fragility of the red cells, and the occurrence of hæmoglobinuria; and from the paroxysmal hæmoglobinuria of syphilis by the negative Wassermann reaction, absence of relation to exposure to cold, and persistence of anæmia between the paroxysms. There is no curative treatment; splenectomy has little effect and the disease usually leads to death after a few years.

7. CHRONIC ACQUIRED HÆMOLYTIC ANÆMIA

Synonym.—Hæmolytic Anæmia (type Hayem-Widal).

Chronic hæmolytic anæmias are occasionally encountered which are difficult to fit into any of the foregoing categories. Acholuric jaundice, like other hereditary diseases, does not always run true to type, and many of these cases are undoubtedly sporadic and atypical examples of acholuric jaundice. Others are probably larval or atypical forms of hæmolytic anæmia (type Marchiafava-Micheli) in which the hæmolytic process is not of sufficient

intensity to produce hæmoglobinuria. Syphilis and Hodgkin's disease may occasionally produce a hæmolytic anæmia; a Wassermann reaction should therefore be performed and careful search made for enlarged lymph glands. Leuco-erythroblastic anæmia must also be excluded. Iron and parenteral liver should be given a fair trial, as a deficiency dyshæmopoietic anæmia may occasionally simulate a hæmolytic process, more especially when complications such as intestinal ulceration are present. If the spleen is enlarged and anæmia persists after investigation and treatment on these lines, splenectomy should be advised, though improvement cannot be promised with the same confidence as in straightforward familial acholuric jaundice. Transfusion may be necessary to make the patient fit for operation; but it is sometimes followed by severe reactions in hæmolytic anæmia, and it is wise therefore to begin with a small " pilot " transfusion.

ANÆMIA IN PREGNANCY

The *physiological anæmia of pregnancy* is due to dilution of the blood in pregnancy owing to altered circulatory conditions and increased blood volume. The hæmoglobin rarely falls much below 75 per cent. in healthy women, the colour index is unity, and there is no hypochromia or poikilocytosis. It often gives rise to unnecessary anxiety. It is distinguished from pernicious anæmia by its mildness and from iron-deficiency anæmia by the normal colour index. It requires no treatment. The same circulatory phenomena are likely to aggravate *idiopathic hypochromic anæmia in pregnancy*, and in women who have suffered from anæmia in a previous pregnancy or who are unable to take an optimal diet, it is wise to prescribe iron as a prophylactic throughout the period of gestation and lactation. Megalocytic or hyperchromic anæmia is very rare in pregnant women in this country, though it is common in tropical or sub-tropical zones. The condition may have different causes, and the prognosis differs accordingly. The following causes of megalocytic anæmia in pregnancy have been differentiated.

1. *Nutritional macrocytic anæmia* is much aggravated by pregnancy, and then assumes a frankly megalocytic type.

2. Pregnancy may occur in a patient with *pernicious anæmia*, or pernicious anæmia may first begin in pregnancy, persisting after gestation; achylia gastrica is present, and subacute combined degeneration may develop.

3. Pernicious anæmia may occur as a temporary phenomenon during pregnancy, disappearing after gestation. The secretion of free hydrochloric acid may be normal, but there is evidence that the hæmatinic ferments are depressed, presumably as a result of the pregnancy. Subacute combined degeneration does not occur. The disease responds well to treatment by liver or stomach. It may or may not recur in subsequent pregnancies. This is the true *pernicious anæmia of pregnancy*, and it is very rare.

Hæmolytic anæmias, which should be separable from pernicious and allied anæmias by the Price-Jones curve and the reticulocytosis, also occur in pregnancy. Most frequently they result from infection by hæmolytic streptococci in the puerperium. It is also probable that the hæmolytic anæmia of Lederer occurs in pregnancy.

ANÆMIA IN CHILDHOOD

Anæmia in children is more difficult to classify than in adults, not merely because of the difficulty of making detailed studies of the blood and the other systems, but also because of the great lability of the blood-forming organs of children. A condition which in an adult induces a mild secondary anæmia, with slight leucocytosis and perhaps an occasional normoblast, in a child may induce profound anæmia, with the appearance of myelocytes and even myeloblasts and megaloblasts in the circulating blood; the spleen and the liver are more often enlarged. Both on this account and on account also of the small blood volume, anæmia is a more urgent disease in the child than in the adult; hæmorrhage is ill-tolerated, and a moderate nutritional anæmia may be fatally aggravated by a trivial intercurrent infection. Treatment should therefore be prompt, and it is often wise to give a transfusion of 50 to 200 c.c. of blood to tide over the interval before medical treatment can take effect. For similar reasons the results of treatment are often better in the child than the adult, and aplastic conditions of the bone-marrow which are almost inevitably fatal in the adult may be repaired in the child. Apart from certain rare congenital anæmias, the causes of anæmia in childhood are identical with those in later life, and with careful clinical and hæmatological examination, supplemented if necessary by the van den Bergh reaction, the fragility test and the Price-Jones curve, a satisfactory diagnosis should usually be obtained. In this way the vague titles formerly used, such as anæmia mitis and gravis, and pseudo-leukæmia, are gradually being replaced by more exact diagnoses.

Symptomatic Anæmia is little different from the same condition in the adult. Hæmorrhagic anæmia is rather unusual in childhood, while causes more peculiar to this age are cyclical vomiting, diphtheria, pyelitis and acute rheumatism. Anæmia may also be secondary to diseases of the blood-forming organs, such as splenic anæmia and Hodgkin's disease. Any type of anæmia in childhood may be complicated by infection, when very bizarre leukæmoid blood pictures may result. Cases characterised by the rapid development of anæmia, jaundice and hæmoglobinuria at one time appeared in epidemics among new-born children in hospitals and institutions (Winckel's disease), but they have practically disappeared with the introduction of antiseptic methods. They were probably due to infection by streptococci or hæmolytic colon bacilli, and sporadic cases still occur as a result of umbilical sepsis.

Dyshæmopoietic Anæmia.—There is a group of mild hypochromic anæmias in childhood which link the nutritional anæmia of infancy with the idiopathic hypochromic anæmia of later life. The condition has been described as *anæmia mitis* or *chlorotic anæmia of childhood*, but it is essentially due to errors of diet and impaired digestion. Treatment is by large doses of iron, and is very successful. Severe anæmia may occur in the course of cœliac disease, and in occasional instances it is of a megalocytic type and requires liver for its treatment; the anæmia may dominate the clinical picture and the fatty diarrhœa be overlooked. True pernicious anæmia rarely, if ever, occurs in childhood.

Aplastic Anæmia is by no means uncommon in childhood, occurring with

special frequency at the age of 12 or 13. It may be of any of the types described in the adult, and is sometimes known as *anæmia gravis*. The prognosis is bad, though perhaps less hopeless than in the adult.

Anæmia pseudo-leukæmica infantum is the term applied by von Jaksch to a group of cases of severe anæmia in children under 3 years of age, most frequent between 6 and 20 months. It is a disease of the poorer classes, and among them it has become uncommon in recent years. The onset of the disease is insidious, with increasing pallor and irregular fever. The abdomen is protuberant, owing to the size of the spleen, which often reaches the iliac crest and the middle line of the belly; the organ is hard, smooth and free from tenderness. The liver and superficial lymph-glands may be slightly enlarged, and purpura and hæmorrhage may occur. The erythrocytes are diminished to 2,500,000 or 3,000,000 per c.mm., and show some slight alteration in shape and size. Nucleated cells are always present—sometimes in large numbers. The hæmoglobin shows a decrease to from 20 to 40 per cent. of the normal, so that the colour index is low, from 0·5 to 0·7. There is nearly always a leucocytosis at some time during the course of the disease, but it is moderate, rarely reaching above 30,000, and sometimes the number may sink as low as 5,000. The feature of the blood films is the constant presence of myelocytes, which occur in numbers greatly above those found in any other disease except leukæmia, though seldom in numbers sufficient to suggest that disease. Not infrequently there is evidence of excessive blood destruction. It is now held that the syndrome described by von Jaksch is not a single disease-entity, but that it includes various types of anæmia of congenital, nutritional, or infectious origin, modified by the peculiar lability of the blood-forming organs in childhood. If gross lesions, such as leuco-erythroblastic anæmia, acholuric jaundice and splenic anæmia are not present, the prognosis is generally good; the anæmia is completely repaired and the spleen can no longer be palpated. Death may, however, occur from intercurrent maladies, such as acute diarrhœa or broncho-pneumonia.

It is obviously important to remove the cause when this can be ascertained, and malnutrition, rickets, tuberculosis and syphilis should receive their appropriate treatment. Iron and liver are usually of great service, and transfusion is indicated when the anæmia is severe. For the rest, every effort should be made to improve the diet and the general hygienic conditions. The patients do best with abundance of fresh air and light, and if possible should be nursed in the open air. Splenectomy is contra-indicated.

POLYCYTHÆMIA

Polycythæmia is a condition in which there is an increased number of erythrocytes per unit of circulating blood. It may be due to known causes, when it is called secondary polycythæmia, or *erythrocytosis*; or it may be an independent disease of the blood-forming organs, when it is called polycythæmia vera, or *erythræmia*. The following causes of erythrocytosis are known:

1. Concentration of the circulating blood, such as occurs in the dehydration of choleraic diarrhœa.

2. Diminution of the oxygen tension in the circulating blood or tissues.

Examples of this are—(*a*) residence at high altitudes; (*b*) cardiac diseases with cyanosis, especially congenital pulmonary stenosis and acquired sclerosis of the pulmonary arteries (Ayerza's disease, or cardiacos negros); (*c*) condi, tions interfering with normal pulmonary ventilation, such as emphysema-asthma, fibrosis and neoplasms of the lungs.

3. Chronic poisoning by a number of chemical agents, such as arsenic, phosphorus, carbon monoxide and aniline derivatives.

4. Cirrhosis of the liver, tuberculosis of the spleen, and similar conditions associated with splenomegaly or portal stasis, in rare instances.

5. A transient erythrocytosis may occur in the stage of recovery from anæmia.

These causes should always be excluded before diagnosing polycythæmia vera; in doubtful cases estimation of the blood volume is helpful, for polycythæmia vera should not be diagnosed unless the blood volume is considerably increased.

1. Polycythæmia Vera.

Synonyms.—Erythræmia; Splenomegalic Polycythæmia; Osler-Vaquez Disease.

Definition.—A disease characterised by well-marked and persistent increase in the number of red corpuscles due to an excessive erythroblastic activity of the bone-marrow.

Ætiology.—Erythræmia occurs more commonly in males in middle or later life, and in some studies there is evidence that it is especially prevalent among Jews born in eastern Europe. A recent theory is that erythræmia is related to Buerger's disease and is caused by sclerosis of the vessels supplying the bone marrow, so that anoxæmia develops and stimulates erythrogenesis. Familial cases of polycythæmia occur; they tend to be mild.

Pathology.—The marrow of most of the shafts of the long bones is converted into active red marrow. The spleen is enlarged and engorged, and often contains thrombotic infarcts. The liver is congested, but no anatomical change is present in it.

Symptoms.—Early symptoms are nervousness, headache, digestive disturbances and hæmorrhage from the distended vessels. The nervous symptoms take the form of lack of concentration, headaches, vertigo, or paræsthesiæ, on account of which the patient may be regarded as suffering from neurasthenia or hyperpiesia. Sometimes temporary disturbances of vision, aphasia or paralyses occur, which recover completely in a few hours. The patients are usually spare, with fair complexion and thin, often narrow, faces. There is cyanosis of the exposed surfaces, especially the cheeks, the tip of the nose and the ears. The colour varies with the temperature, being scarlet in a warm atmosphere and dark blue in the cold. The eyeballs are often bloodshot, the conjunctivæ deep red, the retinal vessels engorged and tortuous, the discs a little swollen. The spleen is palpable in three-quarters of the cases; it rarely extends beyond the umbilicus and varies in size, shrinking after a hæmorrhage or successful treatment. The liver is palpable in about one-half the cases. The urine may contain a little albumin. The blood contains from 7 to 14 million red corpuscles per c.mm., and the hæmoglobin may reach 200 per cent. The red cells are usually smaller than

normal, and the colour index is less than unity. The white cells are normal or moderately increased by a polymorphonuclear leucocytosis. In a few cases many myelocytes appear, as if there were a combination of erythræmia and leukæmia (erythro-leukæmia). The reticulocytes and the platelets are normal.

Complications.—The most important complications are vascular, and result from the increased volume and viscosity of the blood and its sluggish flow. It is noteworthy, however, that hypertension is no more common than in normal individuals in the same age-groups. Not uncommonly there are massive hæmorrhages, especially from the stomach, but also from the nose, lungs, bowel, uterus and bladder, or internally. Thrombosis is not infrequent, and in the cerebral vessels or the portal vein its consequences may be grave. It is rare for a case to progress any length of time without symptoms of peripheral arterial disease. In the beginning these take the form of acro-paræsthesia and vasomotor disturbances of a dilator (erythromelalgia), or spastic type (Raynaud's syndrome). Later, intermittent claudication and gangrene may follow. Peptic ulcer is probably a little commoner than in normal people. When the illness runs a long course leukæmia, myelosclerosis, purpura hæmorrhagica and anæmia may supervene, but it is not clear whether these conditions are the effect of the primary malady or of prolonged depression therapy.

Course and Prognosis.—The disease is very chronic, and sometimes it may exhibit long remissions. Life may be cut short by one of the vascular accidents or by infection, but many cases live to an advanced age.

Treatment.—Venesection relieves the symptoms, but its effects are temporary. The blood may be used for transfusion, and in hospital practice these patients are useful as donors. Phenylhydrazine is the most popular remedy. It destroys the excess of blood, and great care must be taken to avoid over-dosage. The dose is 1½ to 5 grains every other day until the count approaches normal; it should then be possible to find a dosage which will maintain a normal blood count, 2 grains a week frequently being sufficient. Some patients have been made dangerously anæmic as a result of incorrect diagnosis, overdosage with phenylhydrazine, or lack of supervision during treatment; jaundice, thrombosis, and necrosis of the liver and kidneys have also been observed. If phenylhydrazine produces gastro-intestinal disturbance, acetylphenylhydrazine may be tolerated; it is given in the same dosage. Arsenic is often effective if prescribed in high dosage (p. 822). X-ray treatment may also be used, though it is much slower and less certain in effect than in leukæmia. The rays should be applied over the long bones and the chest. This form of treatment is especially to be recommended when the white count is high, and in elderly patients who do not tolerate phenylhydrazine. Splenectomy is contra-indicated.

2. Methæmoglobinæmia and Sulphæmoglobinæmia

Synonym.—Enterogenous cyanosis.

Definition.—A condition characterised by cyanosis without cardiac or pulmonary lesions, associated with the presence of methæmoglobin or sulphæmoglobin in the circulating red cells.

Ætiology.—In the vast majority of cases the condition is due to the

use of drugs, especially aniline derivatives, and it has become much more common since the introduction of the sulphonamide group. Other drugs which have been incriminated are acetanilide, phenacetin, antipyrine, trional, sulphonal, potassium chlorate, and nitrites. Methæmoglobinæmia is produced by the direct action of the chemical or a breakdown product of it on the red cells. In sulphæmoglobinæmia the chemical sensitises the red cells, so that the hæmoglobin combines with hydrogen sulphide absorbed from the intestine. Sulphæmoglobinæmia is therefore much more likely to develop in constipated patients. A common sequence of events is: constipation; headaches; the use of headache powders which contain phenacetin or acetanilide; and sulphæmoglobinæmia. In very rare cases methæmoglobinæmia occurs spontaneously, apparently as a result of excess production and undue absorption of nitrites from the gastro-intestinal tract; this condition is known as *enterogenous cyanosis*. Equally rare is a familial form of methæmoglobinæmia attributed to an inborn error of metabolism—*familial idiopathic methæmoglobinæmia*. Chronic methæmoglobinæmia and sulphæmoglobinæmia are more common in women than men, and should always arouse suspicion of drug addiction, hysteria or malingering.

Symptoms.—The degree of cyanosis is sometimes out of proportion to the amount of methæmoglobin or sulphæmoglobin present, and it is probably aggravated through absorption by the red cells of coloured derivatives of the drugs themselves. The colour varies from a slight muddiness of the complexion to a deep blue. In marked cases the appearance of the patient is indeed ghastly, and yet it is belied by the comfortable general condition, the absence of any respiratory distress, and the extreme rarity of a fatal issue. In acute cases there may be no symptoms. In chronic cases the patient complains of weakness, nervousness, vertigo or fainting attacks, palpitation, headache and constipation. The blood may show a slight polycythæmia.

Prognosis.—In patients who are anæmic or who have to work at a high altitude, the condition may encroach dangerously on the reserve of functioning hæmoglobin. In other respects it is harmless.

Diagnosis.—The diagnosis depends on the spectroscopic examination of the blood for methæmoglobin or sulphæmoglobin. The brown colour of the blood can often be recognised with the naked eye. Methæmoglobinæmia, in which the altered hæmoglobin is within the corpuscles, must be distinguished from methæmalbuminæmia, in which altered hæmoglobin is present in the plasma; in the latter, there is no cyanosis, and the patient may be jaundiced. The use of drugs should always be suspected, especially in chronic and apparently inexplicable cases in women. It is surprising how skilfully they deceive their attendants and escape detection. I have known more than one woman who has lived many months in hospital and has been shown at medical meetings as a rare and mysterious case when all the time the symptoms were being produced by a bottle of phenacetin tablets concealed in the locker.

Treatment.—Recovery occurs spontaneously in 24 to 72 hours after the drug is discontinued. The cyanosis can be promptly relieved by the intravenous injection of methylene blue, 1 or 2 mg. per kilo, but it will return again if the offending drug is continued. It can be prevented, however, by the continuous administration of methylene blue by mouth, grains 1 or 2 four-hourly. Articles of diet and purgatives containing sulphur should be

avoided in patients under treatment by drugs likely to cause sulphæmoglobinæmia.

LEUCOCYTOSIS

It is important to be familiar with the normal fluctuations of the white cells. In healthy individuals the total number of white cells may vary from 3500 to 12,500 per c.mm., the average being 7500. A typical differential count is: neutrophils 66 per cent., eosinophils 2·5 per cent., basophils 0·5 per cent., lymphocytes 24 per cent., monocytes 7 per cent.; but there are great physiological variations which are best illustrated by the absolute values of the different cells. The total number of neutrophils may vary from about 1500 to 10,000; eosinophils from 0 to 1000; basophils from 0 to 500; lymphocytes from 600 to 4000; and monocytes from 0 to 1750. The total white count is at a minimum or basal level when the subject is at rest in the morning; activity, mental or physical, increases it by 60 or 100 per cent.; in addition there are rhythmical fluctuations in the number of polymorphonuclears, lymphocytes and monocytes, which are probably associated with the replacement of dead or emigrated cells. It is unwise to draw far-reaching conclusions from a single count of the white cells, and the test should always be repeated when an anomalous result is obtained, or when it is uncertain whether the figures fall within normal limits. The most obvious task of the white cells is to protect the body from attack and invasion by bacteria or similar agencies. They may be compared with a standing army which performs no useful service in times of peace, but which possesses great reserves which may be mobilised in time of war. We might press the analogy further and compare the three main groups of blood cells, the granulocytes, the lymphocytes and the monocytes, with the different fighting branches, for just as different types of warfare require different arms, so the three main groups of blood cells show independent variations in the various phases of an infection, and respond differently to different kinds of disease. An increase in the neutrophil leucocytes should strictly be called neutrophil leucocytosis or neutrophilia, but when the term leucocytosis is used without qualification it is taken to mean a neutrophil leucocytosis. Leucocytosis occurs physiologically during the later stages of pregnancy and for about a week after delivery; in the newly born infant; and after exercise, as many as 35,000 cells per c.mm. having been found after violent exertion. The causes of pathological leucocytosis are:

1. Hæmorrhage, or trauma in which tissues are injured and blood is extravasated.
2. Acute infections, especially by the pyogenic cocci.
3. Acute intoxications, such as diabetic coma, uræmia, gout, lead colic, coal-gas poisoning, and poisoning by a number of organic and inorganic substances.
4. Malignant disease, especially when the tumour grows rapidly, or involves the alimentary tract or the bone-marrow, and some cases of Hodgkin's disease.

The number of white cells in these conditions commonly varies from 12,000 to 40,000 per c.mm., according to the acuteness of the infection or intoxication, and the patient's ability to respond; in exceptional cases

the count may even exceed 100,000. The neutrophils are less mature than normal, or are altered by the toxæmia, so that many of the cells have only one or two lobes to their nuclei—a phenomenon described as the "shift to the left." In profound infections in which the patient's resistance is overcome there may be no increase in the total number of white cells but a considerable shift to the left is present; this is a sign of very ill omen. When there is a considerable leucocytosis, as in pneumonia and scarlet fever, small numbers of myelocytes may appear in the peripheral blood.

EOSINOPHILIA

The function of the eosinophil cells is not known, though it is suggested that they protect the body against the absorption of foreign proteins or of abnormal products of protein metabolism. Their number is increased by certain drugs, such as emetine, and also by feeding with whole liver. There is a rare condition of *hereditary eosinophilia* which sometimes manifests itself in different members of a family, and in which the normal proportion of eosinophils and neutrophils is reversed; in such cases infection is attended by a neutrophil leucocytosis and a temporary diminution of the eosinophilia. A constitutional tendency of the same kind is probably present in a number of individuals, and explains the high eosinophilia that may sometimes appear from trivial or unusual causes. In the symptomatic eosinophilias tabulated below it is rare for the total white count to be much increased, or for the eosinophils to exceed 20 per cent., but occasionally they may constitute over 50 per cent. of a total white count of 50,000 to 100,000. The eosinophils are usually increased in:

1. Infestation by parasites, especially hydatid cysts, ancylostomiasis and trichiniasis. *Loeffler's syndrome*, a condition in children in which transient pulmonary infiltrations are associated with blood eosinophilia, has been ascribed to the migration of larvæ of ascaris lumbricoides through the lungs.
2. Convalescence from acute diseases; they are diminished in the acute stage, except in cases of scarlatina in which there is a slight eosinophilia at the time of the eruption, and sometimes in acute rheumatism.
3. Allergic states, such as asthma and hay fever.
4. In many skin diseases.
5. In Hodgkin's disease in about one-quarter of the cases, but rarely to a high degree; and in rare cases of malignant growths, more especially when the peritoneum is involved.
6. In myeloid leukæmia and erythræmia.

Eosinophilia with Splenomegaly.

Synonym.—Eosinophilic Leukæmia.

This is an uncommon syndrome in which enlargement of the spleen is associated with persistent eosinophilia; the liver and the lymph-glands may also be palpable. The total white count is usually between 10,000 and 25,000, but it may exceed 50,000 cells per c.mm.; eosinophils constitute from 20 to 80 per cent., the majority being mature and only a small fraction myelocytes. Anæmia, if present, is of moderate degree. Post mortem the hyperplastic

bone-marrow is seen to be filled with eosinophils in all stages of development. Eosinophil cells are present in the other organs, especially the spleen and the lymph-glands, but here they are mainly adult cells. Areas of hæmorrhage and fibrosis may be found in the spleen and the lungs, and granulomatous tumours have also been observed. The benign course of the disease in many instances, the absence of anæmia, and the small percentage of myelocytes in the blood and tissues are arguments against regarding the condition as a true eosinophilic leukæmia. It is probably not a disease entity, but a syndrome of varied ætiology. Some cases are examples of hereditary eosinophilia in its severer form; others are acquired on the basis of asthma and bronchitis, syphilis, malaria, hepatic cirrhosis, myeloid leukæmia, Hodgkin's disease and other known causes; and a few cases remain obscure. The prognosis is moderately good, but death may occur from intercurrent infection. Splenectomy is contra-indicated, as it aggravates the eosinophilia. Great improvement follows anti-syphilitic treatment in cases with a positive Wassermann reaction.

LYMPHOCYTOSIS

Little is known about the function of the lymphocytes, though they are believed to play an important part in the protection of the mucosæ and the defence of the body from chronic disease. They are increased by exposure to ultra-violet light, and diminished by excessive X-radiation and by vitamin deficiency. Lymphocytes are more numerous in the blood of children than of adults, constituting from 40 to 60 per cent. of a total count of 7000 to 9000 white cells per c.mm., and their reactions to disease are much greater in early life. There are few infections in childhood which may not now and again be associated with an extraordinarily high lymphocyte count. The lymphocytes are especially increased in whooping-cough, chicken-pox, small-pox, typhus, malaria, and most constantly in glandular fever (acute mononucleosis). In isolated instances of these various infections the lymphocytes may rise as high as 75 per cent. or more of a total count of 100,000 white cells per c.mm., and leukæmia may be suspected. Usually the absence of anæmia should quiet this suspicion. The lymphocytes are moderately increased in the stage of healing of acute infections, and in tuberculosis which is progressing favourably. They are diminished in miliary tuberculosis and lesions of the lymphoid tissues, such as glandular tuberculosis, Hodgkin's disease, carcinoma and lymphosarcoma.

MONOCYTOSIS

The monocytes have only been differentiated from the lymphocytes in recent years, and not much is known about their behaviour in disease. They are increased during and after the crisis in acute infections, and also in active tuberculosis, sympathetic ophthalmia and undulant fever. Very high counts are occasionally obtained in miliary tuberculosis and infective endocarditis.

BASOPHILIA

The basophils are moderately increased in a number of diseases of the blood-forming organs, such as leukæmia, erythræmia and acholuric jaundice. The

increase of basophil cells in myeloid leukæmia is sometimes of diagnostic importance, as it may be the only abnormality present during a remission.

LEUCOPENIA

The strict meaning of the word "leucopenia" is a diminution in the total white cell count, but as the granulocytes are chiefly diminished in leucopenia, the word is often used to mean a diminution in the granulocytes. In the interests of accuracy it is better to use the terms *granulocytopenia* or *neutropenia* to indicate a diminution in the number of granulocytes or neutrophils respectively. While the majority of infections induce a leucocytosis, it is characteristic of certain diseases that the white count is normal or diminished. The most important infections in which there is leucopenia are the enteric fevers, undulant fever, influenza and measles. Leucopenia may also occur in septic infections when the resistance is overwhelmed by the severity of the infection; it is nevertheless unusual for the white blood count to sink to the low levels characteristic of agranulocytosis, and a total white count below 2500 should arouse the suspicion of an underlying abnormality in the blood-forming organs. Leucopenia resulting from septic infections differs from agranulocytosis in the presence of septic foci, positive blood cultures, and at autopsy the septic type of splenitis. As might be expected, leucopenia occurs in cachectic and debilitated states and in diseases of the blood-forming organs in which the leucopoietic tissues are depressed. There is a temporary fall in the number of leucocytes in the peripheral blood in anaphylactic shock and similar conditions, owing to the collection of the cells in the internal organs.

In the conditions already discussed the leucopenia is usually moderate in degree and produces no obvious clinical effects, the symptoms being those of the primary disorder. Leucopenia of a much more severe degree occurs in aplastic anæmia and leucopenic leukæmia. The bacteria which are constantly present on the surfaces of the body are then able to invade the tissues, and the trivial infections to which all of us are exposed take on a malignant character. The most common invaders are Vincent's organisms, with the production of fetid ulceration in the mouth and throat or elsewhere. Lesions such as cancrum oris, noma and putrid sore throat rarely develop unless the white blood cells are depressed. Such extreme leucopenia is nearly always accompanied by signs of damage to the other hæmopoietic tissues, such as anæmia and a tendency to bleed. The leucopenia is indeed only one manifestation of a general depression of marrow function. There are, however, cases in which the lesion is strictly confined to the white cells and the leucopoietic tissues, so that the red cells and platelets remain intact. It is to cases of this last type that the term *agranulocytosis* should strictly be confined, as they form a clinical entity with characteristic pathological changes, but the term is often loosely applied to any condition in which the white cell count is greatly depressed and necrotic ulceration is present.

AGRANULOCYTOSIS

Synonyms. — Malignant Neutropenia; Primary Granulocytopenia; Agranulocytic Angina.

Definition.—A disease characterised pathologically by profound leucopenia due to arrest in the development of the granulocytes, and clinically by an acute febrile illness, necrotic ulcerations and a high mortality.

Ætiology.—The majority of cases are due to an idiosyncratic reaction to drugs, especially amidopyrine and the sulphonamide group. The effect is to arrest the maturation of myeloblasts into myelocytes and polynuclear cells. Patients who have an idiosyncrasy to amidopyrine may become sensitive to the drug after taking quite a small quantity, and in the sensitised subject a dose as small as 0·2 g. may be followed by an abrupt diminution in the white cells and changes in the marrow. Agranulocytosis therefore occurs typically in patients who are taking amidopyrine in small doses or at long intervals. When a patient has taken a total of 50 g. amidopyrine with impunity (in divided doses of course) it becomes progressively less likely that he will become sensitive, though there can be no absolute surety of safety. The position with the sulphonamides is different. Agranulocytosis from the sulphonamide group rarely occurs until at least 30 g. of the drug has been taken. It is therefore infrequent before the tenth day and is more likely to be found with second or later courses of treatment. Agranulocytic syndromes may also occur after most of the poisons mentioned under aplastic anæmia (p. 785), but they are rarely so clear-cut and tend to be complicated by anæmia and hæmorrhage. Chronic and recurrent types of agranulocytosis are occasionally met with, especially in females, for which no explanation can be found. There is also a very rare disease, *hypoleukia splenica* or *primary splenic granulocytopenic leucopenia*, in which chronic agranulocytosis occurs in association with splenomegaly, without cirrhosis or drug and bacterial idiosyncrasies, and is completely relieved by splenectomy.

Pathology.—Necrotic, ulcerative or gangrenous lesions are present, most constantly in the mouth and pharynx, but they may affect any part of the alimentary canal, the rectum and in women, the vagina. Œdematous or brawny swellings may be present about the teeth, the neck, in the subcutaneous tissues, or elsewhere. The bone-marrow contains its normal complement of megakaryocytes, and erythropoiesis is normal, but granular leucocytes and myelocytes are absent; in cases dying early, small islands of myeloblasts are seen, but in the later stages these too may disappear and the only white cells seen in the marrow are focal accumulations of lymphocytes.

Symptoms.—In cases due to amidopyrine, there is often a long history of mental or physical over-exertion, followed by chronic fatigue, loss of weight and vague pains in the limbs. If the blood is examined in this prodromal phase, leucopenia of moderate degree will be found. Acute symptoms are often precipitated by dental extraction or an influenzal attack. The onset is abrupt, sometimes with rigors, and the patient complains of aching pains in the limbs and sore throat, and is rapidly prostrated. The temperature is high, ranging from 100° to 105° F. In the majority of cases ulcero-membranous lesions soon appear on the tonsils and gums, and the cervical glands may be enlarged, with surrounding brawny induration. As already indicated, other mucous surfaces may be involved, and in rare cases the sole infective lesion may be a mild redness of the throat without any other tissue or blood infection. The patient is pale but not anæmic. The liver and the spleen may be palpable, and jaundice is an occasional complication. As the disease advances the usual symptoms of a profound toxæmia appear. Examination of the

blood at this stage shows a total white count below 2000, often only a few hundred cells per c.mm.; the reduction affects especially the granulocytes, which may be diminished to about 5 per cent. or even completely absent.

Diagnosis.—Cases arising in the course of another illness which has been treated by amidopyrine or one of the sulphonamides may be very difficult to recognise. The diagnosis depends chiefly on the history and the blood picture. Specific inquiry should be made as to the use of amidopyrine, which is contained in many analgesic and hypnotic preparations, and sulphonamides, which are now very extensively prescribed. I have seen several cases in which the amidopyrine hypothesis had been discarded, but further questions revealed the fact that the drug had indeed been used or was still being used. Aplastic anæmia and leukæmia can be excluded by the blood picture, as the red cells and platelets are not affected in agranulocytosis, and there are no primitive white cells such as appear in acute leukæmia.

Course and Prognosis.—Spontaneous recovery from an acute attack may occur, but the mortality of untreated cases is about 75 per cent. In the fulminating type the patient succumbs in two or three days. In the usual acute type death or recovery occurs within a few weeks. In patients who have recovered from an acute attack and in cases where the disease has been recognised before the onset of acute symptoms, the leucocytes gradually return to a normal level if no more drug is taken; it may be six months before the normal figure is reached. The duration of sensitivity to amidopyrine and sulphonamides is not known—it may be life-long—and patients who have had symptoms of agranulocytosis should never use the drugs again.

PROPHYLACTIC.—No one should ever be given a prescription which allows amidopyrine to be taken without close medical supervision. If drugs of the sulphonamide group are given for more than a week, the blood should be examined at frequent intervals. The occurrence of drug fever 7 to 10 days after beginning sulphonamide treatment may herald the onset of agranulocytosis. Sudden deterioration in the condition of a patient who is being treated with amidopyrine or sulphonamide should always suggest a white blood cell count.

Treatment.—Treatment is disappointing; hence the importance of careful supervision of patients who are taking amidopyrine and sulphonamides, and their immediate prohibition in agranulocytosis. The remedy most commonly used is pentose nucleotide (pentnucleotide), 10 to 50 c.c. of which are injected intramuscularly every day; it often causes troublesome reactions, such as præcordial distress, rigors and fever. Liver extract may be tried in a dosage of 4 to 5 c.c. intramuscularly daily. Other remedies which have been used are neoarsphenamine injections, stimulating doses of X-rays to the bones, and transfusion, but there is no convincing evidence that they are efficacious. For local treatment the mouth may be sprayed with a saturated solution of potassium chlorate, and ulcerated areas then swabbed with a solution of copper sulphate, 10 grains to an ounce of water. Abscesses and areas of cellulitis should be drained but only essential surgery should be done. General treatment suitable to an acute febrile illness should not be neglected. In the chronic cases in which there is leucopenia but no fever or infection a ten-day course of pentose nucleotide, 20 c.c. intramuscularly daily, may be given once a month until the white count is stabilised at a normal level. A long holiday by the sea or in the mountains, away from crowded centres of

infection, is the ideal prescription. If this cannot be procured the effects of ultra-violet irradiation may be tried. The diet should be rich in vitamins and in purin foods. Teeth may be scaled and cleaned, nasal sinuses treated by postural drainage, and pyelitis treated by mandelic acid; but dental extractions and the radical extirpation of septic foci should be postponed until the white count is stabilised at a normal level.

LEUKÆMIA

Synonym.—Leukosis.

Definition.—Leukæmia is a morbid condition characterised by widespread hyperplasia of the leucopoietic tissues, either myeloid or lymphatic, which is usually associated with qualitative and quantitative changes in the white cells of the circulating blood.

Ætiology.—The ætiology is unknown, and the disease appears to occupy an intermediate position between the reaction to infections and noxious agencies on the one hand and the true neoplasms on the other. Leukæmia occurs in the lower animals also, and (like the sarcomata of these animals) it is sometimes transmissible by cell-free filtrates. In its more acute forms in man it often resembles an infection, and very similar changes in the blood and the blood-forming organs may sometimes be produced by infections and similar clearly apprehended agencies; it is difficult, however, to reconcile the tumour-like growths which sometimes develop in leukæmia with a hypothesis of infection. It differs from the ordinary neoplasms in being a system-disease, and affecting the whole organ simultaneously. The neoplastic hypothesis presents fewer difficulties, the diffuse character of the lesion being explained by the labile character of the leucopoietic tissues and being paralleled by the diffuse carcinomas of the breast and the cirrhotic liver. In experimental animals leukæmia has been induced by indole, benzole and tar, and in man it has been thought to be unduly frequent in those whose work exposes them to benzol, X-rays and radium. There is much similarity between leukæmia and erythræmia, and at times the two diseases appear to occur simultaneously, an erythro-leukæmia. Heredity is not known to play any part in the incidence of leukæmia. In a few instances the disease has followed injuries to the bones.

Classification.—We might expect to find forms of leukæmia corresponding to each of the different types of white blood cell, and classify them accordingly. In practice it is found that the only forms of leukæmia which occur at all frequently are those which involve predominantly the neutrophils and their precursors, or myeloid leukæmia, and those which involve the lymphocytes, or lymphatic leukæmia. Eosinophilic leukæmia has already been discussed; in exceptional cases of myeloid leukæmia basophil cells may predominate. Monocytic leukæmia has recently attracted much interest, but many cases so described are actually myeloblastic leukæmia, and in the majority, at any rate, myeloblasts or myelocytes as well as monocytes are present in the blood and tissues. In cases in which monocytes predominate, the leukæmia is usually acute or subacute, with fever, severe anæmia and necrotic mouth lesions, and a tendency to temporary remissions and aleukæmic phases. In leukæmia the immaturity of the cells is just as important

as the type of cell present, and for clinical work the leukæmias are therefore described as chronic myeloid leukæmia, chronic lymphatic leukæmia, and acute leukæmia. Whichever strain of cells is affected, the disease breeds true, and the two groups of cells are never involved simultaneously. Confusion has sometimes arisen owing to the ease with which very immature cells of the myeloid series, the myeloblasts, can be mistaken for lymphocytes. In acute leukæmia the cells may be so very immature that it is impossible to determine their origin, but the clinical features of acute lymphatic and acute myeloid leukæmia are identical.

1. Chronic Myeloid Leukæmia.

Synonyms.—Myelocytic Leukæmia; Spleno-Medullary Leukæmia; Chronic Leukæmic Myelosis.

Ætiology.—The disease is more common in males, who make up 60 per cent. of the cases. It is very rare before puberty, and more than half the cases begin between 30 and 50, the greatest incidence being between 35 and 45.

Pathology.—The changes which are found in the body are almost confined to the hæmopoietic organs. The bone-marrow is firm and fleshy, pale pink or grey in colour, rarely of a greenish hue. The predominant cell is the myelocyte, but there are also large numbers of myeloblasts and nucleated red cells. The spleen is usually enormously enlarged, but its outline is preserved; its surface is smooth, its consistence firm, its colour on section a greyish-red, usually mottled with infarcts. Microscopically the Malpighian corpuscles are obliterated, and the pulp is filled with myeloid cells and resembles the bone-marrow. The liver is large, firm, and of a pale yellow tint, and its capillaries contain large numbers of myelocytes. The other organs may show anæmia, hæmorrhages, and infiltration with myelocytes.

Symptoms.—Early symptoms are easy fatigue, slight loss of weight and strength, and gastro-intestinal disturbances, but the patient may first complain of the enlargement of the abdomen due to the increasing size of the spleen. The anæmia at this time is not marked, indeed the appearance is not seldom one of good health. Pain in the left side is sometimes felt, either as a result of the dragging weight of the enlarged spleen or from perisplenitis over an infarct. The average duration of symptoms before medical advice is sought is about a year. Fever is commonly slight, and there are often long periods of normal temperature interrupted now and then by small rises of short duration to 101° F. or 103° F. The basal metabolic rate is increased. Tenderness is often present over the sternum, more marked during exacerbations of the disease.

On examination the striking feature is the size of the spleen. It occupies the greater part of the left side of the abdomen, often reaching to the iliac crest below the middle line at the umbilicus. It forms a hard smooth tumour, with rounded edges, not tender to palpation and easily recognised by the characteristic notches in the anterior margin. The size tends to vary in the course of the disease, often leading to false hopes as to the efficacy of treatment. Sudden enlargement is due to hæmorrhage or infarction, and marked diminution nearly always occurs with the approach of death. The liver is larger than normal, and smooth. The lymph-glands are rarely palpable, except sometimes near the end. Impairment of vision may occur

from leucocytic accumulations or hæmorrhages in the retina, while involvement of the inner ear may lead to deafness and Ménière's syndrome.

In the later stages the anæmia becomes severe and cachexia develops. Ascites and œdema make their appearance, the heart weakens, and the patient becomes emaciated. Hæmorrhage is frequent, but rarely lethal. Death occurs from exhaustion or from intercurrent infection. It should be noted that infection may produce a temporary improvement in the blood picture, but such a remission is often followed by an aggravation of the disease, which then pursues an acute and rapidly fatal course. Conversion of chronic into acute leukæmia may also happen spontaneously.

The Blood.—The principal characteristics are progressive loss of hæmoglobin and of red cells, and increase, frequently enormous, of the leucocytes. The white count ranges from 100,000 to 1,000,000 cells per c.mm., values about 400,000 being most usual. The increase is mainly composed of cells of the granulocyte series. The typical cell is the neutrophil myelocyte, which constitutes 20 to 40 per cent. of the total; but the neutrophil, eosinophil and basophil polymorphonuclears are also increased, eosinophil and basophil myelocytes are present, and occasional myeloblasts are encountered. The anæmia is of the orthochromic type, and as it becomes more severe, anisocytosis and polychromasia develop, and nucleated red cells appear in the blood. The platelets are normal or slightly increased at the beginning of the disease, but decrease in the terminal phase.

Diagnosis.—This is usually made with ease from the characteristic blood picture and the great splenic enlargement, though difficulty may arise when the white cells fall to normal or subnormal values as a result of excessive treatment or of a natural remission of the disease. In these circumstances the presence of immature white cells and of basophilia may indicate the correct diagnosis. Myeloid leukæmia usually runs true to type and rarely presents an aleukæmic phase. The differential diagnosis of chronic myeloid leukæmia and myelosclerosis may be very difficult but will rarely be of great clinical importance.

Course and Prognosis.—Chronic myeloid leukæmia is invariably fatal. The average duration of life is just over 3 years from the onset of the disease, or 2 years after coming under treatment. There is no evidence that treatment prolongs life, though it greatly increases the comfort of the patient. In any large series exceptional cases are observed in which life is prolonged for 10 to 20 years. One of my cases was under observation for 22 years from age 38 to her death from bilateral hydronephrosis at the age of 60; in her the disease seemed to be of a benign character, and though there was great splenic enlargement, the highest white count was only 35,000, with 26 per cent. myelocytes. At the other extreme are subacute cases which shade indefinitely into acute leukæmia. The prognosis in an individual case will depend on the general condition of the patient and the presence or absence of cachexia, the degree of anæmia, and the height of the white count, very high and also very low values being unfavourable. Enlargement of lymph nodes and the appearance in the blood of large numbers of myeloblasts are each unfavourable signs. (See also under Treatment.)

Treatment.—The treatment of chronic myeloid leukæmia is practically confined to the use of X-rays and arsenic. Both agents owe their reputation to their remarkable power of producing a temporary remission in the disease.

The natural course of chronic myeloid leukæmia is steadily downhill, and during the latter half of the untreated disease the patient is confined to his bed, cachectic and miserable. After a course of treatment with X-rays or arsenic, the patient is restored to what he feels his normal condition. The spleen usually remains enlarged and the blood abnormal, but in rare cases the blood returns almost to normal and the spleen recedes beneath the costal margin. Such a remission lasts from a few months to a year, when repetition of the treatment again produces improvement, though not so complete as before. After a varied number of cycles treatment finally becomes ineffective, and a time arrives when despite all efforts the patient becomes steadily worse. The period of decline is usually swift, and in the majority of cases death occurs within four or five months of entering this final phase. Iron and to a less extent liver are valuable adjuvants to X-ray therapy. Splenectomy is contra-indicated in leukæmia, and leucotoxic drugs such as benzol and thorium-X are not without danger. Anti-leucocytic sera have been employed, but have not emerged from an experimental stage.

2. Chronic Lymphatic Leukæmia.

Synonym.—Chronic Lymphadenosis.

Definition.—A chronic overgrowth of the lymphatic tissue throughout the body, accompanied by an increased number of lymphocytes in the blood.

Ætiology.—The disease is one of middle and later life, and is never met in children. The average age of incidence is 55, over ten years later than chronic myeloid leukæmia. Males are affected about four times as often as females. The cause is not known. Chronic lymphatic leukæmia is much the rarest of the three main types of leukæmia, and it accounts for less than one-sixth of all the cases.

Pathology.—Post mortem, the striking feature is the enlargement of the lymph-glands and other lymphoid tissues. The glands are seldom larger than a walnut, discrete, homogeneous, and pinkish-grey on section. The lymphoid tissue of the pharynx is hypertrophied, and lymphoid nodules may be present in the intestines, the kidneys and elsewhere. The liver and spleen are uniformly enlarged, the bone-marrow is hyperplastic, and grey or greyish-red in colour.

Symptoms.—The disease may be present for months or years before the patient feels it necessary to consult a physician. Swelling of the glands is usually the first symptom to attract attention, or the patient may complain of increasing tiredness and loss of weight. Less frequently enlargement of the tonsils is first noticed, or enlarged glands and spleen are discovered by chance during a routine examination. In exceptional cases a tumour extirpated by the surgeon is found to be a lymphoma, and subsequent examination of the blood reveals chronic lymphatic leukæmia. Other early symptoms are itching eruptions of the skin, and impotence.

In typical cases all the superficial lymph-glands are enlarged. The enlargement is moderate and the glands are rarely so big as in Hodgkin's disease or lympho-sarcoma. They are freely movable and not adherent to one another, moderately hard, and do not alter in consistence during the course of the disease. Spontaneous fluctuations in their size may occur. In atypical cases only one group of glands may be enlarged. The tonsils may

be hypertrophied, the spleen is nearly always palpable, though it does not often extend more than a hand's breadth below the costal margin, and the liver is enlarged. Tenderness of the sternum or of the long bones is unusual. Hyperplasia of the lymphoid tissue in various parts of the body may lead to the formation of tumours or other unusual symptoms. Nodular lesions, infiltrations and actual tumours may develop in the skin. Enlargement of the thymus and the mediastinal lymph-glands may produce the signs of an intrathoracic tumour. Lymphomata may develop in the breast or other organs. The salivary and lachrymal glands may be symmetrically enlarged, producing one of the varieties of Mikulicz's syndrome.

The Blood.—The red cells and hæmoglobin are unaffected in the early stages, but, later, severe anæmia develops, with anisocytosis, polychromasia and nucleated red cells. The platelets are unaffected till the end, and hæmorrhage is rare. The total white count is increased, usually to about 200,000 cells per c.mm., but not to the high level seen in chronic myeloid leukæmia. Lymphocytes predominate and may constitute 95 to 99 per cent. of the white cells. The majority are small lymphocytes, though a few large lymphocytes are nearly always present. The nuclei may be more deeply indented than normal, and azur-granules are usually absent. The absolute number of polymorphs is unaltered, and no myelocytes are present. It is probable that the proliferation of lymphoid tissue in the glands and elsewhere may precede by some time the increase of lymphocytes in the blood stream. In rare cases the blood is normal when the patient first comes under observation, but, later, the characteristic picture develops (*aleukæmic leukæmia*); or the total white count may not be increased, though there is a high percentage of lymphocytes (*leucopenic leukæmia*).

Diagnosis.—Only in the rare aleukæmic cases is diagnosis difficult. Points of importance are the generalised enlargement of the lymph-glands, their uniform consistence and moderate size, and the enlargement of the liver and spleen. Biopsy of a gland or sternal puncture may assist.

Prognosis.—The disease is invariably fatal. The average duration is 3½ years from the onset, or about 18 months after coming under treatment. A few cases are more chronic, and exceptionally life may be prolonged for 10, 15 or 20 years. Death occurs from cachexia, hæmorrhage, or most commonly from intercurrent infection, sepsis being a very dangerous complication. It is doubtful whether treatment greatly modifies the course of the disease.

Treatment.—X-rays should be applied to the lymph-glands, but not to the spleen, as irradiation of the spleen produces little benefit and is often followed by severe reactions. Arsenic and ultra-violet radiation may also be employed.

3. Acute Leukæmia.

Ætiology.—Acute leukæmia is not a very rare disease, but many cases go unrecognised, because of the close simulation of other diseases and the difficulty of diagnosis without careful examination of the blood. It is more frequent in childhood and early adult life, but may affect any age. Males predominate in a ratio of about 2 to 1.

Symptoms.—The onset is usually abrupt, and more than half the cases begin with symptoms regarded as a cold, influenza or bronchitis; it is only

when the infection fails to respond to treatment and the patient remains prostrated that a more serious disease is suspected. Other early symptoms are ulcerative stomatitis, or tonsillar enlargement with sore throat, and some cases first come under the physician's care after a prolonged hæmorrhage from tonsillectomy, dental extraction or some trifling operation, which has left the patient exsanguinated. The course of the disease varies from fulminating cases in which the patient succumbs within a week, through cases of average acuteness with a duration of less than 2 months, to subacute cases which shade indefinitely into chronic leukæmia. Usually the rapid development of anæmia, weakness and loss of weight soon compels the patient to take to his bed. He complains of sore throat, headache and pain in the bones. The temperature becomes high and purpuric manifestations set in, which aggravate the anæmia or bring the patient's sufferings to an abrupt termination by loss of blood or cerebral hæmorrhage.

On examination the extreme pallor and the enlargement of the superficial lymph-glands, especially those in the neck, first attract attention. The pallor is most striking when there are in addition purpuric hæmorrhages into the skin, varying in extent from a pinpoint to large patches which may break down and ulcerate. The size of the spleen varies; usually it is easily palpable, but it may not be felt, or it may be greatly enlarged. The liver may be enlarged. The lungs may show bronchitis, broncho-pneumonia, or pleurisy, with or without effusion. Pericarditis and endocarditis may occur. The mind usually remains clear to the end. Certain symptoms may be so prominent as to colour the whole clinical picture and give a special aspect to the disease. In the anginal type, there is necrotic ulceration of the tonsils or other areas of the buccopharyngeal mucous membrane, or bleeding from the gums, complicated by secondary infection. In the hæmorrhagic type, purpura and hæmorrhages are the predominant features, and the disease may be mistaken for purpura hæmorrhagica. There may be hæmorrhage from any of the mucosæ, and in one of my cases there was so much blood in the urine that firm clots formed in both pelves and ureters, leading to death from suppression of urine. Disturbances of vision or deafness may result from hæmorrhage into the retina or the labyrinth. The fever and slight splenomegaly may be suggestive of some systemic infection, and there may be leucopenia and an eruption resembling the rose spots of typhoid fever. Bone pains may suggest the diagnosis of acute rheumatism, and there may even be serous effusion into the joints.

In the more subacute forms of the disease, tumours may develop in various parts of the body. They are composed of undifferentiated white cells and infiltrate the surrounding tissues like a malignant growth. Plum-coloured nodules appear in the skin or in the gastro-intestinal tract, in the latter situation leading to vomiting or profuse diarrhœa, often blood-stained in character, or to intussusception of the bowel. In the abdomen or in the mediastinum large growths may develop from the lymph nodes or the thymus, compressing and infiltrating the adjacent structures. Tumours of the bones have been distinguished by the special title of *chloroma*, owing to the greenish colour sometimes seen in the freshly cut surface of the growth. They have a predilection for the subperiosteum of the orbit, and cause headache, deformity of the temporal and frontal bones, exophthalmos, proptosis, papilloedema and swelling of the veins of the head, neck and

face. They may, however, occur in other parts of the skeleton, and sometimes seem to arise within the bone, which is expanded over them in a brittle shell. The spinal meninges may be invaded, with consequent transverse myelitis, while infiltration of the nerve roots leads to peripheral nerve palsies. It is a curious feature of these neoplastic phenomena that they often begin with a very atypical blood picture, the total white count not being greatly increased and in rare cases the differential count being normal at the onset, though the typical blood picture of leukæmia appears later.

Hæmatology and Pathology.—The outstanding feature of the blood in acute leukæmia is the presence of a large number of mononuclear cells of a primitive type, except in rare cases of acute lymphatic leukæmia in which the predominant cells may be typical lymphocytes. In something like 90 per cent. of all cases of acute leukæmia these primitive cells belong to the myeloid series, the majority being myeloblasts. They are usually larger than the normal white cells; their nucleus, which is round or oval, consists of a pale-staining chromatin reticulum in which 4 or 5 nucleoli may be distinguished; the deep blue cytoplasm contains no granules. Careful staining often reveals some cells with a few myelocyte granules, and a larger or smaller number of typical myelocytes may be present, especially in the more chronic cases. The total white count is rarely high in the early stages of the disease, usually not exceeding 25,000 to 30,000 per c.mm., but as a rule there is a rapid rise to 100,000 or more before the termination. Primitive cells constitute 90 per cent. or more of the white blood cells. Sometimes the total number of white cells is diminished and the count may be below 1000, the majority of the cells being myeloblasts. Such *leucopenic* cases are very prone to necrotic ulcerations and infectious complications. Much more rarely both the total and the differential white count are normal at the onset of the disease, as if the morbid process had not yet invaded the blood stream—*aleukæmic leukæmia*. The overgrowth of the primitive white cells in the marrow and the hæmorrhages soon lead to a profound anæmia, usually of an aplastic or hypochromic type. In very exceptional cases numerous normoblasts and megaloblasts appear in the blood stream, there may be frank megalocytosis, van den Bergh's reaction is positive, and at post-mortem excess of iron pigment may be found in the liver and spleen. The number of platelets is diminished in almost all cases, and sooner or later this is reflected in the hæmorrhagic character of the disease. The bleeding-time is prolonged, the tourniquet test is positive, and the clot may not retract well.

The post-mortem findings vary only slightly from those of chronic leukæmia. There is diffuse hyperplasia of the leucopoietic tissues in the marrow, lymph-glands and spleen, and all the tissues are infiltrated with myeloblasts, which may form nodules or tumour-like masses in various situations. Terminal hæmorrhagic and infectious lesions are rarely absent.

Diagnosis.—Acute leukæmia may simulate a number of diseases, among which may be mentioned the severe systemic infections, septic or diphtheritic inflammation of the mouth and throat, scurvy and the hæmorrhagic diseases, malignant disease or tumours of bone. Usually the blood picture will be decisive, but the possibility of agranulocytosis or of septic infection should be remembered in cases in which only a few immature white cells are present

in the blood. Glandular fever may cause confusion in the early stages, but the benign course and the absence of anæmia and hæmorrhages will soon differentiate it from leukæmia; in doubtful cases the heterophil antibody reaction, a serological test which is positive in glandular fever and negative in leukæmia, may be employed. The blood picture in acute leukæmia is sometimes suggestive of pernicious anæmia, but the other symptoms of that disease and its favourable response to liver are absent. In difficult cases examination of a bone-marrow smear obtained by sternal puncture may be decisive.

Prognosis and Treatment.—Few diseases are more tragic than acute leukæmia, as it is invariably fatal and it so often affects lives which seemed full of promise. Onset at an early age, high fever and great immaturity of white cells, all point to a speedy fatal issue. Death often comes by intercurrent infection, especially in the leucopenic cases, or as a result of hæmorrhage. Rarely the disease may pass into a subacute or chronic form, and death be postponed for a year or longer. Treatment is mainly directed to checking infection, especially about the mouth and throat, and preventing hæmorrhage. Intravenous injections of neoarsphenamine may cause the necrotic ulcerations to heal, and they may also be swabbed with a paint of equal parts of Fowler's solution, tincture of ipecacuanha and glycerin. Blood transfusion may bring the patient into a suitable condition for X-ray treatment, which is otherwise contra-indicated by the low number of normal polymorphonuclear cells, but any improvement is usually evanescent and it rarely does more than protract a painful situation.

THE HÆMORRHAGIC DISEASES

The hæmorrhagic diseases may be arbitrarily classified into those which are due to defective coagulation of the blood and those in which the blood clots normally. According to the theory of blood coagulation most widely held at the present time, a ferment precursor prothrombin is converted into thrombin in the presence of calcium and tissue derivatives (thrombokinase or thromboplastin). The thrombin then reacts with the fibrinogen of the plasma to produce fibrin. It is doubtful whether the clotting process is ever affected by shortage of calcium. Deficiency of fibrinogen has been observed as an excessively rare congenital abnormality—*fibrinopenia*. The only two important conditions in which coagulation is impaired are hypoprothrombinæmia and hæmophilia. Prothrombin is formed in the liver under the influence of the fat-soluble vitamin K. Prothrombin deficiency may therefore occur under the following conditions:

(i) In the newly-born (*melæna neonatorum*). The factors here are the small amount of prothrombin in the blood at birth, deficient intake of vitamin K in the first few days of life and absence of saprophytic bacterial activity in the intestine—bacteria synthesise vitamin K.

(ii) Deficient intake of vitamin K in states of extreme malnutrition.

(iii) Deficient absorption of vitamin K in intestinal diseases and fatty diarrhœa, as in obstructive jaundice, cœliac disease and sprue.

(iv) Deficient utilisation of vitamin K when the liver parenchyma is diseased.

Hypoprothrombinæmia is recognised by the fact that the blood does not coagulate normally even in the presence of an excess of thrombokinase. It can be prevented or treated by the administration of vitamin K. This can be given by mouth, together with bile salts to ensure its absorption, but at the time of writing the best method appears to be the injection of the synthetic vitamin derivative, methyl-naphthoquinone, 5 to 10 mg. dissolved in oil by intramuscular injection daily. In hæmophilia the blood coagulates normally on the addition of thrombokinase, and the disease is therefore probably due to inadequate release of thrombokinase.

1. PURPURA

In the narrow sense purpura refers merely to the occurrence of bleeding in the skin in the form of petechiæ, macules or larger areas. In the wider sense it connotes a group of diseases which are characterised not only by these cutaneous lesions but also by bleeding from the mucosæ and internally. Purpura is often classified into thrombocytopenic and non-thrombocytopenic forms, but there is so much overlap between these two that the distinction often falls to the ground. Hæmostasis appears normally to occur in two stages, first, contraction of the damaged vessel, and second, occlusion by thrombosis. In all the purpuras, whether thrombocytopenic or non-thrombocytopenic, the first stage of hæmostasis appears to be at fault, the capillaries do not retract properly when they are injured and the bleeding time is prolonged. In hæmophilia the second stage is at fault and though hæmostasis begins normally, bleeding recurs after a short interval.

The blood platelets.—The platelets are the third formed element in the circulating blood. They are spherical or oval, non-nucleated disks, with an average diameter of 2 to 3 microns, and with a hyaline cytoplasm which contains numerous granules. The average number of platelets is from 250,000 to 450,000 per c.mm., but there are great variations in health and according to the method of estimation employed. The platelets are believed to be produced by the megakaryocytes in the bone-marrow, and after a brief life of a few days they are phagocyted by the cells of the reticulo-endothelial system. Large numbers of platelets are present in the spleen, but it is not certain whether they are held there in reserve or in process of destruction. The platelets play an important part in the arrest of hæmorrhage, sealing wounds in the endothelial lining of the vessels, promoting the coagulation of the blood and securing the firm adhesion of the clot. Purpuric symptoms commonly appear when the blood platelets fall below 40,000 per c.mm. The following signs may also be observed in thromobocytopenic purpura: 1. The platelets are very variable in size and shape, and giant platelets may be present. 2. The blood clots in the normal time, but the clot does not retract and express the serum as rapidly and completely as in health. 3. The bleeding time is greatly increased. If the blood from a sharp prick in the finger is soaked off with a filter paper without pressure every 30 seconds, bleeding normally ceases in one to two and a half minutes, but if the platelets are defective it may be prolonged even to an hour or more. 4. The capillaries are more fragile than normal. The sphygmomanometer is applied to the upper arm and the pressure is maintained midway between the systolic and

diastolic level for five minutes. When the platelets are defective, a coarse purpuric rash may appear on the lower arm.

The endothelium.—A hæmorrhagic tendency due to a pure endothelial lesion is characteristic of scurvy, in which the plasma and the platelets are normal but the fragility of the capillaries is much increased. The same is true of the purpura of old age and nervous purpuras, such as stigmatisation. The hæmorrhagic states present in uræmia and other cachectic conditions are probably due to endothelial damage. When hæmorrhagic states are due to lesions of the capillaries, plasma may also pass through the endothelial lining, producing wheals, local œdema of the tissues and urticaria, and the purpuric areas may be elevated above the surrounding skin.

2. SYMPTOMATIC HÆMORRHAGIC STATES

Acquired hæmorrhagic states due to defective coagulation of the blood have already been discussed and it has been pointed out that the most important of them are due to defiency of prothrombin. Hæmorrhagic tendencies in which the blood coagulation is normal may develop in a heterogeneous collection of diseases, and it is difficult to present the subject at all formally.

1. The most important group is constituted by the *infectious diseases.* Purpura and a hæmorrhagic tendency have been observed in infections with the pyogenic cocci, scarlatina, chicken-pox, diphtheria, the enteric fevers, typhus, malaria, and gonococcal and meningococcal septicæmia. They have also been observed in chronic septic infections, such as focal sepsis and malignant endocarditis, and in tuberculosis, especially the miliary form. In all such conditions we have reason to believe that the endothelial lining of the vessels is damaged. The platelet count varies from case to case. It may be increased, and then thrombosis may develop in the midst of hæmorrhagic manifestations; it may be normal; or it may be diminished, when the hæmorrhagic tendency may be very severe, such cases being known as purpura fulminans. In typical cases the platelets are diminished during the acute period of the illness, but increase in convalescence and afterwards fall to normal limits. The cause of the thrombocytopenia of infections is not known. It has been suggested that there is an increased utilisation of platelets in such illnesses, either to combat the infection or to repair the lesions of the vessel walls. In some cases it is undoubtedly due to depression of the function of the bone-marrow in producing platelets, and this should be suspected more especially when there is leucopenia also. We shall see later that the spleen plays an important part in one group of hæmorrhagic states associated with thrombocytopenia, but I do not think there is any evidence to inculpate the spleen in the hæmorrhagic states which complicate infectious illnesses, and the splenectomy should not be performed. Treatment should be directed to the primary malady, and the hæmorrhages should be controlled by local measures, supported if necessary by transfusions.

2. A second group of symptomatic hæmorrhagic states is constituted by *chronic nutritional disturbances and cachexias,* of which chronic nephritis is an example. Here also we may mention the purpura which occasionally occurs in pregnancy. Malignant disease of the stomach is occasionally complicated by purpura hæmorrhagica; in the cases I have seen there was extreme thrombocytopenia.

3. A third group is produced by *organic and inorganic poisons*, such as salvarsan and sanocrysin. Here there may be both endothelial damage and thrombocytopenia.

4. A fourth group is associated with *chronic splenomegaly*, such as occurs in splenic anæmia and Gaucher's disease. Here there is thrombocytopenia, which is usually relieved by splenectomy.

5. A fifth group is the result of *diseases of the blood-forming organs*. The proliferation in the bone-marrow of the megaloblasts in pernicious anæmia, or of the immature white cells in leukæmia, may cause a pressure atrophy of the megakaryocytes and consequent thrombocytopenia. The same effect may be due to other tumour-like lesions of the bone-marrow.

Aplastic anæmia requires special mention. In discussing this disease I have already described cases in which the red cells are predominantly affected (aplastic anæmia), and others in which the white cells are predominantly affected (agranulocytosis). Cases also occur in which the platelets are chiefly affected, and they are known as *malignant thrombocytopenia*, or aleukia hæmorrhagica. The term "aleukia hæmorrhagica" is unnecessary, but it stresses the leucopenia, which is nearly always present in these cases. The disease should be recognised by its acute and rapidly fatal course and by the absence of any signs of regeneration in the white cells or the red cells. The spleen is not enlarged, and splenectomy is useless. Treatment should be directed to keeping the patient alive by transfusions in the hope that the bone-marrow may recover its functions.

Treatment.—General and local measures of value in all forms of hæmorrhagic tendency may conveniently be discussed here. The only reliable general remedy is the administration of normal human blood, as an ordinary transfusion in severe cases and as intramuscular injections of 10 to 20 c.c. daily in mild cases. Cotarnine hydrochloride, three to four intramuscular injections of 1 c.c. of a 10 per cent. solution daily, is believed to be of value in uterine bleeding, while Congo Red 10 c.c. of 1 per cent. solution intravenously, may be used in any hæmorrhage, though it is most commonly employed for hæmatemesis, melæna and hæmoptysis. Liver and vitamin C, more especially by injection, have been recommended for all kinds of hæmorrhage; I have never been persuaded that they have any effect other than their specific action in pernicious anæmia and scurvy respectively. In more chronic cases ultraviolet radiation and high vitamin diets are used, but again with little real assurance. Recently the injection of Moccasin snake venom was recommended for chronic and recurrent bleeding, especially of a purpuric type, but it is now generally held to be worthless. On the other hand, local treatment of hæmorrhage, especially in hæmophilia and purpura, has been revolutionised by the local application of snake venom, which is a powerful coagulant. The venom of Russell's viper (1 in 10,000 solution) or of the Australian tiger snake (1 in 5000 solution) has been chiefly used. Loose clot is washed away from the bleeding point with hot water, and tampons or other appropriate dressings soaked in the venom solution are then applied. With the use of snake venom it is now possible to repair wounds which would previously have been fatal. Heat is a valuable agent for checking hæmorrhage and may be applied as hot water (42° C.) or better, especially in hæmorrhage from an inaccessible cavity, as a stream of hot air.

3. MELÆNA NEONATORUM

Synonym.—Hæmorrhagic Disease of the Newly-born.

Ætiology and Pathology.—The blood is cytologically normal and the condition is essentially due to hypoprothrombinæmia. Both the bleeding time and the clotting time may be greatly prolonged. The incidence has been placed as high as 1 per cent. of all births, male and female. Heredity seems to play no part. In some cases acute gastric and duodenal ulcers have been found at autopsy, but it is more probable that these represent necrosed areas from submucous hæmorrhages than that they are the cause of the bleeding.

Symptoms.—The bleeding is spontaneous, commencing at any time in the first week or two of life, most commonly on the third or fourth day. The bowel is the usual site of hæmorrhage, but blood may also ooze from the mouth, nose and urinary tract, or be extravasated into the viscera or the cavities of the body. If the disease is not immediately treated, death from hæmorrhage and shock soon occurs.

Diagnosis.—This can be confirmed if necessary by estimating the prothrombin time. Hæmorrhagic states may occur in the new-born as a result of sepsis, syphilis, thrombocytopenia and other blood dyscrasias, but all are rare.

Prognosis and Treatment.—The prognosis depends on the promptitude of the treatment and the amount of blood already lost. It has been suggested that vitamin K, given prophylactically to the mother, will diminish the incidence of both intracranial bleeding and hæmorrhagic disease in the newly-born. By the time the condition develops, it is too late to use vitamin K, which has a latent period of 12 to 24 hours before acting. For treatment, 10 to 15 c.c. of fresh human blood should be injected subcutaneously once or twice daily, when the bleeding usually stops quickly and the infant makes a good recovery. No typing of the blood is necessary ; a little citrate may be added to prevent coagulation. During treatment the infant is kept as quiet as possible and not lifted from the cot. He can be fed by a bottle or spoon with breast milk, or if necessary, with an artificial food.

4. ESSENTIAL THROMBOCYTOPENIA

Synonyms.—Idiopathic Purpura Hæmorrhagica ; Hæmogenia ; Morbus Maculosus Hæmorrhagicus of Werlhof.

Definition.—A disease characterised by multiple hæmorrhages in the skin or from the mucous membranes, a reduced platelet count, a prolonged bleeding time, but a normal coagulation time.

Ætiology and Pathology.—Some 30 per cent. of the cases occur in the first decade of life, and the disease is infrequent after the age of 40. A few cases have been traced to idiosyncrasy for certain foods, such as milk, and for certain drugs, such as quinine or sedormid. Ingestion of the offending food or drug is followed within a few hours by the onset of thrombocytopenia and purpura. Another group of cases, occurring from one to three weeks after an infection such as tonsillitis, is suggestive of sensitisation to the infecting organism or its products. A small group is associated with malignant

disease, particularly metastases in the bone-marrow. The majority remain unexplained. The bone-marrow contains rather more than its normal complement of megakaryoblasts and megakaryocytes, and this is suggestive of an arrest of maturation of the platelets comparable with the arrest of maturation of the megaloblasts in Addison's anæmia and of the leucocytes in agranulocytosis. The spleen shows no pathognomonic changes.

Symptoms.—An acute and a chronic form are described. The acute form is uncommon. It begins suddenly and without warning, though sometimes there is a history of an acute infection a couple of weeks before. There is no pyrexia and the spleen is not palpable. Purpuric patches appear in the skin, of variable size and of irregular distribution. There is no erythema or whealing. Hæmorrhages occur from any of the mucosæ, the nose and mouth, the alimentary canal and the urogenital tract. The slightest injury gives rise to excessive bleeding, or the formation of large hæmatomata. The bleeding time is greatly prolonged, and the tourniquet test is positive. Examination of the blood reveals a thrombocytopenia, platelets being perhaps completely absent; there is usually a slight leucocytosis, and immature red cells and even normoblasts may be poured out to combat the anæmia. Recovery occurs in a few days or at most a few weeks, and the platelet count returns to normal. This may be the only attack, but in other patients a recurrence months or years later reveals that the disease is present in a relapsing form.

The chronic form of the disease, which accounts for 75 per cent. of the cases, may be of a continuous or of a relapsing type. In many cases the disease first manifests itself in childhood. In the continuous type there is persistent thrombocytopenia, with exacerbations of symptoms due to fluctuations of the platelets above and below the critical level of about 40,000 per c.mm., or to the effects of trauma or intercurrent infection. In the relapsing type there are long intervals of freedom during which the platelet count is quite normal. There may be persistent purpura, especially on the legs, or the parts exposed to trauma, or purpura may be completely absent. The spleen may be enlarged. There is a tendency for hæmorrhages to recur from the same site, as if it were an area of predilection, so that one patient may suffer from hæmatemeses, another from hæmaturia, another from menorrhagia. In my experience the disease becomes less troublesome in later life, even though the platelets remain at the same low level.

Diagnosis.—The diagnosis depends on the thrombocytopenia and the associated symptoms of platelet shortage, but it should be remembered that the platelets may be normal in the free intervals. For differential diagnosis the section on symptomatic hæmorrhagic states should be consulted; the absence of toxæmia and of joint pains is an important difference from these conditions and also from Henoch's purpura. Acute leukæmia is an important cause of purpura hæmorrhagica, which should be excluded by the differential white blood count. Most difficulty will be experienced in distinguishing the acute form of essential thrombocytopenia from the malignant purpura of aplasia of the bone-marrow. In malignant thrombocytopenia there is usually leucopenia and no sign of regeneration of red cells. In the chronic form of essential thrombocytopenia it is rather easy to overlook the possibility of a hæmorrhagic disease altogether, especially when there is no purpura and the bleeding is always from one organ. On this account this diagnosis should

always be considered in cases of symptomless hæmaturia, or hæmatemesis, or the like, or ill-advised operations may be performed.

Prognosis.—Death may occur in the acute attacks, or irretrievable damage be done, as by hæmorrhage into the vitreous humour of the eye or into the central nervous system. Nevertheless the disease is relatively benign, and the physician should not allow his judgment to be impaired by the alarm that is always felt in the presence of a hæmorrhagic disorder. One of my patients had multiple cerebral hæmorrhages, in addition to external bleeding which made him profoundly anæmic. He was treated with transfusions and symptomatic remedies, as he firmly refused splenectomy, and he remained thrombocytopenic, anæmic and ill for several months. A year later he was perfectly well, working as a railway guard with a normal blood count. This is by no means an isolated example, and the natural tendency of the acute attacks is to recovery.

Treatment.—The remarkable alleviation of the symptoms by splenectomy is very mysterious. The operation was introduced on the theory that the spleen was destroying an excessive number of platelets, but there are many facts which cannot be adapted to this theory. The bleeding may cease immediately the pedicle of the spleen has been tied, and before the platelets have had time to increase. The operation is usually followed by a great rise in the platelet count, but later the platelets may fall to subnormal levels without the recurrence of hæmorrhage. Operation should rarely be performed in acute cases, as the majority recover quickly on medical treatment and those that do not are usually of a type that is not likely to benefit from splenectomy. It is a good working rule to rely on transfusion and general treatment for at least a fortnight before having recourse to splenectomy. In the chronic cases the mortality of splenectomy has fallen to 7 per cent.; of those who survive the operation the immediate results are 85 per cent. cured, 10 per cent. improved and 5 per cent. not improved. Experience has nevertheless shown that splenectomy does not eradicate the cause of the disease, for after an interval of months or years the symptoms recur in about half the patients, though as a rule they are much less troublesome than before the operation. Operation should therefore be restricted to patients in whom the disease is really disabling or is subject to acute exacerbations. Operation should not be performed in patients with a family history of purpura hæmorrhagica. General treatment is on the lines already described (p. 812). Septic foci should be removed and efforts made to exclude sensitisation to foods or drugs. The results of X-ray treatment are at present discordant, but there is some evidence that remissions may be induced by irradiation of the spleen or the bones, and this treatment is worthy of further trial.

5. HENOCH'S PURPURA

Synonyms.—Anaphylactoid Purpura; Hæmorrhagic Capillary Toxicosis; Toxic Purpura.

Definition.—Although the term Henoch's purpura is sometimes restricted to cases characterised by purpura, colic and gastro-intestinal lesions, it is profitable to extend it to a group of non-thrombocytopenic purpuras, which are of obscure origin, and which may be accompanied by urticaria, œdema, swollen joints and various visceral manifestations. For

this reason the milder cases which are known as purpura simplex, and also the peliosis rheumatica or arthritic purpura of Schoenlein are considered under this same heading, for all appear to be manifestations of the same pathological state.

Ætiology and Pathology.—The disease is related to allergic conditions, such as erythema multiforme, erythema nodosum, angioneurotic œdema and serum sickness. The lesions probably result from an abnormal permeability of the capillaries, which allow plasma and blood to escape through their walls. The sensitising agent is not always the same. In some instances it is the streptococcus, the attack following a sore throat, or persisting until a septic focus is drained. In other instances sensitisation to foods has been demonstrated, and the disease has been cured by removing them from the diet.

Symptoms.—The attack is usually preceded by symptoms of general bodily disturbance, such as headache, malaise, loss of appetite, and a rise of temperature. In the mildest cases (purpura simplex) a fine purpuric eruption appears, often affecting the limbs rather symmetrically, and with a special tendency to develop round the hair follicles. In severe cases there may be extensive, irregularly distributed ecchymoses, and there is much œdema of the face. Wheals and pemphigoid lesions may develop, and careful examination will often show that the purpura is not a pure hæmorrhage, but that it is raised or surrounded by a zone of erythema. Successive crops of purpura appear. Bleeding is not necessarily confined to the skin, but may be subperiosteal, intramuscular or intravisceral. Joint pains are rarely absent, though the joints are seldom much swollen, and there may also be myalgia or neuralgia. The gastro-intestinal symptoms take the form of colic, bilious vomiting, and diarrhœa, with blood-mixed stools. The abdominal wall may be rigid, and it may be difficult to differentiate the lesion from an intussusception, which may indeed occur from invagination of a piece of intestine whose walls have been stiffened by the exudation of serum and blood. Similar lesions occur in the urinary tract, but extensive hæmorrhage from the mucosæ is rare. The spleen may be palpable and the urine may contain albumin, blood cells and casts. In rare instances death has occurred from cerebral convulsions, suggestive of acute uræmia; nephritis is, indeed, the most important complication.

The blood is normal, save for a slight anæmia or a mild leucocytosis. The platelets are normal or only slightly diminished, and the coagulation and bleeding times are normal. The tourniquet test may be positive, but in general there is little tendency to spontaneous or excessive external bleeding, and the mucosal hæmorrhages are small and attributable to oozing from areas of œdema and congestion.

Diagnosis.—The disease is not sharply divided from the symptomatic purpuras. It should, however, be clearly differentiated from essential thrombocytopenia and similar blood disorders by the absence of specific changes in the blood, and the presence of signs of toxæmia and increased capillary permeability. Cases with intestinal lesions may closely simulate intussusception, and they may occasionally be complicated by intussusception or peritoneal effusion.

Prognosis.—The disease tends to spontaneous recovery after an illness of a few weeks. Chronic and relapsing cases occur which are very

troublesome, though rarely dangerous. The prognosis is good, except for complications, such as nephritis and intestinal obstruction.

Treatment.—Treatment should be symptomatic and conservative. Incautious attempts at desensitisation may aggravate the disease. Splenectomy is not indicated. In view of the risk of renal damage the patient should be at rest, the diet should be lacto-vegetarian, and the urine should be kept alkaline. No further treatment is necessary in the majority of cases. Chronic cases should be investigated for persistent infection, foci of sepsis, or evidence of protein sensitisation. Large doses of calcium are frequently prescribed, but it is doubtful if they have any value. Non-specific desensitisation may be attempted by subcutaneous injections of horse-serum, 10 to 20 c.c. daily till improvement begins, or by minute doses of tuberculin.

6. HEREDITARY HÆMORRHAGIC STATES

As case histories are more carefully analysed, we are discovering that there are many instances of hereditary hæmorrhagic tendency which differ in pathology from hæmophilia, a disease which has obtained an exaggerated importance because of its prevalence in the royal households of Europe. Further experience may show that the symptoms and the mode of inheritance differ considerably in different family groups of bleeders. A practioner faced with a case which does not square with the classical description of hæmophilia will do well to prepare a careful pedigree and submit the data to an expert hæmatologist or eugenist, for these diseases can rarely be cured and patients are often anxious for advice whereby their transmission can be prevented. In the present state of knowledge we can distinguish the following hereditary tendencies to bleed :

(*a*) Classical hæmophilia (p. 818).

(*b*) Hæmophilia not uncommonly occurs sporadically, in the absence of a family history. Some of these cases are examples of hæmophilia arising *de novo* as a spontaneous mutation ; others are compatible with the transmission of the gene from a remote ancestor, for by the laws of chance there are bound to be some families where the males have escaped inheritance of the defect for several generations and yet it remains latent in the females.

(*c*) Hæmophilia may be atypical in affecting males as well as females, or in combining the features of hæmophilia and hereditary hæmorrhagic purpura. Both these variants of hæmophilia are so uncommon that an error of diagnosis should be suspected.

(*d*) Hereditary fibrinopenia is exceptionally rare.

(*e*) Hereditary hæmorrhagic states in which the coagulation of the blood is normal but the bleeding time is prolonged are by no means infrequent. These states are variously known as hereditary purpura hæmorrhagica ; constitutional hæmogenia ; thrombasthenia of Glanzmann ; thrombopathia of Willebrand-Jürgens ; and hereditary pseudo-hæmophilia. They bear a closer affinity to purpura hæmorrhagica than hæmophilia, and in some families the platelets are reduced. Nevertheless, the patients may suffer from hæmarthrosis. The condition may be transmitted direct from one generation to another, and it often affects females more severely than males. Sporadic cases occur. Splenectomy has no influence on the disease.

(*f*) Hæmorrhagic states apparently hereditary in origin occasionally

occur in which no abnormality can be detected in the blood or vessels by current methods of investigation. Clinically they bear most resemblance to the hereditary purpuras. It is always wise to take seriously the statement that a patient is a bleeder, even though no confirmation can be obtained from the laboratory.

(*g*) Hereditary hæmorrhagic telangiectasia (p. 819) is probably at least as common as hæmophilia.

(*a*) Hæmophilia

Definition. — A rare hereditary disease of males, characterised by a tendency to uncontrollable hæmorrhage and a great prolongation of the coagulation time.

Ætiology.—The disease is inherited by the law of Nasse, according to which it is transmitted only by females and manifested only by males. In Mendelian terminology it is a sex-linked recessive, and theoretically it might be expected to occur in females in the proportion of 1 to 200 affected males.

Pathology.—In contrast to prothrombin deficiency, the blood in hæmophilia clots normally in the presence of excess of thrombokinase. The disease has therefore been attributed to inadequate release of thrombokinase, and this again to undue stability of the platelets.

Symptoms.—The disease usually manifests itself in early life, but not at birth, so that there is no excessive hæmorrhage from the cord. Severe bleeding at circumcision is common, and in 60 to 70 per cent. of recorded cases the disease was recognised before the second year. It is doubtful whether the bleeding is ever spontaneous, and there is no purpura, but excessive hæmorrhage may occur from a mere scratch, and great bruises or ecchymoses from trivial injuries. Some patients cannot use a tooth-brush on account of bleeding from the gums. Epistaxis is common, but internal bleeding is unusual, though hæmaturia, melæna and hæmatomyelia have been described. Trauma and dental extraction are the most usual causes of severe hæmorrhage, and a rick of the muscles which would pass unnoticed in an ordinary boy may lead to an extensive intramuscular hæmorrhage which leaves the patient exsanguinated. The bleeding is not so much severe as persistent; hence it is rare for the hæmophiliac to die of a sudden profuse hæmorrhage, he rather fades out of life owing to the inability to stop the slow continued loss of blood.

The most remarkable form of hæmorrhage, and one which is common, is into the cavities of the joints. The joints which suffer most often are the knees and elbows, but any joints may be affected. The swelling and effusion take place with great rapidity, and with a great deal of pain. The joint is hot, tender, reddened, and the surrounding tissues swollen. The temperature is raised to 101° or 102° F. The effusion is almost pure blood, but as absorption proceeds it becomes a dirty brown colour, which stains the synovial membrane and the cartilages of the joint. It is sometimes absorbed rapidly, and the joint restored to complete mobility. When absorption is slow or effusions repeated, contraction and ankylosis may cripple the patient permanently. In a joint often affected, there is always considerable destruction of the cartilages and of the ligaments, with the result that the bones are exposed and undergo changes resembling those of osteo-arthritis. Osteophyte formation is, however, rare, and so is bony ankylosis. Fibrous ankylosis is, on the

other hand, common. The spleen is not palpable. Hæmophiliacs are usually weakly individuals.

Diagnosis.—The diagnosis is based on the family history and on the delayed coagulation of the blood; the cytology and chemistry of the blood are normal. The joints are sometimes mistaken for tuberculous joints. A more serious error is to incise a hæmatoma on the mistaken diagnosis of an abscess. Hæmophilia should be differentiated from other hereditary hæmorrhagic states and from acquired conditions, such as essential thrombocytopenia.

Prognosis.—It is said that less than 12 per cent. of hæmophiliacs survive to puberty, but the disease undoubtedly becomes less severe in later life, though still present. A peculiar feature of the disease is its variability, the blood at times clotting almost normally, at other times seeming almost incoagulable, and if the patient survives a severe hæmorrhage there is often a temporary improvement in the blood.

Treatment.—Treatment is unsatisfactory, and it is much better to try to stamp out the disease by discouraging the reproduction of affected families. The only members of a hæmophiliac family who can safely beget children are the unaffected males. Sufferers from the disease should be protected from trauma as far as possible, and operations should be discouraged unless they are essential to life. Transfusion is the best general treatment and snake venom the best local treatment. When a joint is distended with blood it should be aspirated; needle punctures rarely bleed much.

(*b*) Hereditary Hæmorrhagic Telangiectasia

Definition.—A hereditary disease characterised by multiple telangiectases, which cause hæmorrhages from various sources, especially the nose.

Ætiology.—The disease is not strictly a blood disease, but a hereditary dystrophy of the capillary system, which is transmitted directly from generation to generation, affecting both sexes equally and behaving as a Mendelian dominant. It is, in my experience, at least as common as hæmophilia.

Symptoms.—Epistaxis generally begins in childhood and before any cutaneous telangiectases have been recognised, but it tends to become more frequent and severe with advancing years. The telangiectases are not present at birth, and are sometimes not noticed till middle life. They vary in kind, appearing as dilated venules; spider capillary networks; punctate red or purple spots and blebs; and raised nævi up to an inch in diameter. They are most common about the face, nose and mouth, and the trunk and limbs are generally spared, except for the tips of the fingers. Epistaxis is the common complaint, but external bleeding, hæmoptysis, gastrostaxis, hæmaturia, or cerebral hæmorrhage may occur. The blood is normal, except for the anæmia induced by the bleeding.

Diagnosis.—This depends on the family history and the presence of telangiectases, and both these may be missed if they are not sought for. Few telangiectases may be visible, and epistaxis or alimentary hæmorrhage may be the presenting symptom. Many cases are first seen by the rhinologist.

Prognosis and Treatment.—There is no curative treatment, and death from hæmorrhage occurs in a considerable percentage of the cases. Affected members of these families should, therefore, be strongly advised against having children, as half of their offspring will inherit the disease. Treatment of the nævi by cauterisation or radium is only moderately successful.

PROPHYLAXIS AND TREATMENT OF ANÆMIA

Prophylactic.—A number of the diseases of the blood-forming organs, such as acholuric jaundice and hæmophilia, are pure hereditary dystrophies, and rational treatment should be directed not to the individual but to the stock, all those who carry the morbid trait being advised against reproduction. Prophylaxis of the acquired forms of anæmia is not often feasible, but the relation of anæmia to nutritional disturbances should be emphasised and especial care should be taken in the growing periods of life, childhood and pregnancy, that the diet contains a sufficiency of iron and protein.

Treatment.—Good treatment is not possible without exact diagnosis, and if a patient is ill enough to be treated for anæmia, then he or she is ill enough for an examination of the blood to be necessary. It is surprising how often debility is mistaken for anæmia, but the distinction is often difficult on clinical examination. Much time and money are wasted by the prescription of remedies which are not indicated, and the physician is confused and unable to evaluate the effects of treatment. It is a simple matter to test the hæmoglobin, after which a more detailed examination of the blood can be advised if anæmia is found. Many disturbances of the blood are of a highly specific nature, and the appropriate treatment can only be elucidated by careful clinical and hæmatological study. It is no use prescribing iron for the anæmia of scurvy, or vitamin C for the anæmia of myxœdema.

Symptomatic disturbances of the blood-forming organs, which are far commoner than their primary diseases, usually recover spontaneously if the cause can be removed ; if it cannot, they rarely respond well to symptomatic treatment. Many remedies for anæmia have gained an unfounded reputation by being administered to patients who would have recovered equally rapidly without treatment. It is surprising, for example, how swiftly the blood may be regenerated after a severe hæmorrhage. On the other hand, in chronic and persistent anæmias the dosage of the drugs which are useful in treatment is much higher, and the period necessary for treatment is much longer, than is often realised. Treatment can be checked by the reticulocyte crisis, which should occur in the first fortnight, and by the rise in hæmoglobin, which should be over 1 per cent. a day, or approximately 10 per cent. a week in a severe anæmia receiving optimal treatment. Patients who are severely anæmic should be confined to bed, for this makes a great difference to the speed of regeneration of the blood. A generous mixed diet should be given, rich in vitamins, and liver or kidney should be taken two or three times a week. Fresh air and sunshine or ultra-violet therapy also improve the patient's condition, but too much should not be expected from these ancillary treatments, which by themselves will rarely influence a severe anæmia.

Iron is of value in the majority of anæmias of low colour index, especially those which are due to chronic hæmorrhage, or to defective absorption of iron (idiopathic hypochromic anæmia). Recent studies have shown that the various preparations of iron differ greatly in their activity. Elemental iron as in ferrum redactum, is rather inactive, on account of its insolubility. The ferrous salts are the most active, next the scale preparations, and then the ferric salts; organic preparations of iron, such as hæmoglobin, in which the iron is "masked," have no therapeutic activity. Effective doses of substances in common use are: ferrous chloride, or exsiccated ferrous sulphate, in each case 3 grains thrice daily after food; Blaud's pill (ferrous carbonate), which must be fresh and is often best prescribed as a powder, in a dosage of 10 to 15 grains thrice daily after food; and iron and ammonium citrate, in a fluid mixture, 20 to 40 grains thrice daily after food. Intolerance of iron is very unusual, and is usually due to suggestion; the digestion improves in most cases, and with large doses diarrhœa is a more common complaint than constipation. Menorrhagia sometimes occurs, especially in women about the menopause, and may require special treatment. Iron should not be given by injection. The majority of ampoules of iron preparations which are sold contain infinitesimal amounts of the metal, and are ineffective; potent preparations cause much pain, and the injections may lead to iron poisoning—headache, vomiting, paralysis and even death. A patient too ill to take iron by mouth should be transfused.

Liver and stomach are often prescribed as if they were a panacea for all forms of anæmia, but in my experience they are of no value except in the small and well-defined group composed of pernicious anæmia and allied megalocytic anæmias. Whole liver, whether raw or cooked, is not to be recommended, as it is impossible for a patient to take it in adequate dosage or for a sufficient period of time. Whenever possible parenteral therapy should be used as it is the most economical and effective. Superconcentrated extracts such as anahæmin have been introduced recently. They are often better tolerated than the cruder extracts but there is evidence that something may be lost by these processes and such extracts may fail in nutritional macrocytic anæmia and anæmia due to intestinal disease unless given in extravagant amounts. The Anti-Anæmia Preparations Advisory Board of the United States Pharmacopœia in 1938 decreed that it would not assign any preparation of injectable liver extract a strength greater than 15 units per c.c. liquor hepatis purificatus, U.S.P., contains 10 units per c.c. and there are numerous British intramuscular extracts of the same type. In a case of pernicious anæmia of average severity treatment should be begun by the intramuscular injection of one of these extracts in a dosage of 2 to 4 c.c. daily for the first 3 days. The interval between doses is gradually increased to a week or 10 days, and finally a maintenance dose is determined, which will usually vary from 4 to 6 c.c. at intervals of 3 to 6 weeks. In very severe cases treatment may begin with a single injection of 5 c.c. of an intravenous extract, or 4 c.c. of an intramuscular extract every 6 hours for the first 24 hours. Desiccated stomach or oral extracts of liver may be given by mouth when treatment by injections is inconvenient. The usual dose of desiccated stomach is ½ oz. twice daily. Fluid extracts of liver are more palatable than dry, and they should be given in a dose equivalent to from ½ lb. to 2 lb. of liver a day. When a patient

comes under treatment for subacute combined degeneration, recovery may be accelerated by a course of massive liver therapy, 4 to 8 c.c. of an intramuscular extract daily for 6 weeks. I am convinced that subacute combined degeneration can be prevented, and that its progress in the early stages can be arrested by adequate treatment. It has been well said that the daily maintenance dose is " not some liver, but enough liver for the given case." The blood should be kept at 5 million red cells per c.mm., and 100 per cent. of hæmoglobin, and it should be examined at intervals to ensure that this level is maintained. Patients should be told that treatment must be continued for the rest of their lives and they should also be warned of the folly of relaxing treatment. The disappearance of macrocytosis is probably the most reliable laboratory test that treatment is adequate. Whatever the level of the blood count, paræsthesiæ or similar nervous symptoms suggest that enough effective substance is not being given. Infections and old age both increase the dosage necessary for the control of pernicious anæmia.

Hydrochloric acid is of value in the treatment of the dyspepsia of simple achlorhydric and pernicious anæmia, but it has no effect on the anæmia. Heroic doses are unnecessary, 20 to 30 minims of the dilute acid at mealtime being sufficient. If desiccated stomach is employed, hydrochloric acid is not usually required.

Arsenic is a drug which was formerly administered in all forms of anæmia, but its use is now becoming restricted to leukæmia and erythræmia. It is usually given as liquor arsenicalis, beginning with 2 minims and increasing to 10 to 15 minims thrice daily, after meals, until the desired effect is produced, or signs of intoxication begin to appear. The drug is then discontinued for 4 to 6 days, and resumed in a smaller daily dosage, the maintenance dose being determined by the clinical condition and the blood picture.

X-rays and to a less extent *radium* are employed in two ways in diseases of the blood-forming organs : in small doses as a stimulant, and in large doses as a depressant. Stimulating doses are used in agranulocytosis and in purpura hæmorrhagica, but this form of treatment can hardly be said to have established itself yet. Depressant doses are employed in leukæmia and polycythæmia : the rays may be applied to the bones, to the spleen or to enlarged glands. The best results appear to be obtained with small doses frequently repeated. In leukæmia treatment is stopped when the white count has fallen to about 15,000, as the fall may continue for 2 or 3 weeks after cessation of treatment ; it should be resumed whenever the white count rises above 50,000 cells per c.mm.

Transfusion is essentially an emergency measure, and it has little curative value except in the rare hæmolytic anæmia of Lederer. It has a definite mortality, and should be advised with as much circumspection as a surgical operation. It is indicated when the patient is too ill to react to curative treatment, or when it is necessary to bring him into condition for treatment directed at the cause of the anæmia. The very greatest care should be taken, fresh sera always being employed for the grouping, and a direct compatibility test being carried out immediately before transfusion. Donor and recipient should always belong to the same group, for experience has shown that members of group O cannot safely be employed as universal donors. Under ordinary conditions the advantages of working with citrated

blood outweigh any theoretical disadvantages; the blood should be kept warm and should be administered slowly. Even when every care is taken reactions occur, especially in febrile patients. The anaphylactic type of reaction occurs during or immediately after the transfusion. It is characterised by dyspnœa, cyanosis, swelling of the face, and urticarial rashes, and it responds to treatment by adrenaline or morphine. The hæmolytic type of reaction may occur during the transfusion, or some hours later. It is characterised by tingling pains in the veins, præcordial oppression, cyanosis, rigors, high fever, hæmoglobinuria and jaundice; death may occur at once, or later from suppression of urine. It has been shown that suppression of urine will not occur if the urine is dilute and alkaline, and it is therefore advisable to prescribe fluid and alkalis for 24 hours before and after a transfusion. A single transfusion of a pint of blood raises the hæmoglobin on an average about 10 per cent. This is rarely sufficient for patients who are severely collapsed and anæmic, as after a bad hæmatemesis, and in such cases a cannula may be tied into a vein and 2 or 3 litres of blood may be slowly introduced at a rate of 90 to 150 c.c. an hour.

L J. Witts.

SECTION XI

DISEASES OF THE SPLEEN AND THE RETICULO-ENDOTHELIAL SYSTEM

INTRODUCTION

The spleen is a composite organ made up of various tissues which are also found elsewhere in the body. Any individual tissue, not only in the spleen but wherever else it occurs, may be simultaneously attacked by disease. Thus, the *classification* of diseases of the spleen is difficult, because few of the diseases are confined to this one organ, and many are fully described, in their clinical aspects, in other sections of this volume.

In order to understand some of the difficult and, in many ways, still anomalous diseases of the spleen, it is essential to consider briefly the structure and functions of the organ. An important general point is the essential "lobularity" of the spleen, which explains the features of many pathological conditions (*e.g.* infarctions) and abnormalities.

The tissues which make up the human spleen are:

1. The Hæmopoietic or Blood-forming Tissues.—In the fœtus the liver and spleen are the chief blood-forming organs. In post-natal life the bone-marrow takes over this function, which, however, can be called into great activity again in both the liver and the spleen in a number of blood diseases.

2. The Lymphoid Tissues.—These are found in the spleen as the Malpighian bodies, and elsewhere as the lymph nodes and collections of lymphoid tissue scattered widely through the body.

3. The Reticulo-Endothelial Tissues.—The cells of this tissue line the splenic blood sinuses, and occur abundantly in the pulp. Elsewhere they are met with as the Kupffer cells of the liver, in the bone-marrow, in the lymph glands and in other situations.

4. The Vascular Structures.—These are peculiar, and are described subsequently. The spleen is in direct connection with the portal venous system and, of necessity, is involved in many diseases and abnormalities of that system. This fact, together with others already mentioned, bring the liver and spleen into close relationship in disease.

5. The Supporting Tissues.—These consist of the capsule, the trabeculæ, and the reticulum of the pulp.

A diagrammatic sketch of a splenic lobule is provided (Fig. 19). It may require modification or correction in future, but without some such scheme in mind, it is difficult to correlate structure with functions, and to explain the reactions of different parts of the spleen in disease.

Functions.—It has long been known that the spleen, by itself, performs

no function essential for life, and that the organ can be removed without permanent harm to the individual. The functions of the spleen are those of its component parts, and nothing need be said here of splenic functions in relation to the hæmopoietic and lymphatic systems, as these are dealt with elsewhere. The activities of two structural parts, namely, (1) the spleen as part of the Reticulo-Endothelial System, and (2) the spleen as a blood reservoir, require more detailed consideration.

1. The Spleen as part of the Reticulo-Endothelial System.—The spleen contains the largest collection of cells of this system in the body, and is necessarily involved in all diseases in which these cells react. Some diseases, particularly affecting the reticulo-endothelial system, are, for the sake of clarity, dealt with separately (p. 833), and it is important to summarise the main functions of the spleen as part of the reticulo-endothelial system. These are :

(*a*) *Phagocytosis.*—This is a most active splenic function, resulting in the destruction of bacteria, protozoa and red blood corpuscles. This "filtering out" activity at once brings to mind the splenic changes in infections (typhoid fever, malaria), and the enlargement of the organ in hæmolytic anæmias (pernicious anæmia, acholuric jaundice).

(*b*) *Storage.*—These cells of the reticulo-endothelial system play an important part in the intermediate metabolism and storage of fats, lipoids, hæmoglobin and iron. These functions are referred to in greater detail in connection with Gaucher's and other diseases.

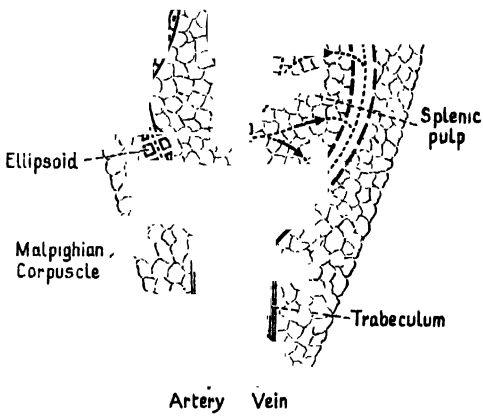


Fig. 19.—Diagrammatic sketch of a splenic lobule.

(*c*) *Formation of blood cells.*—Cells of this system (monocytes) enter the blood stream, and alter the blood picture in a number of diseases.

(*d*) *Development of immunity reactions.*—One such reaction is the phagocytosis of invading micro-organisms, referred to previously. Much work has also been done suggesting that the reticulo-endothelial cells are the main source of antibodies, antitoxins, precipitins and agglutinins. It is certain that in chronic infective diseases these cells most abundantly react and proliferate (*e.g.* the giant cells and histiocytes of tuberculosis and syphilis). Some hitherto unexplainable examples of splenomegaly (reticulo-endotheliosis of the spleen) may come into this category.

2. The Spleen as a Blood Reservoir.—The contractility of the spleen has long been recognised, but its significance was not appreciated. It enables an extra supply of blood to be suddenly withdrawn from the organ and poured into the general circulation in bodily emergencies—hæmorrhage,

exercise, emotion. Study of this function involved an inquiry as to how blood is stored in the spleen, and this not only emphasised the peculiar vascular arrangements and structures of the organ but also explained, in part at least, some well-known pathological changes in enlargement of the spleen which previously were puzzling.

No hypothesis of the mechanism of the splenic circulation fits the facts so well as the " two-way " blood flow through the organ suggested in Fig. 19. Taking this view, blood normally flows through the splenic artery, arterioles and blood sinuses, to return at once through the veins. Some blood is, however, deflected in order to be stored in the spongy pulp among the reticulo-endothelial cells, and ready to be restored at once to the venous outflow on contraction of the spleen. Blood reaches the pulp through the walls of the " ellipsoids," and a short description of these structures, which are peculiar to the spleen, is essential.

Ellipsoids are thickenings of reticulo-endothelial tissue surrounding the terminations of the fine " penicillar " arterioles. They act potentially as valves, and through channels in their loosely formed walls blood-cells reach the pulp. It is at or about the ellipsoids that perivascular hæmorrhages, with their peculiar end-result referred to subsequently, occur so commonly in many forms of splenomegaly.

It is evident, judging from clinical results in purpura hæmorrhagica (p. 810), that the spleen must have some important influence on blood-platelet formation or destruction, but the mechanism is not understood.

Another fact concerning the spleen, difficult to explain but well recognised clinically, is the apparent resistance of the splenic tissues to tumour growth.

A. DISEASES OF THE SPLEEN

ABNORMALITIES OF THE SPLEEN

The spleen may be completely absent, or may take the form of small spleniculi (syn. splenunculi, accessory spleens) scattered throughout the upper abdomen. A few small accessory spleens, in close proximity to an otherwise normal spleen, are quite common, and share in all pathological processes of the main organ.

Congenital lobulation is occasionally found, and emphasises the essential lobular structure. Normally only the characteristic notch or notches on the anterior border persist as evidence of this fact.

FLOATING SPLEEN

Synonyms.—Wandering Spleen; Movable Spleen; Dislocation of the Spleen.

Ætiology.—This condition occurs almost exclusively in females, and may either form part of a general visceroptosis or follow enlargement of the organ from disease. Trauma may be a direct ætiological factor, especially when the spleen is enlarged, and dislocation may occur quite suddenly. The question

of whether supporting ligaments are torn or only stretched has been much disputed.

Pathology.—A floating or dislocated spleen has been found in almost every part of the abdomen, even in the pelvis. Perisplenitis generally supervenes, and the organ becomes fixed in position. If diseased, the organ may continue to enlarge in its new location.

Symptoms.—Apart from those caused by complications, the symptoms may be very indefinite, and consist chiefly of localised pain from perisplenitis, and the effects of pressure on adjacent organs or on the intestine.

Certain complications may arise. Prior to fixation, acute twisting of the pedicle may lead to abdominal symptoms resembling those following twisting of the pedicle of an ovarian cyst. Slower torsion of the pedicle leads to simple atrophy, without symptoms. A number of other rare abdominal complications, due to traction on abdominal viscera, have been described.

Diagnosis.—This depends on the discovery by abdominal palpation that the spleen is absent from its normal position (although clinical proof of this is difficult), and of the presence of a tumour. Diagnosis may be easy if the characteristic shape and notches can be felt through a lax abdominal wall. If, however, the organ is fixed, carcinoma may be closely simulated. Examination under an anæsthetic may afford help, but often a correct diagnosis is only made by laparotomy.

Treatment.—Splenectomy is to be recommended in the majority of cases.

INFARCTION OF THE SPLEEN

Infarction of the spleen may be aseptic or septic. *Total aseptic infarction* is probably commoner than is supposed, especially in cardiac disease. It does not give rise to symptoms, and may be found accidentally at necropsy. *Total septic infarction* is very rare, but may lead to abscess formation. *Partial infarction* or *multiple infarctions*, both aseptic and septic, are common in a great variety of diseases. Apart from local treatment for pain, they generally require little attention, unless abscess supervenes.

ABSCESS OF THE SPLEEN

This may be single, but is more often multiple and the sequel to multiple septic infarctions. It occurs in typhoid fever, phlebitis, erysipelas and other infective conditions, and is dangerous because it so often escapes detection until rupture and peritonitis ensue. The diagnostic signs—which, however, are not confined to this disease—are sudden pain, tenderness and acute perisplenitis with an audible friction rub.

RUPTURE OF THE SPLEEN

Ætiology.—Rupture of the spleen may occur in a healthy individual as the result of injury, but is more common when the organ is enlarged and diseased. The first is chiefly of interest to surgeons. The second (sometimes

called " spontaneous rupture ") is of much importance to the physician and also in medico-legal work. Spontaneous rupture may take place in acute infective diseases (*e.g.* typhoid fever), in chronic infections (*e.g.* malaria), in leukæmia, and in other varieties of splenomegaly. In all of these the splenic capsule is altered by inflammation, by distension, by disease, or by a combination of these conditions. When a spleen has undergone great and rapid enlargement from any cause the danger is particularly severe, and too robust clinical examination of a leukæmic spleen has resulted in rupture of the thin and stretched capsule. Trauma, to cause rupture of an acutely enlarged spleen, may in fact be so slight as to escape notice, and may be very indirect in its application.

Pathology.—The rupture may occur in any part of the organ, and the tears may be longitudinal or transverse, single or multiple. As a rule, both the capsule and splenic tissues are torn, but " delayed rupture " may ensue when the splenic tissues are only bruised, and a collection of blood finally bursts through the capsule.

Symptoms and Diagnosis.—In most cases the patient experiences sudden violent pain in the region of the spleen, followed almost immediately by dizziness and collapse. The clinical picture is soon simply that of a severe internal hæmorrhage, and if the patient is unconscious an accurate diagnosis may be impossible in the absence of a previous medical history.

Prognosis.—This is improving with the advances in emergency surgery, but is still very serious, especially in conditions of actual splenic disease.

Treatment.—This is surgical.

SEPTIC SPLEEN

Synonym.—Acute Splenic Tumour.

This condition is an accompaniment of a great variety of infective diseases, and the recognition of splenic enlargement may be important in the general diagnostic picture (*e.g.* typhoid fever, infective endocarditis, abortus fever). Pathologists divide septic spleens into two types—the " red " spleen, most characteristically seen in typhoid fever; and the " grey " spleen, common in pneumonia, infective endocarditis, and in most septic conditions.

In the recognition of slight splenic enlargement, percussion is difficult and far less trustworthy than palpation of the tip of the organ below the ribs. It should be remembered that the spleen may be felt in various situations below the left costal margin, sometimes nearer the xiphisternum and sometimes in the extreme flank. Palpation is easier in an individual with a broad chest and wide costal angle than in the opposite type.

CHRONIC VENOUS CONGESTION OF THE SPLEEN

This occurs in congestive heart failure, but is of no clinical significance, and the spleen is seldom obviously enlarged during life. In portal hepatic cirrhosis, enlargement may be very considerable and form a real splenomegaly. It is tempting to suggest that the enlargement is due simply to back-pressure and congestion of the portal venous system, but all attempts to bring about chronic

splenic enlargement experimentally in this manner have been a signal failure. The considerable splenomegaly noted in some cases of hepatic cirrhosis must therefore be due to some unknown factor or factors.

CYSTS OF THE SPLEEN

Three varieties of cysts of the spleen have been described, namely, dermoid, echinococcus (hydatid) and serous or hæmorrhagic. All are uncommon. *Serous* or *hæmorrhagic cysts* will alone be dealt with.

Ætiology.—It has been claimed that this variety of cyst is congenital, and also that it may follow injury. The exact facts, however, are unknown, but when once formed they continue to grow slowly and indefinitely.

Pathology.—Serous or hæmorrhagic cysts may be single or multiple. They contain a mixture of fluid and light chocolate-coloured debris, with abundant cholesterol crystals producing a distinct sheen. Perisplenitis is common, but rupture is rare. A cyst may be deep within the splenic tissues, or may project backwards.

Symptoms.—The cysts may be large enough to bring about splenomegaly. If they project backwards, a thinned-out but apparently normal anterior margin, with the characteristic notches, may be felt through the abdominal wall and simulate other forms of splenomegaly.

The only pathognomonic sign is fluctuation, but even when this is detected the diagnosis from congenital cystic kidney may require to be made. Repeated attacks of acute perisplenitis are a noteworthy feature.

Treatment.—Splenectomy should be performed as early as possible, before dense perisplenitic adhesions have formed.

PERISPLENITIS

Perisplenitis, or inflammation of the splenic capsule, is mentioned in connection with a great many acute and chronic diseases, and is of considerable clinical importance. When acute, there is generally associated pain. Perisplenitis may be detected either by manual palpation or frequently only by the aid of the stethoscope over the tender area. It may, when acute, as already indicated, be of real diagnostic importance, while in the chronic stages it may present a serious problem to the surgeon and hinder or prevent successful splenectomy. Dense perisplenitic adhesions between the upper pole of the spleen and the vault of the diaphragm are the gravest danger in the technique of splenic surgery. Perisplenitis over the anterior surface of the spleen, even when of long duration, seldom gives rise to adhesions, and may show the same " sugar-iced " appearance as in Pick's disease.

CHRONIC ENLARGEMENT OF THE SPLEEN

Synonym.—Splenomegaly.

Chronic splenic enlargement may be simulated by: (1) Tumours, enlargements and displacements of the left kidney. (2) A greatly enlarged

left lobe of the liver. (3) A rolled-up carcinomatous or tuberculous omentum. (4) Carcinoma of the splenic flexure of the colon. (5) Carcinoma of the body of the stomach. If these can be excluded, then a mass felt in the left upper abdomen is almost certainly an enlarged spleen.

In this section only the chronic enlargements of the spleen not dealt with elsewhere will be considered. Splenomegaly is a feature of many diseases, both in the tropics and in temperate climates. Mention may be made of a few examples—malaria, kala-azar, schistosomiasis (including Egyptian splenomegaly), anæmias, leukæmias, tuberculosis, syphilis and Hodgkin's disease.

The composite structure of the spleen in relation to the pathology of many of the above diseases is discussed elsewhere.

In most splenic enlargements, as chronicity increases, changes occur in the trabeculæ and reticulum, which become thickened, and the whole spleen becomes dense and fibrous.

Changes in the vascular system are common in splenomegaly, and are of such peculiar type as to require description.

Vascular changes in splenomegaly.—These are of two main types:

1. Thrombosis, often followed by tunnelling of the organised thrombus so as partially to restore the circulation of the main splenic vein or even of the portal vein. This thrombo-phlebitic lesion, to which particular attention was drawn by Warthin, is found at necropsy in a number of patients who have suffered from long-standing splenomegaly. The splenic enlargement may be enormous; hepatic cirrhosis and ascites are common in the late stages; and clinically it is impossible to separate this type of splenomegaly from that shortly to be described as "splenic anæmia." The exact cause and significance of "thrombo-phlebitic splenomegaly" are not understood, but the condition may be simply a complication of the more ordinary type of splenic anæmia.

2. "Fibro-siderotic nodules," due to organisation of perivascular hæmorrhages in the neighbourhood of the ellipsoids. This lesion, which appears to be entirely non-specific, may be present or absent in almost any form of splenic enlargement. It is often particularly well seen in chronic "splenic anæmia," but may be found abundantly in the spleen removed from a child suffering from acholuric jaundice. In a cut section of the spleen the nodules present a striking appearance as small firm yellowish-brown nodules, standing out from the surface, and aptly compared to "flakes of tobacco-leaf." Originally described by Stengel, they have recently attracted much attention under the name "Gandy-Gamna bodies." It was claimed that they were evidence of a streptothrix infection invading the spleen and the cause of the splenomegaly, but this view is now given up. How they arise is uncertain, but they are readily recognised to be the result of organisation of a hæmorrhage round a small arteriole, and consist of fibroblasts, crystals of iron phosphate, and phagocytic cells containing abundant golden-yellow hæmosiderin.

SPLENIC ANÆMIA

Synonym.—Hepato-lienal Fibrosis. *Old synonyms:* Banti's disease; Banti's syndrome.

Splenic anæmia is the most common, and also the most difficult, form of chronic splenomegaly met with in this country. There has been much trouble with nomenclature, much difficulty in interpreting the splenic histology, and much discussion as to whether we are dealing merely with a clinical syndrome or a true pathological entity. Originally described as "anæmia splenica" (1866), and as "splenic pseudo-leukæmia" in the days before the pathology of the leukæmias was understood, the name "splenic anæmia" was again brought into clinical use by Osler (1902). Confusion has always been rife over the relations of the disease first described by Banti in 1883, and amplified in subsequent descriptions by him up to 1910. It may be said at once that the *clinical* phenomena in splenic anæmia and Banti's disease are identical in all respects. Argument has centred round the problem of Banti's somewhat varied description of the pathology of the spleen in his cases, and whether the changes described by him are peculiar and diagnostic of a distinct pathological entity, rarely if ever found elsewhere. The matter is now of no clinical importance unless or until a definite ætiological cause for this common type of splenomegaly is discovered, but to avoid confusion it would be better if the term "Banti's disease" were omitted altogether from clinical use, and the older term "splenic anæmia" retained. The synonym "hepato-lienal fibrosis" is an attempt to indicate the main gross pathological changes characteristic of this syndrome or disease.

Definition. — A chronic disease or syndrome characterised by splenomegaly, moderate anæmia of the hypochromic type with low colour-index, leucopenia, and a tendency to hæmorrhage, especially from the stomach. The terminal stage is associated with hepatic cirrhosis, jaundice and ascites.

Ætiology.—This is unknown. It is usually stated that the splenic changes appear first, and the hepatic fibrosis subsequently. Heredity plays no part. The condition is generally held to be more common in males than females, but in a personal series of 45 cases, 22 were males and 23 females. It is a very chronic disease, probably never recognised at its outset, but the first symptoms often appear (25 out of 45 cases) before the age of 30 years.

Pathology.—The characteristic histological changes in the spleen may be briefly summed up as peri-arterial hæmorrhages (some of which may develop into fibro-siderotic nodules); dilatation of the blood sinuses; proliferation of histiocytic (reticulo-endothelial) cells around the sinuses and in the pulp; and generalised fibrosis of the trabeculæ and reticulum. The Malpighian bodies also share in the fibrosis. The liver changes vary greatly in degree; the earlier changes are little known, but the later stages differ in no way from those of ordinary hepatic cirrhosis. There are no other primary pathological changes of importance.

Symptoms.—Splenomegaly is essential, but its degree varies. The average weight in a series of cases was about 900 g., though the weight may be as much as 3000 g. The spleen feels smooth, firm and uniform. Moderate anæmia is the rule, unless the case is complicated by recent hæmorrhage. An average red cell count is perhaps 2 to 3 millions per c.mm. or more; hæmoglobin 30 to 50 per cent., and the colour-index always below unity. The leucocytes are diminished, being seldom over 5000 per c.mm., and a common average count is 2 to 3000 per c.mm. There are no characteristic features in stained films.

Hæmorrhage from the stomach (derived especially from large veins passing in the gastro-splenic omentum "vasa brevia" or occasionally from œsophageal veins in the late stages of the disease) occurs in a large percentage of cases, and may be copious and repeated. More rarely, intestinal bleeding occurs, or the skin may show purpura simplex. The skin is generally light yellow in tint, but brownish pigmentation is not uncommon.

The terminal stage of the disease is identical with that of ordinary hepatic cirrhosis, with signs of portal obstruction, ascites and jaundice.

Course.—This is chronic, the duration varying from several to many years, and in the majority from 5 to 12 years.

Diagnosis.—The diagnosis is made merely by a process of exclusion after considering all other forms of chronic splenomegaly. The spleen is larger than in most cases of ordinary hepatic cirrhosis. The association of anæmia and leucopenia is important.

Prognosis.—This is invariably bad, but greatly depends on the onset of complications, such as hæmorrhage, hepatic cirrhosis, ascites and possibly thrombosis of the splenic or portal vein. Most patients die from hæmorrhage or hepatic insufficiency, but a few simply from asthenia.

Treatment.—This remains unsatisfactory, since the ætiology is unknown. The constant hypochromic anæmia has received insufficient attention in the past, and in the absence of actual hæmorrhage it is generally possible by intensive iron therapy to raise the hæmoglobin percentage considerably, with great improvement to health. After severe hæmatemesis blood transfusion may be required.

Apart from this general treatment, splenectomy has been the chief therapeutic measure recommended, based on the view that the changes in the spleen, whatever their origin, occur first and later influence changes in the liver. This hypothesis is by no means universally held, and some maintain that the course of this chronic disease is unaltered by splenectomy at any stage. It is certainly true that splenectomy does not prevent the occurrence of severe and even fatal hæmatemesis, which has been met with several years afterwards. On the other hand, striking improvement has been obtained even in late and unpromising cases with ascites. It is clear, moreover, that some of the failures of splenectomy must now be set down to errors in diagnosis, since the differentiation of diseases such as leuco-erythroblastic anæmia (p. 783) is comparatively recent. On the whole, while opinion remains divided through lack of positive knowledge, both of ætiology and progress, splenectomy should be reserved for cases in which reasonable health is not being maintained in spite of active treatment of the anæmia. Enormous splenomegaly or repeated attacks of perisplenitis are other indications for surgery. If splenectomy be decided upon, the blood platelet count should be carefully watched (as in every operation of splenectomy), and, if the count is high, the operation should be deferred. A rise in the platelet count occurs after splenectomy, and if figures of 750,000 or more per c.mm. are reached, there is some danger of widespread and even fatal thrombosis in abdominal veins or elsewhere.

The alternative to splenectomy is X-ray treatment applied over the spleen, which may reduce the size of the organ, but does not influence the course of the disease.

TUBERCULOSIS OF THE SPLEEN

Although the spleen shows tubercles in almost every fatal case of tuberculosis, localised infection leading to chronic splenomegaly is rare. This does occur, however, and the splenic enlargement, which may be considerable, presents a difficult problem in diagnosis. The true pathology is seldom suspected, unless active tuberculosis is known to exist in other organs. In such circumstances, however, an amyloid spleen might first be suspected. The treatment must obviously vary in relation to the presence and course of tuberculosis elsewhere, but massive tuberculosis of the spleen should be regarded as dangerous and splenectomy is indicated.

TUMOURS OF THE SPLEEN

Simple tumours are very rare, but fibromas, hæmangiomas and lymphangiomas have been noted.

Sarcoma is the only primary malignant tumour. Primary carcinoma of the spleen, because of the absence of epithelial tissue, cannot exist, and the rarity even of secondary carcinoma has been commented upon.

Sarcoma is of two types—one diffuse and the other arising in, and producing great enlargement of, the Malpighian bodies. There may be great difficulty in deciding whether true tumour growth exists, or merely excessive proliferation of reticulo-endothelial cells. Secondary nodules in lymphatic glands may afford the only proof. Diagnosis is impossible without laparotomy. Splenectomy should be carried out, and cases of permanent cure are on record.

B. DISEASES OF THE RETICULO-ENDOTHELIAL SYSTEM

The position of the cells of the reticulo-endothelial system within the body and the main functions attributed to them have already been discussed. Some confusion often arises because different terms are applied to the cells of this system, and it may be well to mention that monocytes, histiocytes, macrophages, endothelial cells and large mononuclear cells may all belong to this group, the cells being derived from reticular cells and from endothelium.

The following diseases, not described elsewhere and associated with hypertrophy of this system of cells, are recognised :

MONOCYTIC LEUKÆMIA

A variety of acute leukæmia only recently identified, and not easy to separate from the acute myeloblastic type (see p. 802).

HYPERCHOLESTEROLÆMIC SPLENOMEGALY IN DIABETES MELLITUS

This is a rare condition, arising in conjunction with lipæmia in the blood. The enlarged spleen is filled with foamy cells containing lipoid, which, however, may not show double refraction to light when viewed through crossed Nicol's prisms, as does ordinary cholesterol-ester. For this reason, confusion with Gaucher's disease may easily arise. Chemical analysis, however, proves the presence in the tissue of a great excess of cholesterol. These cases clinically often exhibit xanthomatosis of the skin, and some have shown the interesting complication of hepatic cirrhosis and jaundice.

XANTHOMATOSIS. (See p. 1468.)

SARCOIDOSIS. (See p. 1467.)

GAUCHER'S DISEASE

Definition.—An uncommon chronic disease, arising in early life and first characterised clinically by progressive splenic enlargement; hepatic enlargement soon follows the splenomegaly; and, finally, the two organs are enormous. The condition is due to a peculiar type of reticulo-endothelial hyperplasia, in which the cells (in spleen, liver, bone-marrow and elsewhere) are filled with a lipoid substance named kerasin.

Ætiology.—This is unknown, but it is possible that the condition is due to an inborn error of metabolism. The disease begins very insidiously in early life. Most cases are recognised before 10 years of age, but in a few, only in adult life. In a well-known published series, females outnumber males as much as 7 to 1. The Jewish race exhibits a special proclivity to this disease, but it is found in other races. Familial incidence is important, as affording some evidence of an inherited abnormality. As many as four children in a single generation of one family have suffered from the disease.

Pathology.—The reticulo-endothelial cells, wherever they occur, become enormously distended with " kerasin," which is not doubly refractive to light. In paraffin sections the large foamy cells are very characteristic. The spleen, and later the liver, are grossly enlarged and smooth, and large collections of the cells in the bone-marrow may ultimately lead to spontaneous fractures. (See p. 1392).

Symptoms.—Slowly progressing splenic enlargement is the first and cardinal sign. The enlargement soon forms a distinct bulge on the left side of the abdomen, and ultimately is enormous. This is followed later by enlargement of the liver. Ultimately the two organs may be so enormous as to appear to fill the whole abdomen. The lymph glands are never enlarged. The eyes show a phenomenon which is so constant as to be almost pathognomonic: a brownish-yellow wedge-shaped thickening, or pinguecula, appears first on the nasal, and later on the temporal, side of each eye. The skin of the face, neck, forearms and hands frequently shows a peculiar brownish-

yellow solid pigmentation, or mottling, which may also be seen over both legs and ankles. The pigment does not appear to be hæmosiderin. Hæmorrhage from mucous membranes (epistaxis, bleeding from the gums) is common, but never severe. Small hæmorrhages and hæmorrhagic pimples are frequent in the skin, particularly in areas liable to slight trauma. There are no characteristic changes in the blood, and anæmia is absent except in the very late stages. Apart from the inconvenience due to the enormous abdominal distension, the patients may complain little, and the mental faculties are unimpaired.

Course and Termination.—The disease is very chronic, but exhibits a slow and progressive advance. Cases are on record of over 40 years' duration, and of 20 years after splenectomy in adult life. Death often ensues from some intercurrent disease.

Diagnosis.—The familial history; early onset; great and progressive splenomegaly; hepatic enlargement; changes in the eyes; pigmentation; and great chronicity—these constituting an almost characteristic and unmistakable picture. Von Gierke's disease (Glycogen disease) (p. 692) is distinguished by the great hepatic enlargement, together with an absence of splenomegaly.

Treatment.—Splenectomy is to be recommended, in childhood if possible. Even if cure cannot be promised, the patient is relieved from the enormous subsequent abdominal distension.

NIEMANN-PICK'S DISEASE

Synonym.—Pick-Niemann's Disease.

Definition.—A rare more or less generalised disease of the reticulo-endothelial system, confined to infancy or very early childhood and rapidly fatal. First described by Niemann (1914) and Pick (1924), the affected cells are filled with a peculiar complex lipoid. At least 50 per cent. of the patients are of Jewish stock, and although a review of most of the recorded cases shows that there is some familial tendency, this is not very striking.

Pathology.—Reticulo-endothelial cells, wherever they occur, are filled with a complex lipoid mainly composed of phosphatides. The liver, spleen and to a less extent the lymph glands are in consequence enlarged. Histological examination also reveals the presence of many foamy cells containing the lipoid in the bone-marrow and elsewhere. The blood picture is normal.

Symptoms.—The disease begins in the first year, the infant does not thrive, and the exposed skin shows a brownish pigmentation. A mongoloid facies is occasionally noticed. The liver and spleen rapidly enlarge, and may soon almost fill the distended abdomen. Groups of lymphatic glands are also swollen.

Diagnosis.—Confusion may arise with: (1) Waren Tay-Sachs' Disease (Amaurotic Family Idiocy), a disease of infants, strongly familial, almost always affecting the Jewish race, and due to a lipoid degeneration of cells of the central nervous system. In this malady, however, the liver and spleen are not enlarged. (2) Gaucher's Disease. This begins later in childhood and persists into adult life. (3) Von Jaksch's Anæmia. This is at once

differentiated by the blood picture. (4) Congenital Syphilis with hepatic enlargement.

Prognosis and Treatment.—Death occurs almost invariably within two years of birth, and no treatment is possible.

HAND-SCHÜLLER-CHRISTIAN'S DISEASE

Synonyms.—Hand's Disease; Schüller-Christian's Disease or Syndrome.

Definition.—This is a rare lipoid disturbance of the reticulo-endothelial cells, but it is of greater importance than Niemann-Pick's disease because some sufferers survive to adult life. First described by Hand in 1893, cases were also recorded by Schüller in 1915 and Christian in 1919; in all, over one hundred have been reported.

Ætiology.—This is quite unknown. There is no hereditary, family or racial tendency, and either sex may be affected. The disease usually first shows itself in early childhood, but occasionally somewhat later. Mental changes are absent.

Pathology.—The diagnostic feature is the presence of localised deposits of cholesterol-ester in the bones of the skull, most easily recognised in the flat bones of the vault but also occurring elsewhere. Other bones of the body are rarely involved (see p. 1393). Histologically the lipoid is contained in "foamy" cells, and giant cells are numerous. The lesion, in fact, closely resembles xanthoma (p. 1468), and the clinical features of the disease under discussion are due to the peculiar and characteristic sites of the lipoid deposit. The cholesterol content of the blood is often, but by no means invariably, raised.

Symptoms.—The three outstanding features of the disease are: (1) Bony defects of the skull, visible as areas of decreased density in X-ray films; (2) diabetes insipidus, due to localised involvement of the pituitary; and (3) exophthalmos, on one or both sides.

The clinical signs which usually first attract attention in a child are diabetes insipidus or exophthalmos; the former is present in 70 per cent. of all cases, the latter not so frequently. When X-ray films are taken defects in the skull are invariably visible.

Diagnosis.—The three points mentioned above are characteristic. The changes in the skull, seen by X-rays, are essential; but the diagnosis may still be made when one or even both of the others are absent. Various clinical features have been described in individual cases, but none of these form an essential part of the syndrome or aid diagnosis.

Prognosis.—This is not good, and one third of the patients die in childhood. The earlier the onset (before 5 years) the worse the outlook. The initial acute phase is evidently the danger. If the patient survives this and the chronic stage (presenting itself chiefly as diabetes insipidus) is reached, he may live for many years.

Treatment.—X-ray therapy may benefit the local condition in the bones of the skull, and should be tried. Dietetic restriction of foods rich in cholesterol has been recommended, but is of doubtful value. No treatment is known to remove the exophthalmos, but the diabetes insipidus responds quite well to the usual therapy for that disease (p. 483).

RETICULO-ENDOTHELIOSIS OF THE SPLEEN

Here may be mentioned a number of cases of chronic splenomegaly, often with enormous enlargement, and of unknown ætiology. The clinical picture resembles splenic anæmia, but on histological examination the organ exhibits extreme reticulo-endothelial hyperplasia, and frequently giant-cells are present. In some cases the liver has been found to be cirrhosed. The exact status of this group of cases is still undetermined, but the histological changes in the spleen are quite unlike Hodgkin's disease, or any other type of splenomegaly.

J. W. McNee.

SECTION XII

DISEASES OF THE LYMPHATIC SYSTEM

INTRODUCTION

THE lymphatic system consists of the lymphatic vessels (lymphatics), the thoracic duct, the lymph nodes or glands, and multitudes of large or small collections of lymphoid cells scattered throughout almost every organ and tissue of the body. Examples of large collections are the tonsils, the Peyer's patches of the intestine, the Malpighian bodies of the spleen, and the thymus gland. Small collections are well seen in the liver, the bone-marrow, the lungs, the thyroid gland, and in many other situations.

Our knowledge of the functions of this abundant tissue is still meagre. It seems certain that the larger collections of lymphoid tissue, and especially the lymph nodes, may be regarded as filters of the blood plasma. How is this function carried out? It is now recognised that the lymph nodes are not made up merely of lymphocytes and lymph-follicles, but contain both lymphoid and reticulo-endothelial tissue. The sinuses of the lymph glands are lined by reticulo-endothelium, through which all substances entering the glands must pass. The functions of the reticulo-endothelial cells have already been discussed (p. 824), and it is this part of the lymph gland which is believed to filter out, or store, foreign particles, bacteria, and metabolic products. As a result, the gland may often be damaged or diseased.

A lymph gland is arranged in follicles, and it was long claimed that the centre of each follicle, which contains pale and larger cells, is the "germinal centre" in which new lymphocytes, large and small, are formed. It is now considered more probable (although still unproved) that the large pale central cells are essentially reticulo-endothelial in function.

The purely lymphoid parts of the glands are the source of the lymphocytes, but the functions subserved by these cells, in the blood stream and elsewhere, are still unknown.

The thymus gland is also double in structure, the larger cortical part being chiefly composed of ordinary lymphoid tissue, while the smaller medulla (Hassall's corpuscles) is epithelial in origin.

DISEASES OF THE LYMPHATIC VESSELS

(i) DISEASES OF THE THORACIC DUCT

Apart from obstruction of the duct, caused by intrinsic or extrinsic tumours (usually malignant in nature), and less often by tuberculosis, aneurysm and lymphadenoma, lesions in this situation are rare and are very difficult of

recognition during life. The results of obstruction are chylous pleural effusion and (or) chylous ascites. Since chyliform ascites may occur without obstruction to the thoracic duct, as in tuberculous peritonitis, peritoneal carcinomatosis and even in cirrhosis of the liver, the presence of a milky pleural effusion is better evidence of a thoracic duct lesion than is a milky ascites. But even here the diagnosis is by no means certain on this fact alone. Chyluria, with chylous œdema of the genitals and lower extremities, if concurring with one or both of the above do, however, make diagnosis of obstruction to the thoracic duct almost certain.

(ii) DISEASES OF THE LYMPHATIC VESSELS

(i) LYMPHANGITIS.—Acute inflammation of the smaller lymphatics is a very common infection, and is mainly of surgical significance. When present in septicæmia, however, its importance lies in the fact that it indicates the area of primary septic infection, or that pyæmic metastases are threatening in the neighbourhood of the inflammation. The appearance is that of reddish lines on the skin, running in the long axis of the limb, or of a red blush, here or elsewhere, associated with pain, tenderness and slight œdema. Chronic lymphangitis is usually tuberculous or syphilitic in nature.

(ii) LYMPHANGIECTASIS.—This condition is usually the result of obstruction of the larger lymph vessels, causing dilatation of the smaller radicles, as by carcinoma, scar tissue, etc., or by infiltration of the walls of the vessels by tubercle or syphilis. *Elephantiasis* is a chronic affection, usually of one or both legs, leading to great increase in size of the limb. It may be congenital or acquired. In the latter case the condition may be due to infection by *Filaria sanguinis*, which causes lymph stasis and also inflammation of the skin and subcutaneous tissues.

DISEASES OF THE LYMPH NODES

A. LOCAL

(i) ACUTE LOCAL LYMPHADENITIS is generally associated with acute lymphangitis and is due to the same causes—acute septic inflammation of the skin or mucous surfaces of the part drained by the lymphatics affected. The lymphatics associated with the fauces are those most often involved, for obvious reasons. The tender and swollen nodes may suppurate, in which case the inflammation spreads, leading to peri-adenitis and involvement of the skin.

(ii) CHRONIC LOCAL LYMPHADENITIS is more often due to tuberculosis than to pyogenic infection.

CHRONIC TUBERCULOUS LYMPHADENITIS

Synonym.—Lymph Gland Tuberculosis.

This manifestation of tuberculosis, when localised, is seen chiefly in children. The cervical glands are most commonly affected, but the bronchial glands and mesenteric glands are also frequently involved.

The *cervical glands* may be invaded on one or both sides of the neck, and by their enlargement may cause much deformity. It should be remembered that frequently many more glands are diseased than can be detected by the eye or by palpation. The enlarged glands may subside spontaneously under conservative treatment, but on the other hand may become adherent and matted together. Later, caseation may ensue, the skin becomes involved and a sinus results, with discharge of sterile tuberculous pus. Secondary pyogenic infection should then be guarded against. Tuberculous glandular enlargements are always painless.

Nowadays attempts to remove masses of non-caseous tuberculous glands in the neck are rarely justified, if at all, since other infected lymph nodes must be left behind. The best treatment is general and nutritional, as advised for other forms of tuberculosis, and an open air life in a sunny coast resort is to be strongly recommended. If local caseation occurs and fluctuation is clearly detected, surgical excision must be employed, since in this way involvement of the skin, sinus formation and an ugly depressed scar may be avoided. The site of the surgical scar should be carefully chosen for its cosmetic effect, and by skilful retraction of the skin may be placed in some suitable fold away from the lesion.

The treatment of tuberculosis of the *bronchial glands* and *mesenteric glands* is discussed elsewhere.

Local tuberculous enlargement of lymph nodes in the axillæ or groins, both in children and adults, is so rare that other diseases should always be suspected.

B. GENERAL

(i) Acute Generalised Lymphadenitis. This occurs in every one of the acute infectious diseases, but is particularly frequent, and therefore of special diagnostic importance, in German measles, measles, scarlet fever and diphtheria. In glandular fever there is generalised lymphadenitis associated with mononucleosis.

(ii) Chronic Generalised Lymphadenitis. This is seen in the secondary stage of syphilis, and rarely in tuberculosis. In the latter infection the character of the nodal enlargements varies with the histological reaction to the bacillus and with the tendency to caseation, which may be well, or ill, marked. It is in cases in which caseation is delayed, or absent, that the diagnosis from lymphadenoma is sometimes very difficult, or quite impossible, in the absence of biopsy.

C. NEOPLASTIC

Lymphatic glands are invaded both by carcinoma and sarcoma. In carcinoma the involvement is secondary, and the situation and line of spread of the enlargement is often of critical importance in the diagnosis of the seat of the primary growth. Primary lympho-sarcoma is dealt with separately (p. 844), but secondary invasion by sarcoma is not infrequent.

Enlargement of lymphatic glands, local or general, in Hodgkin's disease and chronic lymphatic leukæmia, is discussed elsewhere.

HODGKIN'S DISEASE

Synonym.—Lymphadenoma.

Definition.—A disease characterised by painless, progressive enlargement of lymph nodes, usually beginning in one group and spreading to other groups, and associated with hyperplasia of lymphoid tissue in the spleen, liver and other organs, with anæmia.

The disease appears definitely to be a specific entity. Its causation is unknown. In nosology it is by some placed amongst the microbic infections, and by others amongst the neoplasmata; it has affinities with both of these processes.

Ætiological Factors.—The disease occasionally follows upon known infections—pyogenic, tuberculous or syphilitic—but in these cases it would appear to be of the nature of a secondary infection rather than an expression of any one of these diseases. It may coexist with tuberculosis. Though it may arise at almost any age, the chief incidence is during the first four decades of life. It is about twice as common in males as in females. Though sometimes seen in two or more members of the same family, there seems to be little or no real hereditary tendency.

Pathology.—The enlarged lymph nodes tend to remain discrete, and the capsule of the node is rarely, if ever, infiltrated. The masses are sometimes very large and may weigh several pounds. Individual nodes are seen to be of a pinkish-grey colour, smooth, "leathery" to the feel and, on section, show yellowish strands passing in from the capsule, with rather translucent whitish tissue between them. Areas of necrosis are unusual. Microscopic examination reveals great proliferation of the reticular endothelium, hyperplasia of the lymphoid cells and a mixture of large hyaline cells, plasma cells and eosinophil leucocytes. Some of the endothelial cells are very large and are multinuclear. These cells have some resemblance to giant cells, but their outlines are more regular and their nuclei are superposed and placed in a mass near the centre of the cell rather than ranged around the periphery. The presence of these large multinuclear endothelial cells, together with eosinophil cells, constitutes the most characteristic feature of the lymphadenomatous lesion histologically.

The *spleen* is generally enlarged at the time of death, but great enlargement, though it does sometimes occur, is unusual. The organ is quite firm, preserves its natural contours, and adhesions are often present. The surface is sometimes slightly nodular. On section the well-known "hardbake" appearance is seen—whitish-grey areas (of lymphadenomatous material) embedded in a dark red matrix (of spleen pulp).

The *liver* is the organ most often affected next to the spleen. The deposits are found to lie chiefly in the portal canals. There is usually associated fatty change.

Of other organs and tissues, the lungs, kidneys, bones and intestines are those chiefly affected.

Symptoms.—In the great majority of the cases the first symptom is the appearance of enlarged lymph nodes in the neck. The first nodes to be involved are more often in the posterior than in the anterior triangle. At this time the patient is not ill, nor does a full investigation, as a rule, discover

signs of disease elsewhere; there is little or no anæmia. Other, but less common, situations for the initial node swellings are the axillæ, the groins, the mediastinum and the abdomen. There is usually an interval of some months before general symptoms appear, and their onset is usually insidious. In some cases, however, the general symptoms advance rapidly. There is an acute type of the disease, associated with early generalisation of the node involvements, and if the original local lymph node enlargement is overlooked, the simulation of some such acute infection as miliary tuberculosis may be very close.

The features of the lymph node swellings are important. They soon become visible. They are painless, insensitive, and in the early stages of the disease they mobilise easily. To the feel, the nodes are firm and leathery. They tend to remain discrete, without involvement of the capsule and therefore without coalescence. The skin is only rarely involved; and when it is, or when, with equal rarity, the nodes undergo caseation or suppuration, this is due to secondary infection by pyogenic organisms or by tubercle. After a while the enlarged nodes tend to become massive tumours, and certain of the above features change—their mobility lessens and the individual nodes are difficult to recognise.

Two sets of symptoms now become added to the initial superficial node enlargements—the general symptoms of the disease, and symptoms referable to pressure and infiltration of the lymphadenomatous tissue in different parts of the body.

The *general symptoms* include a sense of lassitude and weakness, shortness of breath on exertion, sweating and loss of weight. Pruritus is rather common and may be very intractable. The colour of the skin changes to a *café-au-lait* tint, and in some cases a well-marked general pigmentation develops. *Pyrexia* is quite common. The form most often seen is a mild grade of remittent pyrexia, similar to that seen in tuberculosis. Not at all infrequently, however, the pyrexia assumes an undulant character, and the recognition of this type of fever is of great importance in diagnosis. It is not at all uncommonly overlooked, especially if morning and evening charts are not kept. Sometimes the undulant feature is very regular, a wave of pyrexia of some 10 to 14 days' duration is followed by an apyrexial period of somewhat shorter duration, when the pyrexial period is repeated, and so on. The symptoms wax and wane with the pyrexia, not only the general symptoms but, at times, symptoms of a focal kind. The writer has seen a case of this sort in which acute pulmonary symptoms were present, and the disease was thought to be a relapsing broncho-pneumonia. Such pyrexia as is here referred to is termed the "Pel-Ebstein type," after the two observers who first described it. There is a third, and less common, form of pyrexia: the continued type somewhat resembling typhoid fever. It occurs in severe and rapidly progressive cases.

The *anæmia*, though it may be severe, has not, despite tradition to the contrary, any special features, nor is the blood picture often helpful in diagnosis. The red blood count and the hæmoglobin estimate are those of a "secondary" anæmia. The white cells vary much in number and in kind. Leucopenia is present in some of the more acute cases, and is occasionally a striking accompaniment of the pyrexial phases in a marked Pel-Ebstein fever. In the majority of cases, however, the leucocyte count shows a

moderate rise (10,000 to 20,000). The absolute eosinophil count quite frequently lies above the top figure of the range in health (400), and this fact may therefore be of some diagnostic help.

Focal symptoms, as already stated, are due, in the main, to pressure by the lymphadenomatous masses. Mediastinal pressure causes distressing dyspnœa, cyanosis and stridor; laryngeal palsy may be bilateral and may require tracheotomy—in which case the operation may tax the resources of the most experienced surgeon. Enlarged hilum glands and invasion of the peri-bronchial tissues produce collapse of lung, pleural effusions (sometimes hæmorrhagic or chyliform), and bronchiectasis with hæmoptysis. Masses in the transverse fissure of the liver may cause jaundice and ascites.

An interesting and not very uncommon complication is a paraplegia due to meningeal involvement about the lumbo-sacral region or the cauda equina.

Diagnosis.—This is from other causes of lymphadenopathy, both local and general, such as tubercle, syphilis, the less acute form of glandular fever, leukæmia and generalised neoplasmata. There are two diseases which confuse with Hodgkin's disease in particular: these are tuberculous adenitis and lympho-sarcoma. Especially does the uncommon form of tuberculosis, termed "endothelial," cause difficulty. In such circumstances *biopsy* alone may serve to establish the diagnosis. But even then the problems may not be solved, because the node removed may not show characteristic changes, being as yet inconclusive in its early morbid appearances or being too fibrotic. Care must be exercised in the choice of the lymph node to be excised: the one most easy to remove is not necessarily the best for diagnostic purposes. M. H. Gordon has recently found that an extract of the affected lymph nodes causes an encephalitic syndrome in rabbits which he regards as specific. This biological test may therefore be used in diagnosis; its specificity requires confirmation.

Course and Prognosis.—Trousseau's description of the disease as having three stages—the stage of local lymph-node enlargement, the stage of general lymphatic enlargement, and the stage of cachexia—holds good for the great majority of cases. But cases may be acute throughout, the total duration not exceeding three months. In other instances, long periods of remission occur, and these, with modern irradiation methods of treatment, are much more frequently seen nowadays than formerly. The average duration of the disease is perhaps about five years. Patients in whom the diagnosis has been well established may be found in moderately good health ten years later. But complete arrest must be quite rare if, indeed, it occurs at all. Rather rapid "lighting up" in a quiescent case is one of the striking features of the disease, and though the condition may be, again and again, stabilised by treatment, the level of health after each active phase has passed is found to be lower than it was previously.

Treatment.—Excision of the enlarged nodes, formerly much practised, has to-day been almost completely abandoned in favour of irradiation methods, using either X-rays or radium for the purpose. Of the two methods, X-rays appear more generally useful. It is at present the usual custom to use light and frequent doses, irradiating the nodes, the spleen, the mediastinum and other parts known to be affected, mapping out the areas to be treated and selecting the angles of application with great care. These light doses may be given daily over a period of two or three weeks, and repeated after an

appropriate interval. A course of arsenic may now be administered, and nothing seems better for this purpose than the old-fashioned Fowler's solution (liq. arsenicalis) in an alkaline draught, commencing with min. 3 and gradually increasing to min. 10 or min. 15 t.d.s.p.c. General hygienic measures should be attended to throughout the treatment. Antigen therapy, based upon Gordon's researches, is on trial.

LYMPHOSARCOMA

Definition.—A disease arising in different parts of the lymphatic system, locally malignant and invading neighbouring structures; and later, spreading by the lymphatics to give rise to metastases in distant organs.

Ætiology.—The incidence of lymphosarcoma is very similar to Hodgkin's disease, but this disease is much less frequent.

Pathology.—The commonest site of origin of the disease is in the cervical lymph glands, next in the mediastinal glands, and more rarely in the tonsils, the lymphoid tissues of the naso-pharynx, the retro-peritoneal lymph glands and the lymphoid tissue of the intestine. In section the affected tissues have a homogeneous appearance. Histologically the essential diagnostic point is the uniform replacement of the normal structure of the lymph follicles by cells which are all alike and which generally closely resemble small lymphocytes. Between the cells is a fine reticulum, well shown only by special staining, and absent in ordinary "round-celled sarcoma." When the cells are uniformly larger, and possibly derived from reticulo-endothelial parts of the lymphatic system, a histological diagnosis of *endothelioma* may be justified, but otherwise the disease is identical.

Many, but not all, tumours arising in the mediastinum are examples of oat-celled carcinoma of the lung arising in a bronchus (p. 1219), so that mediastinal lymphosarcoma is less common than was formerly supposed.

In the later stages of the disease distant groups of lymphatic glands may be involved, but the spleen is not often enlarged. At necropsy secondary growths may be widespread, but are often too small to be recognised except by the microscope.

Symptoms.—When arising in the cervical lymph glands, the enlargement is rapid, matting together soon occurs, and local destruction with ulceration may ensue. Otherwise, especially if the glands involved are in deeper situations, the symptoms are chiefly those of pressure and invasion of neighbouring structures. In contradistinction to Hodgkin's disease, general symptoms are few. The patient may appear in good health, and the cachectic state seen in the late stages of lymphadenoma is absent. Fever also is much less common. The blood picture is usually not distinctive, but in a few cases may suggest lymphatic leukæmia.

Diagnosis.—This is principally from Hodgkin's disease, but other diseases of the lymphatic system should also be excluded. Removal of a suitable lymphatic gland or portion of tissue is the only rational means of diagnosis.

Course and Prognosis.—The course is more rapidly fatal than in Hodgkin's disease, but may be greatly influenced by treatment.

Treatment.—Lymphosarcoma is more susceptible to suitable X-ray treatment than almost any of the varieties of enlargement of the lymphatic

glands, and the localised masses generally disappear with great rapidity. Recurrence elsewhere, however, is soon manifest, and most patients die of asthenia. No permanent cure can yet be hoped for.

STATUS LYMPHATICUS

Synonym.—Lymphatism.

Under this term are classed, somewhat loosely, a number of cases met with in which there is hyperplasia of the lymphatic tissues in the body. The note of dramatic significance is given to these cases because, in them, sudden death is prone to occur, whether during anæsthetic administration or otherwise.

Since the thymus is found to be enlarged with great constancy in such patients, considerable importance attaches to this part of the picture, though it is probable that the essential nature of the diseased state is much more general, and that such local hyperplasia alone, though it has serious possibilities, is not responsible for more than a proportion of the fatalities.

Though the diagnosis of thymic hyperplasia is nowadays greatly assisted by X-ray examination of the thorax, by far the majority of instances of lymphatism are only discovered in the post-mortem room. Children who present a pallid and flabby facies are by no means necessarily "lymphatic" in the sense of the word here used. Nor does the presence of "thymic asthma" necessarily denote more than the local lesion of an enlarged thymus. In other words, lymphatism always presents thymic hyperplasia as one of its features, but demonstration of thymic enlargement, whether before or after death, by no means proves the existence of lymphatism. The real nature of this latter condition is quite unknown.

MIKULICZ'S DISEASE

Definition.—A slowly developing bilateral enlargement of the lachryma glands, followed by similar symmetrical enlargement of the salivary glands—the parotid, the submaxillary and the sublingual.

Ætiology.—This is unknown. The condition occurs only in adult life.

Pathology.—This disease, described in 1888, is included here rather than under conditions affecting the salivary glands because the enlargement is due to hyperplasia of the lymphoid tissues, and not of the secretory elements. Excised tissue shows changes resembling sarcoma or lymphatic leukæmia, and the condition has occasionally progressed to true leukæmia.

Symptoms.—The enlargement of the glands is symmetrical, painless and slowly progressive. The ultimate deformity may be very great. The only symptoms complained of are interference of vision and impaired salivary secretion. The general health is unimpaired.

Diagnosis.—This depends on the clinical features described. Leukæmia, Hodgkin's disease, tuberculosis and syphilis, in all of which enlargement of the salivary glands may be present, should be excluded.

Treatment.—Arsenic, potassium iodide and X-ray therapy have all been tried, but the disease pursues a very chronic course

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SECTION XIII

DISEASES OF THE CIRCULATORY SYSTEM

DISEASES OF THE HEART AND PERICARDIUM

PHYSIOLOGICAL CONSIDERATIONS

In normal circumstances it is the left ventricle which gives rise to the clinical apex-beat, and the apex-beat may then be defined as that part which is farthest to the left at which a definite forward thrust is imparted to the finger held perpendicularly to the chest. When the right ventricle is much enlarged, however, that chamber may displace the left ventricle backwards, so that the apex-beat is due to the contraction of the right, instead of the left, ventricle.

The *sino-auricular node* is a small node of specialised tissue which is situated at the junction of the superior vena cava with the right auricle. In it are nerve fibres and ganglion cells, which are connected with the vagus and sympathetic nerves. The *auriculo-ventricular node* is a small node of specialised tissue which is situated in the septal wall of the right auricle. The *auriculo-ventricular bundle*, or bundle of His, is a bundle of tissue connecting the auricles and ventricles. It arises from the auriculo-ventricular node, passes forwards in the interauricular septum, then turns downwards, and at the upper margin of the interventricular septum divides into two main branches, one of which goes to the right and the other to the left ventricle, each eventually terminating in widespread subendothelial arborizations—the Purkinje fibres. Nerve-fibres and ganglion cells are present in the auriculo-ventricular bundle, and its blood supply is mainly derived from a special branch of the right coronary artery.

The heart muscle possesses certain inherent properties, namely: Rhythmicity, by which is meant the power of generating impulses which can excite it to contract rhythmically; excitability, the power to receive impulses for contraction; contractility, that of contracting in response to impulses or stimuli; conductivity, that of conveying waves of excitation or impulses from fibre to fibre; and tonus or tonicity, a condition of sustained partial contraction, independent of systolic contractions, by virtue of which the muscle fibres offer more resistance to stretching during diastole than they would owing to their inherent elasticity or other properties alone.

The function of rhythmicity is more developed in the remains of the primitive cardiac tube than in the auricular or ventricular tissue, especially in the remains of the sinus venosus. Impulses therefore normally arise at the latter site, and there is reason to believe that they begin in the sino-auricular node, for which reason the node has been called the " pace-maker "

of the heart; the rhythm of the sinus governs that of the remaining segments of the organ. The function of conductivity is most developed in the auriculo-ventricular node, the bundle, and its branches; and that of contractility in the muscle fibres of the auricles and ventricles.

From the sino-auricular node, the wave of excitation travels to the other portions of the heart by means of the function of conductivity. It first spreads over the auricles, and auricular systole takes place. It is then conveyed through the auriculo-ventricular node, along the auriculo-ventricular bundle, its branches and ultimately the subendothelial arborizations, and is so distributed to the ventricles, the latter contracting in response to excitation waves received from the auricles.

The interval separating the commencement of auricular and ventricular contraction is of great clinical importance, for it is an index of the time-relations of the contraction of the auricles and ventricles, and of the function of conductivity of the auriculo-ventricular node and bundle above its division. It is called the *As–Vs* interval. The function of the conductivity of the heart may be measured by means of the electro-cardiograph and the clinical polygraph.

But while normally the function of rhythmicity is most developed at the sinus part of the auricle it may be so in any other portion of the remains of the primitive cardiac tube, in which event the impulses are generated at that particular point; for this reason the different parts of the heart are capable of starting independent contractions. They may arise in the auricle; or in the auriculo-ventricular node or the bundle above its division; or in the ventricle itself, probably in the subendothelial arborizations.

When the impulses are generated in the sinus part of the auricle, we speak of normal or sinus rhythm. When they arise at an abnormal point, *i.e.* at some site other than the sinus, the abnormal focus is sometimes termed *ectopic* (Lewis) or heterotopic (Hering), and the contraction an *ectopic* beat. The term *ectopic* rhythm also is sometimes employed.

When the ventricular contraction is the result of an excitation wave which comes from above the division of the auriculo-ventricular bundle, it is sometimes termed supra-ventricular in origin; and when it is due to an impulse generated below the division of the bundle, it is sometimes called of ventricular origin.

When the ventricular contraction is supra-ventricular in origin, but the manner of conduction of the wave of excitation along the normal channels is abnormal, the ventricular beat is sometimes called *aberrant*.

In what is termed *auriculo-ventricular nodal rhythm*, the impulses arise in the auriculo-ventricular node, and travels upwards into the auricles and downwards into the ventricles, giving rise to a simultaneous contraction of both auricles and ventricles.

When the ventricles beat independently of the auricles, the independent rhythm of the ventricles is called "idio-ventricular" rhythm. It is found only in association with auriculo-ventricular block.

Throughout systole the heart muscle is absolutely refractory and so does not respond to a stimulus, whatever its strength. Immediately after systole the muscle is relatively refractory, during which it may respond to a stronger stimulus but not to a weaker one. When stimulated, the cardiac muscle either does not contract at all, or it does so to the fullest possible extent at the

time, whether the stimulus be weak or strong; it is a case of "all or none." The longer the time that has elapsed since the previous contraction, the weaker is the stimulus required to bring about a further contraction. Further, the greater the degree of excitability of the muscle-fibres, the weaker is the stimulus required, and the earlier in the refractory period will the heart contract. The amount of contraction does not depend upon the strength of the stimulus employed, but varies according to the time at which the stimuli are applied. When a contraction occurs early in diastole, the contraction in the succeeding cardiac cycle is weaker than that preceding it. Within certain limits, the degree of contractility depends upon the length of the preceding diastole; the greater the period of rest, the more perfect and full is the recovery. It can, therefore, be readily understood that the greater the heart-rate the greater is the possibility of cardiac failure. Similar laws apply to each of the other special functions of the heart muscle. In the case of conductivity, for example; when conduction occurs, this function has been exercised to the fullest extent possible at the time of stimulation. The refractory period follows immediately after the conduction of a stimulus, and during this brief period the muscle-fibres cannot again conduct a stimulus, conductivity being completely exhausted. Restoration, however, quickly commences, and ultimately the function is restored. The extent of the relaxation between the contractions depends upon the degree of tone present, and upon the rate of the heart-beat. With a slower rate there is, of course, more time for full relaxation. There should be a sufficient period of rest after each function has been exercised. Within certain limits, the greater the period of rest the more perfect and full is the recovery of each special function. In heart failure one or more of the five fundamental functions of the fibres of the heart muscles are at fault, and, if this occur to two or more simultaneously, the different functions are not necessarily equally affected. From what has been said, the value of rest in heart failure can be readily understood.

The pulsus alternans is probably an indication of depressed contractility of the heart. When conductivity of the heart is impaired, there is some degree of heart-block. A lowered state of tonicity results in dilatation of the heart and it may be of the auriculo-ventricular orifices.

The heart has the power of rhythmically contracting and dilating, due to an inherent power possessed by the cardiac musculature, independent of any extrinsic nervous influence. Nevertheless, the activity of the various functions of the muscle-fibres is under nervous control. Both the inhibitory fibres of the vagus and the accelerator fibres of the sympathetic are normally in a state of tonic activity, and the cardiac centres are in a state of continuous slight excitation.

The Cardiac Cycle.—Stated briefly, in the cardiac cycle there occur in rapid succession auricular systole, ventricular systole and ventricular diastole. There are three phases in the systole of the ventricles, namely: (*a*) The period during which all four valves are closed; this is called the pre-sphygmic period. (*b*) The period during which the semilunar valves are open; this is called the sphygmic or pulse-period. (*c*) The period between the closure of the semilunar valves and the opening of the auriculo-ventricular valves; this is called the post-sphygmic period. It should be noted that the sphygmic or pulse-period in a tracing of the cardiac apex, carotid pulse or radial pulse, does not refer to the actual time of occurrence of ventricular systole, but

to a period in the tracing; and, on account of the distance from the heart, the sphygmic or pulse-period will necessarily be later in a radial tracing than the same period in a tracing taken at the cardiac apex or over the carotid. The periods of time which elapse between the apex-beat and the carotid pulse, and between the carotid and radial pulses, have each been found to be $\frac{1}{10}$th of a second; the pulse-period, therefore, in a radial tracing commences about $\frac{1}{10}$th of a second behind the same period in a tracing of the carotid, and about $\frac{1}{5}$th of a second behind that in a cardiogram.

Assuming that in normal health the human heart beats about 72 times per minute, each cardiac cycle, therefore, is completed in about $\frac{8}{10}$ths of a second, this time being divided up in the following manner: systole of auricle, $\frac{1}{10}$th of a second; systole of ventricle, $\frac{3}{10}$ths of a second; diastole, $\frac{4}{10}$ths of a second. The most stable part of the cardiac cycle is the ventricular systole, and the most variable is the diastole. The rate of the heart-beat mainly depends upon the duration of the diastole. When the heart beats unusually quickly, the duration of the diastole is shortened by a greater degree than that of the systole; in other words, when the period of the cardiac cycle decreases it is the long pause which is particularly shortened.

THE CLINICAL POLYGRAPH

The clinical polygraph was the instrument employed by Mackenzie in his epoch-making researches on irregular action of the heart and the results of the administration of the digitalis group of drugs in those suffering from cardiac affections.

By means of this instrument the movements of both auricles and ventricles can be recorded graphically, the time-relations of the contractions studied, and the function of conductivity of the auriculo-ventricular bundle above its division measured. It is possible to identify sinus arrhythmia, the various types of extrasystoles, the various degrees of auriculo-ventricular heart-block, the pulsus alternans, auricular fibrillation, and a proportion of cases of auricular flutter. At the present time, however, the clinical polygraph has largely been superseded by the electrocardiograph in clinical practice, since the latter gives practically all the information to be obtained by the polygraph, its findings are more accurate, and it provides additional information (see p. 999.)

Clinical electrocardiography is dealt with at the end of the Section.

By means of the clinical polygraph it is possible to obtain tracings of any two of the following: The radial or brachial pulse, the apex-beat, the carotid pulse, the jugular pulse, the liver pulsation, and the respiratory movements. A time-marker registers $\frac{1}{5}$th of a second on the recording surface. For clinical purposes, it is usual to take simultaneous records of the radial or brachial pulse, and of the pulsation of the jugular vein at the root of the neck. A tracing of the radial pulse is called a sphygmogram or arteriogram, and a tracing of the venous pulse is called a phlebogram.

THE PHLEBOGRAM.—In a normal phlebogram, in each cardiac cycle, three main elevations, separated by three depressions, are to be observed (Fig. 20). The three waves are called the *a*, *c* and *v* waves respectively. The *a* wave is due to the auricular systole. The *c* wave is probably due to the impulse

of the carotid artery, but a similar wave occurs in intra-auricular pressure curves and, therefore, the *c* wave may be partly venous. The *v* wave is due to stasis; during ventricular systole the pressure in the right auricle and jugular vein rises steadily, falling suddenly with the opening of the auriculo-ventricular valves, and this sudden fall of pressure marks the summit of the *v* wave. Occasionally a fourth wave, the *h* or *b* wave, occurs in diastole



FIG. 20.—Simultaneous tracings of the jugular and radial pulses, showing the normal form of venous pulse. Note that the *a*–*c* interval is $\frac{1}{5}$th second, and that the summit of the *v* wave coincides with the dicrotic notch of the radial pulse.

between the *v* wave and the *a* wave of the next cycle (Fig. 21). The waves of the jugular curve are identified by their time-relations to points on the radial pulse. The commencement of the *c* wave occurs $\frac{1}{10}$th second before the main radial upstroke, and the summit of the *v* wave is synchronous with the bottom of the aortic notch in the radial pulse. When the *v* wave is double (v^1 and v^2), the apex of the second *v* wave is synchronous with the aortic notch. The *a* waves are recognised by exclusion, after identifying the *c* and *v* waves. The period of ventricular systole corresponds in time to the segment of the venous curve between the commencement of *c* to

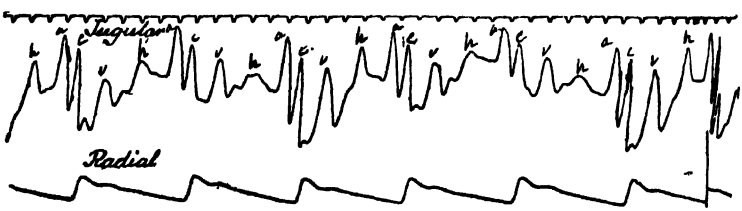


FIG. 21.—Simultaneous tracings of the jugular and radial pulses. The jugular curve shows the *h* or *b* wave.

the summit of *v*. The *a*–*c* interval, from the commencement of the *a* wave to the commencement of the *c* wave, approximately represents the conduction time between auricles and ventricles, and measures normally between 0·15 and 0·2 seconds. If it exceeds $\frac{1}{5}$th second, it indicates depressed conductivity by the auriculo-ventricular node or bundle. When the cardiac rate is unusually frequent, the duration of the diastolic

interval is shortened, so that the *v* wave approaches more and more to the following *a* wave, and *v* and *a* may even coincide and superimpose.

In cases of great distension of the right auricle the *c* and *v* waves coalesce to form a plateau-shaped wave (Fig. 22). This was described by Mackenzie

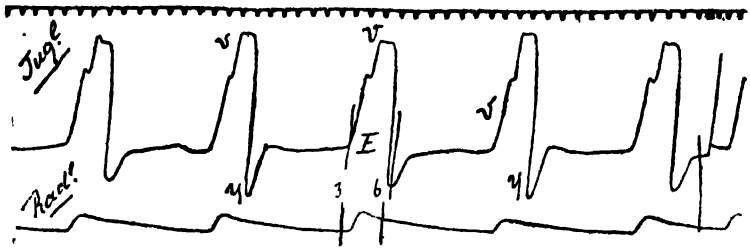


FIG. 22.—Simultaneous tracings of the jugular and radial pulses, from a case of auricular fibrillation, showing the ventricular form of venous pulse, and an unusually slow radial pulse.

as the ventricular form of venous pulse when it occurred in the absence of the *a* waves, but the condition is due to the great distension rather than to auricular fibrillation.

CIRCULATORY FAILURE

It is necessary to point out that there are two varieties of circulatory failure, namely, cardiac or central, and peripheral. In the first variety the fault lies in the heart itself. In the second, there is failure of the circulation at the periphery. In some cases both forms are present, as may occur in diphtheria and pneumonia.

It is important to note that syncope may be cardiac, or peripheral, in origin, and is much more commonly due to the latter.

A. HEART FAILURE

In the study of heart disease it is of fundamental importance that we should have a true conception of the principles which underlie heart failure. It is also of much practical consequence to recognise the beginning of failure, and, in addition, to distinguish between the various degrees which may arise later.

It should be understood that the essential cause of cardiac failure lies in the heart muscle, and is due to changes in the heart muscle which render it unable to maintain an efficient circulation. If this view of the causation of heart failure be correct, valvular defects and disturbances of the cardiac mechanism, such as auricular fibrillation, and diseased conditions of the blood vessels, should be regarded from the point of view of the relation which they bear to the myocardium, as well as specific affections in themselves. Let us take the case of a valvular lesion: First of all, it can be readily understood that it is a mechanical impediment to the heart muscle in its work. But it should be remembered that there are, as a rule, along with the chronic valvular lesion, coincident changes in the cardiac musculature, or the blood

vessels, or both. In all cases of chronic valvular disease, therefore, it is of importance that we should endeavour to ascertain whether the lesion which has invaded the valve has also affected the myocardium, or the blood vessels, or both, and, if so, to what degree.

By the 'reserve force' of the heart is meant the force inherent in the cardiac muscle which is called upon when bodily effort is made; and by the 'rest force' is meant the force inherent in the muscle of maintaining an efficient circulation when the body is at rest.

The reserve force may be estimated by the response of the heart to effort. This includes: (1) The effect of a standard piece of physical exertion on the cardiac and respiratory rates, which is called the 'exercise tolerance test. The pulse rate should not be unduly increased, and it should return to its former level within two minutes after the cessation of the effort. (2) That which is of much greater value, the amount of physical exertion in which the patient can indulge without experiencing abnormal subjective symptoms.

In our investigation of the reserve force of the heart, it is necessary to emphasize the following. The natural standard of the cardiac strength varies in different individuals, each knowing the amount of exertion in which he can normally engage without producing subjective symptoms. Our inquiry should aim at finding out whether there has been a departure from such, and, if so, in what degree. Again, a departure from the normal standard may be due to temporary or extraneous causes, such as deficient tone the result of lack of physical exertion, fatigue, upward displacement of the contents of the abdominal cavity, anæmia, and broncho-pulmonary morbid affections.

Inquiry should also be made whether any departure from the normal standard is increasing, and, if so, whether in spite of an adequate period of rest and the employment of other remedial measures.

By heart failure is meant the condition in which the cardiac muscle is unable to maintain an efficient circulation. It almost invariably begins with a diminution of the reserve force of the heart. This manifests itself by a limitation of the area of cardiac response, *i.e.* an individual cannot indulge in physical exertion which formerly he was able to do without experiencing subjective symptoms. These may appear as the result of less and less effort, until ultimately the 'rest force' is diminished, some or all of the symptoms being present even during rest, and objective signs also become evident.

It may be mentioned here that while the terms 'compensation' and 'decompensation' or failure of compensation sometimes used with reference to chronic valvular disease (see p. 927) are not strictly synonymous with the absence and presence of cardiac failure respectively, for practical purposes they correspond with them.

The onset of heart failure may be gradual, or more or less rapid or even abrupt, usually the former. Among the most common symptoms are difficulty in breathing (dyspnœa), fatigue, palpitation, discomfort or pain, giddiness, and faintness or actual syncope, referred to exertion. I would again emphasize that these may also be the result of temporary or extrinsic causes, some of which have been mentioned.

Difficulty in breathing is the most frequent and earliest symptom, and is more frequent in mitral than in aortic disease. Its degree may be so slight that the patient himself may only observe it on over-exertion. Later, however, the dyspnœa may be induced by less and less effort, until ultimately

it may be brought on by such slight forms as walking slowly on the level, or on changing the position in bed; it may, indeed, be present without any effort. The degree may amount to orthopnœa, that is, the patient may be unable to lie down.

There may be paroxysms of dyspnœa, or what is termed cardiac asthma. In the great majority of cases they occur during the night, and perhaps especially when the patient is falling off to sleep, but very occasionally, especially in mitral stenosis, on over-exertion during the day. The attack comes on suddenly, with a sense of suffocation, the intensity of which may be extreme and compel the patient to breathe in a laboured manner and, if in bed, to sit up. There may be a sense of oppression in the chest, cough, frothy expectoration, which may be blood-stained, wheezing, sweating, and cyanosis. Rhonchi and bubbling râles may be audible, and the second sound in the pulmonary area may be accentuated. After a time, lasting from a few minutes to a few hours, the attack subsides. If due to left ventricular failure, not infrequently there is gallop rhythm, presystolic in time (see p. 856), and less often pulsus alternans, especially in hypertension. Acute pulmonary œdema may occur.

Paroxysmal dyspnœa and acute pulmonary œdema are believed to be due to paroxysmal venous congestion and paroxysmal pulmonary œdema respectively, the result of disproportionate activity between the two sides of the heart. They occur especially in hypertension, aortic incompetence or stenosis, chronic myocardial disease, and atheroma of the coronary arteries, with more or less sudden failure of the left ventricle. They may rarely be met with in marked mitral stenosis with sudden tachycardia, with increased output by the right ventricle, but apparently not if there is gross dilatation of the left auricle or auricular fibrillation. In both groups of cases there is disproportionate activity on the part of the two sides of the heart. Paroxysmal dyspnœa and acute pulmonary œdema are generally relieved if right-sided failure or auricular fibrillation supervenes, and usually recur if these are successfully treated.

Cheyne-Stokes respiration sometimes occurs, and is usually the result of chronic heart disease, especially in left ventricular failure. At first, it is generally during sleep and is slight, consisting merely of waxing and waning of respiration, but later, there may be actual apnœa and hyperapnœa. If during the day, it is of more serious significance.

Fatigue, usually related to physical or mental effort, generally the former, is not an uncommon symptom of cardiac failure. While palpitation may be due to such (see p. 876), it is much more frequently met with apart from it. Discomfort or pain is a relatively infrequent manifestation of heart failure. Some are of opinion that failure is never a cause of such. I do not share this view, although I would point out that even in the subjects of organic morbus cordis pain is generally due to extrinsic causes. For differential diagnosis, see p. 877. The pain of angina pectoris is described on p. 984. There may be a sensation of weight or oppression over the precordium in cardiac failure.

Symptoms due to cerebral anæmia the result of failure on the part of the heart to maintain an adequate supply of blood to the brain are not infrequent. They include early fatigue on mental effort, sleeplessness, disagreeable dreams, giddiness, faintness or actual syncope, lack of power of concentration, impairment of memory, headache, nervousness, loss of emotional control,

mental irritability, and, in severe cases, even insanity. Giddiness may be slight and transient, or severe enough to cause the patient to fall.

It is important to note that syncope may depend upon a fault in the heart itself, *i.e.* it fails to propel an adequate amount of blood into the arteries; or upon failure of the venous return to the organ, due to vaso-dilatation, especially of the splanchnic area.

The latter is much more common. In such there is a preliminary fall of blood pressure. There are two varieties, namely, that associated with posture, and what are called *vasovagal attacks*. The former is more frequent in the elderly or middle-aged. The pulse becomes feeble and may be imperceptible. Vasovagal attacks are more common in the young, and are apt to be associated with emotion, a heated stuffy atmosphere, or fatigue. They rarely occur when the patient is lying down. There is not only a preliminary fall in the blood pressure but also a diminution in the cardiac rate due to increased vasovagal tone, both of which may be marked. There is profuse sweating, respiration becomes slow and may almost cease, the face may become of a greenish pallor, there may be dilatation of the pupils, nausea and vomiting, and occasionally slight convulsions of the face and arms and trunk. Full recovery is usually slow.

Syncope of primary cardiac origin may occur in auriculo-ventricular block (see p. 908), paroxysmal tachycardia, 1 : 1 auricular flutter, and occasionally in organic morbus cordis, most commonly in aortic valvular disease and chronic myocardial disease. It should be remembered, however, that syncope in the last two may also be the result of failure of the venous return to the heart. In paroxysmal tachycardia and 1 : 1 auricular flutter, the amount of blood propelled by the heart at each systole is so small as to give rise to cerebral anæmia. There is a severe fall of blood pressure, whereas in auriculo-ventricular block there is no fall. In aortic and chronic myocardial disease syncope is usually associated with physical exertion.

There may be cough, generally with expectoration, which may be only nocturnal, and slight wheezing. Hæmoptysis is not infrequent, and may be the result of venous congestion or of a pulmonary infarct. Cough and hæmoptysis are most common in left ventricular failure and mitral stenosis. Cardiac asthma and acute pulmonary œdema have been dealt with. There may be physical signs of venous congestion and œdema of the lungs, which may be limited to the bases, or more or less widespread; and, later, of hypostatic pneumonia. The vital capacity of the lungs is diminished, and the pulmonary circulatory rate is decreased. Radiological examination may reveal evidence of pulmonary congestion or œdema. There may be hydrothorax, the result of pulmonary congestion, in which event it is generally left-sided. The pulmonary artery and its branches may become dilated and even atheromatous. There is a tendency to affections of the respiratory system, such as bronchitis and broncho-pneumonia, in heart disease, especially with mitral stenosis.

Digestive symptoms are common, being due either to venous congestion or to deficient blood supply of the alimentary organs, more commonly the former. They may take the form of loss of appetite, gastro- and intestinal flatulence, a sense of fulness, pain in the epigastrium and between the shoulder blades, nausea or vomiting, constipation, or, rarely, diarrhœa. When venous engorgement has become established, the liver may be palpable,

having a sharp edge and smooth surface, and may be tender and rarely pulsating. In severe hepatic congestion there may be a continuous aching pain, sometimes accompanied by rigidity, in the right hypochondrium. Jaundice is infrequent. Ascites may develop.

There may be visible distension and it may be also pulsation of the jugular veins. Cyanosis may be an indication of cardiac failure, especially in congenital morbus cordis and mitral stenosis, being less frequent in aortic disease. There may be lividity of the lips, the cheeks, tips of the ears, and finger nails, while clubbing of the fingers may be present in chronic cases. There may be polycythæmia. It is to be noted that the degree of cyanosis due to heart failure is not a reliable indication of the degree of the latter.

It is important to exclude other causes of cyanosis, such as broncho-pulmonary affections, methæmoglobinæmia, sulphæmoglobinæmia, and cases of a venous-arterial shunt in which at least a third of the venous blood passes directly into the systemic circulation, such as may occur in patent interventricular septum, patent interauricular septum, and patent ductus arteriosus. In these conditions the cyanosis arises in a different manner than when the result of cardiac failure, and there is little or no dyspnœa and an absence of other indications of failure. At the same time it is to be remembered that in the cases of a venous-arterial shunt mentioned, cyanosis due to cardiac failure may supervene.

Œdema is an important and usually a late manifestation of cardiac failure. It is more likely to occur in mitral and chronic myocardial than in aortic lesions, and in the last named tends to supervene much later and to be of much more serious significance than in the case of mitral disease. It is to be noted that generally there is an increase in a patient's weight for some time before pitting can be detected, and a loss of weight for some time after its disappearance. Œdema of cardiac origin almost always commences in the most dependant parts of the body, and in the evenings. In those who are up and about some puffiness round the ankles is first evident. The œdema increases and extends upwards, and may involve the thighs, the genitalia, the trunk, and towards the final stages may become general, but even in severe and prolonged cases occasionally it is limited to the lower extremities. If the patient is confined to bed, the sacral region, the back of the thighs, the back of the malleoli and, it may be, the genitalia are first involved. The serous membranes may be implicated, with resultant hydrothorax, ascites, and occasionally hydropericardium. Hydrothorax may be due to pulmonary or to systemic venous congestion or both. In the first it is usually left-sided, and in the second generally right-sided. Very occasionally, mostly confined to constrictive pericarditis and mitral stenosis, œdema commences in the abdomen and may even be limited to this.

Œdema indicative of cardiac failure may be recognised by the fact that it almost always commences in the most dependent parts, and that there is an increase in the general venous pressure. Hydrostatic œdema is also not uncommon in heavy people, especially of middle age and later, particularly in those who stand or sit much and with little or no movement of the lower extremities, and most often in hot weather. It sometimes occurs in varicose veins, severe anæmia, some nutritional disorders, as a terminal event in great wasting, and in local obstruction of the venous circulation, for example, by pressure from without, as in tumour, or venous thrombosis. In the differential

diagnosis of cardiac œdema, renal œdema, beriberi, myxœdema, and Milroy's disease should be considered. Œdema of renal origin usually commences in the face and in the mornings.

The urine may be scanty, high-coloured, of high specific gravity, exhibit an excess of urates, and may contain albumin or even blood.

Loss of flesh may be present, and when heart disease occurs in the early years of life, development may be arrested. Embolism, as well as arterial and venous thrombosis, may be an expression of cardiac failure.

There is usually tachycardia, but very occasionally bradycardia is to be noted. The volume and force of the pulse are often diminished. The apex-beat may be displaced, chiefly outwards. It is diffuse and weaker or occasionally tapping in character. The area of cardiac impairment is increased transversely, being more so to the left when the left ventricle is chiefly involved, and *vice versa*. The first sound is frequently diminished, and may also become short, sharp and clear, and resemble a second sound. The long pause is sometimes diminished. If there is tachycardia, there may be tic-tac rhythm. There may be a systolic murmur in the mitral or tricuspid area, due to relative incompetency of either of the valves. The arterial blood pressure varies in cardiac failure. It may fall, in which event the diastolic tends to diminish relatively less than the systolic, as is usually the case in left ventricular failure; or it may rise; or it may rise until shortly before death.

Not infrequently there is gallop rhythm, presystolic in time, or, more rarely, pulsus alternans, especially in hypertension. The former is best audible at the apex or between it and the xiphisternum. There are three distinct heart sounds. The third is related to the first sound of the next cardiac cycle, and the intervals between the three sounds are about or quite equal. There is usually reduplication of the apex-thrust. Not infrequently there is associated bundle-branch block or arborization block. Gallop rhythm, presystolic in time, cannot exist with auricular fibrillation. The prognosis in gallop rhythm is in the great majority of cases very serious.

It may be advisable to mention here that there are other varieties of triple rhythm, *i.e.* three actual sounds, at the apex: (1) The result of the third normal sound of the heart. (2) An early diastolic murmur, quickly following the second sound, in mitral stenosis may resemble a third sound, and a reduplication of the second sound and a triple rhythm are simulated. The murmur is separate but quickly follows the second sound, and is short. There is usually auricular fibrillation. (3) A reduplication of the first sound in the first grade of auriculo-ventricular block in which the interval between the contraction of the auricles and ventricles is unusually long. (4) A reduplication of the second sound may also simulate a triple rhythm. This, however, is easily recognised in that it is most evident at the base.

Lastly, sudden death, in the vast majority of cases due either to ventricular fibrillation or to sudden standstill of the ventricles, may occur, even without previous manifestations of heart failure.

The type of cardiac failure associated with chronic venous congestion, either pulmonary, or portal, or peripheral, or two or three together, is often described as *congestive failure*. There are three main clinical types of heart failure, namely: (1) the congestive; (2) that associated with systemic anæmia; and (3) angina pectoris.

Cardiac failure may be left-sided, or right-sided, or both, in which event one side may be affected more than the other. Left-sided failure is much more common than right. The latter is apt to supervene sooner or later. Left-sided failure occurs most frequently in hypertension, aortic valvular disease, atheroma of the coronary arteries, and chronic myocardial disease. Right-sided failure may be primary, among the causes being chronic mitral disease, especially stenosis, pulmonary stenosis, and broncho-pulmonary conditions; or secondary to left-sided failure.

In left-sided failure, there may be symptoms of systemic anæmia. The chief manifestations, however, are pulmonary. These have already been described in detail. They include cough, which may be nocturnal, pulmonary congestion or œdema, confined to the bases or more or less widespread, orthopnœa, cardiac asthma, and acute pulmonary œdema. The vital capacity of the lungs and the pulmonary circulation rate are diminished. If there is hydrothorax, it is usually left-sided. In addition, there may be gallop rhythm, presystolic in time, or pulsus alternans. The rhythm is usually normal, but extra-systoles, or very occasionally auricular fibrillation, may be present. Unless there is also right-sided failure, the venous pressure is not increased.

In right-sided failure, there are manifestations of venous congestion, either peripheral, or portal, or both. These have already been dealt with. They include œdema, diminished output of urine, distension of the jugular veins, enlargement of the liver, and cyanosis. The venous pressure is increased. If there is hydrothorax, it is generally right-sided.

In our inquiry regarding cardiac failure, it is not enough to ascertain whether the patient experiences any cardiac symptoms on physical exertion which formerly he was able to do, and how easily such are induced. The presence and the degree of failure as evidenced by objective signs should also be investigated.

It may be helpful to indicate what, in my opinion, speaking broadly, may be regarded as clinical manifestations of four degrees of cardiac failure, namely: 'slight,' 'moderate,' 'severe,' and 'very severe or extreme.'

Slight.—Shortness of breath, palpitation, fatigue and, it may be, præcordial pain on exertion which the patient formerly could do without experiencing this.

Moderate.—Shortness of breath and palpitation on moderate exertion, such as walking at the ordinary rate on the level; slight œdema of the lower extremities; chronic venous congestion and œdema of the bases of the lungs; slight enlargement of the liver; increased rapidity of the pulse-rate while at rest.

Severe.—Shortness of breath and palpitation on slight exertion, such as walking slowly on the level, or on changing position in bed; a considerable degree of œdema of the lower extremities in mitral cases and a moderate degree in uncomplicated aortic cases; diffuse chronic venous congestion and œdema of the lungs; a considerable degree of enlargement of the liver; orthopnœa; cardiac asthma; slight acute pulmonary œdema; œdema of the serous membranes; tic-tac rhythm; gallop rhythm, presystolic in time.

Very Severe or Extreme.—Pronounced continuous shortness of breath; severe dyspnœa on walking slowly on the level, or on changing position in bed; general anasarca in mitral cases and a considerable amount of œdema

of the lower extremities in uncomplicated aortic cases; marked enlargement of the liver; severe acute pulmonary œdema; persistent pulsus alternans in the absence of a marked acceleration of the cardiac rate.

The degree of cyanosis *per se* is not a reliable indication of the degree of cardiac failure, since it largely depends upon the variety of the cardiac affection.

It might be contended that the fact that an individual cannot engage in physical exertion which formerly he was able to do without experiencing cardiac symptoms does not signify cardiac failure. I would reply that, subject to the conditions mentioned, it does, although the failure may be of slight degree. I would repeat, however, that a departure from the normal standard of an individual may be due to extrinsic or temporary causes.

It is to be observed that the same amount of right-sided failure in uncomplicated aortic cases signifies a more severe grade of failure than in mitral cases.

Having discussed the manifestations and varieties and degrees of cardiac failure somewhat fully, much repetition will be saved in describing the clinical features of the various cardiac affections.

In conclusion, it may be advisable to make a few remarks regarding the pathogenesis of heart failure.

In the early part of the nineteenth century, Hope put forward what is called the back-pressure theory. By this is meant that the chronic venous congestion in chronic valvular affections takes place behind a failing ventricle. This view was generally adopted. Later, it was qualified and amplified by Stokes, who laid stress upon the myocardial factor. In the early part of the present century, a fundamental change took place, *i.e.* what is termed the forward-pressure theory was proposed and generally accepted, notably by Mackenzie. By this is meant that the venous congestion occurs in front of a failing ventricle, the output of which is diminished, with consequent deficient supply of blood to the various organs and an increased amount in the venous circulation. According to the back-pressure theory chronic venous congestion in the systemic circulation is indicative of left-sided failure and venous congestion of the pulmonary circulation signifies right-sided failure; and in the forward-pressure theory chronic venous congestion in the systemic circulation is indicative of right-sided failure and venous congestion of the pulmonary circulation signifies left-sided failure.

Recent clinical, radiological, and experimental evidence, including on the chemistry of the blood, together with post-mortem findings strongly suggest that the forward-pressure theory does not fully explain the phenomena of cardiac failure. It is probable that in cardiac failure both deficiency in output and back-pressure are involved.

B. Peripheral Circulatory Failure

Syncope due to peripheral circulatory failure has already been referred to.

Acute peripheral circulatory failure may occur in the toxæmia of some acute infective diseases, such as diphtheria and acute pneumonia; in traumatic shock after severe injuries; and in post-operative collapse. The blood accumulates in the capillaries, with consequent failure of the venous return of blood to the heart. The veins are depleted.

There is weakness, faintness, it may be restlessness, a small rapid pulse,

a severe fall of both systolic and diastolic blood pressure, rapid and shallow respiration, pallor, cyanosis, and coldness of the body-surface.

Unlike cardiac failure, there is an absence of chronic venous congestion.

PROGNOSIS IN CARDIAC AFFECTIONS

Prognosis in cardiac affections is a subject of considerable importance, and often presents great difficulties. From the nature of the ailment, the reasons for the former are not far to seek. Among these are the fact that the patient and his friends are naturally anxious for an opinion as to the probable duration of life, the ability of the patient to lead within limits a fairly normal existence, and perhaps also his capacity for employment.

In trying to form a prognosis in any given case of cardiac disorder, the following points require consideration: the family history; the age, the sex, the occupation, the mode of life, and the social conditions of the patient; the age-incidence of the cardiac affection; the health of the patient subsequent to the commencement of the cardiac affection; the cardiac affection—its ætiology, its variety, its degree, its duration, and whether it is stationary or progressive; the integrity of the myocardium; the question of cardiac failure; the risk of sudden death; the general health of the patient, and the existence or otherwise of complications; and the response of the patient to treatment.

With regard to the family history, we should note whether any other members of the family have suffered from any form of cardio-vascular disease, and the average period of longevity. The younger the patient the more likely is the cardiac affection to be the result of antecedent acute inflammation, and at or after middle life to a primary chronic affection. In the case of both, after adult age the cardiac reserve is more likely to be less as age advances. Taking all cases of cardiac affections into account, the prognosis is better in females than in males. The former are less subject to physical and mental strain, in them mitral disease is relatively more common than aortic disease, and chronic myocardial disease and arterial disease are relatively of less frequent occurrence. On the other hand, in females mitral stenosis is much more frequent, the strain at puberty is greater, and the risks of pregnancy and parturition have to be considered. Any occupation or mode of life involving undue physical or mental strain or exposure, unhealthy habits, such as over-eating or over-drinking, and unfavourable social conditions cause the outlook to be less favourable.

The younger the age-incidence, the less favourable the prognosis. Among the reasons for this are that: (1) in early life the heart is less able to undergo compensatory changes during the period of active growth, and any form of cardiac affection has a deleterious effect upon the general physique and mental development; (2) in early life rheumatic endocarditis is more likely to be accompanied by myocarditis and pericarditis; and (3) there is a greater liability to the recurrence of the cause of the cardiac affection, with possible increased damage to the heart. If the cardiac affection has existed for a considerable time and the health of the patient is still good, the outlook is correspondingly hopeful; and the converse is the case.

Taking cases as a whole, when a chronic valvular affection is the result of

a previous attack of acute endocarditis, the prognosis is not so serious as when due to a primary chronic degenerative process, because in the latter the lesion is apt to come on after middle life, to be progressive, and to be associated with chronic myocardial disease. It should be remembered, however, that in the case of the former, the patient is liable to recurrent attacks and consequent further crippling of the valve. If a lesion is due to syphilis, taking cases as a whole, the prognosis is very unfavourable.

With regard to the variety of the cardiac affection, the prognosis of aortic is less favourable than that of mitral disease, and lesions affecting both valves graver than when one only is involved. It is difficult to give the order of relative gravity of lesions affecting the different valves, but so far as four varieties of chronic valvular disease are concerned, most writers place in order of gravity, aortic incompetence, mitral stenosis, aortic stenosis and mitral regurgitation. With regard to aortic stenosis, however, a qualification is necessary; it refers only to those cases which are due to antecedent acute endocarditis. Among the points which may be of assistance in trying to estimate the degree of the cardiac affection are the degree of modification of the character of the pulse, of the blood pressure, of the cardiac sounds and cycle, the size of the heart, the time of occurrence, the duration, the character, and the area of propagation of any existing murmur or murmurs, and the degree of any existing auriculo-ventricular block. As examples, in chronic valvular disease: in mitral and tricuspid stenosis, the duration of a presystolic murmur and whether there is also a diastolic murmur, and, if so, its length; and in mitral incompetence and aortic incompetence, whether a murmur merely accompanies or replaces the cardiac sound, its length, and its area of propagation.

When the cardiac affection is the result of a previous attack of an acute inflammation, generally speaking, the shorter its duration the less favourable the prognosis, because (1) there is less chance that the inflammatory process has become quiescent; (2) it is less possible, especially in mitral stenosis, to estimate whether the fibrous cicatricial tissue resulting from the acute inflammatory process has ceased to contract; and (3) the patient is more liable to recurrent attacks of the cause, such as acute rheumatism, with possible consequent further damage. In endeavouring to arrive at a decision whether the cardiac affection is stationary or progressive, the following points should be considered: whether the standard of the response of the heart to effort is diminishing; the question of cardiac failure; whether there is an increase in the degree of modification of the character of the pulse, of the blood pressure, and of the cardiac sounds and cycle; the size of the heart; whether there is an alteration in any existing murmur or murmurs—such as whether a murmur replaces instead of accompanies the cardiac sound, or an increase in the length of an apical presystolic, or the supervention and the length of an apical diastolic murmur; and is there an increase in any existing auriculo-ventricular block?

In chronic valvular disease the integrity of the myocardium is of fundamental importance. Is it involved or not, and, if so, to what degree? In this connection the response of the heart to effort and the question of cardiac failure are of value, and are discussed elsewhere. When the degree of limitation of the response of the heart to effort, and, if present, the degree of other manifestations of failure are in excess of what might be expected considering

the variety and degree of the valvular affection, provided a cause for such can be excluded, the greater likelihood, and the more severe the degree, of myocardial involvement. In addition, the size of the heart, to what extent the cardiac sounds and cycle are modified, the cardiac rhythm, including whether there is auriculo-ventricular block, and, if so, of what degree, whether there is bundle-branch block, arborization or intraventricular block, or some other form of disordered action of the heart, are of moment.

The question of cardiac failure is also of cardinal importance. Whenever cardiac failure is present, two points should be taken into consideration, namely, its degree and the circumstances of its onset. The clinical manifestations of the various degrees of cardiac failure are described on pp. 857, 858. With regard to the second point, inquiry should be made as to whether the failure is due to a cause which might reasonably be expected to account for it, and is either temporary and not likely to recur, or persistent but remediable, or is not.

With reference to the risk of sudden death in cardiac affections, the commonest lesions are those of the coronary arteries themselves or involvement of their orifices (see p. 948). Such an event may be due to coronary occlusion, or independent of it. Sudden death is not uncommon in cases of angina pectoris, and may be due to ventricular fibrillation, coronary occlusion, or possibly apart from these. The liability to sudden death is greater in myocardial than in valvular disease. Rupture of the heart, the result of cardiac infarction, is a rare cause. In such cases, death may occur during the first week after coronary occlusion, or later as the result of aneurysm of the ventricle. Of the valvular diseases, sudden death is most frequent in aortic incompetence, almost always due to the occurrence of ventricular fibrillation. In valvular disease, especially mitral, sudden death may result from a large pulmonary embolism. Other causes of sudden death are Adams-Stokes syndrome, and rupture of the aorta in syphilitic aortitis or dissecting aneurysm.

The prognosis is also influenced by the state of the patient's general health and the existence or otherwise of complications, among the latter being arterial disease, hypertension, renal disease, chronic bronchitis, and emphysema.

Finally, the prognosis in cardiac affections should be considered in the light of response to treatment. For example, given a case of severe cardiac failure with auricular fibrillation with a rapid ventricular rate, it is impossible to say what the future will be until full doses of digitalis have been administered.

Having now reviewed the various points which may arise in the consideration of the prognosis of most cardiac affections, these need not be again referred to when the prognosis of individual cardiac disorders comes under discussion.

TREATMENT IN CARDIAC AFFECTIONS

Importance of Treatment in Cardiac Affections.—In few departments of medicine is skilful treatment of so great consequence as in that of cardiac disorders, and in few is it so well rewarded. The heart possesses enormous reserves and, moreover, in recent years there has been a signal

advance in what can be accomplished. I would, therefore, emphasize the importance of a keen, practical interest in cardiological therapeutics. Another observation I would make is that treatment should not only be correct, but sufficiently inclusive and also resourceful.

It is desirable to devote a section to the consideration of the therapeutic measures which may be applicable to any form of cardiac disorder, in order to save much needless repetition when we come to consider the treatment of the individual cardiac affections.

Objects of Treatment.—The primary object is to prevent the supervention of cardiac failure, or complications. With regard to the former, if the view put forward on pp. 851, 852, that its essential cause lies in the heart muscle be accepted, then, on the one hand, the patient should avoid anything which puts a strain upon the myocardium, and, on the other, the practitioner should do everything in his power to promote its efficiency. In addition to the foregoing, cardiac failure, symptoms and complications should receive prompt and suitable treatment.

In the majority of cases the patient's complaint is a manifestation of cardiac failure. In estimating the degree of such, the extent of the departure from his usual standard is of value.

A primary question is whether rest is required and, if so, how much? The ideal is that it should be sufficient to enable the patient to attain his optimum. The amount of rest may vary very greatly. As examples, speaking broadly, in 'slight' cardiac failure, while in some cases it is preferable that the patient should go to bed for a week or so, partial rest for a longer period is usually sufficient. In 'moderate' failure, the patient should remain in bed for at least 3 weeks; and in 'severe' failure, for a minimum of 6 weeks. In a very exceptional case of a woman, aged 55, with very severe exhaustion of the heart, the result of long-continued very excessive work, I advised 6 months' rest in bed, followed by 6 months' partial rest. The subsequent course of events proved the advice to be both necessary and highly successful. The importance of attending to the matter of mental, as well as physical, rest is not sufficiently appreciated.

It should be pointed out that when a patient has had a good period of rest in bed, it should be succeeded by a period of partial rest, the latter having some relation to the former. Thus, if he has been in bed for 4 weeks, he should remain in his bedroom for at least a further week, getting up gradually; he should proceed downstairs and, later, out of doors, gradually; and, in some cases, it is often an advantage to resume work gradually during the first few weeks or more.

I may be permitted to emphasise the following. I have been much impressed with the relatively frequent lack of appreciation of the amount of preliminary rest which is requisite in some cases. This is not a rare cause of unnecessary loss of life. Another and, taking cases in the aggregate, one of the most important causal factors of all, has reference to the future mode of life of patients, with which I shall deal at once.

Instructions regarding Mode of Life.—A cardinal indication is that the patient should live within the limits of his cardiac strength. On the other hand, his usual mode of life should not be unnecessarily restricted, for otherwise he is apt to become nervous and introspective. Herein lies one of the principal duties of the medical attendant. In this regard, it is not

sufficient to tell the patient to 'take care.' The indication is to investigate the patient's occupation, general mode of life, habits, hours in bed, the amount and character of his sleep, how long he takes off for his meals, his mental and emotional character, and other relevant particulars, and to advise, in detail, accordingly.

Each cardiac patient should be in bed for at least 9 hours each night, and have at least an hour for the midday meal, resting after finishing eating, and a quiet day each week. If the degree of impairment is severe, he should be in bed for 10 to 12 hours each night, rest for one or two hours after the midday meal, and stay in bed the whole, or the greater part, of one day a week. The patient should avoid unnecessary tasks outside those of his occupation. When not actually working, he should rest a good portion of the time. Holidays in adequate amount and frequency, and containing a sufficient element of rest are indicated.

With regard to the question of physical exertion, while it is impossible to lay down hard-and-fast rules, it is possible to enunciate a cardinal principle, which will be found of inestimable service, namely: Any exertion which the patient may undergo should not be attended, or followed, by any subjective symptoms, such as breathlessness, palpitation, a sense of tightness or oppression, or discomfort or pain in any part of the front of the chest, fatigue, giddiness, or faintness; or any objective signs, such as maintained increased frequency of the pulse or œdema. This rule will regulate the kind and the rate and the amount of exertion. If any of the foregoing are present during effort, it means that the rate is too quick and it should be proportionately diminished; failing which, that the kind is unsuitable and should be avoided. If they do not occur during it, but subsequently, it means that the amount has been too much and it should be proportionately diminished.

On the other hand, a sufficient amount of exercise is indicated, and any exertion short of producing symptoms is usually not harmful, subject to the following qualifications: it is advisable to keep something in reserve; sudden and violent effort should be avoided; and, in my opinion, based upon personal observations, in aortic incompetence the more strenuous forms of effort should be prohibited in any case.

Here, also, it is not enough to regulate physical exertion only; the importance of attending to the matter of mental effort in cardiac cases is not sufficiently recognised. All excitement, worry and other forms of emotional stress and strain should be avoided.

If the patient suffers from an unduly excitable nervous system, or is prone to worry or be anxious, sedatives, such as a combination of ext. valerian, ext. sumbul, and asafetida, or the bromides, bromide and valerian, uvaleral, or carbromalum, failing which the barbiturates, may be very helpful. My custom is to advise an adequate daily dosage until a full therapeutic effect is obtained, after which a minimal daily dosage for a time. It should not be forgotten that the bromides are strongly cumulative and, especially in the elderly, even moderate doses if taken long enough may produce toxic effects. The matter of sleep is often neglected, and inquiry should invariably be made regarding both its amount and character, and if any defect be found, it should be treated on the lines laid down later.

In most cases the daily amount of fluid taken should be somewhat restricted, the aim being to lessen the amount of work done by the left ventricle

by diminishing its output. The meals should be as dry as the patient will take them, a sufficient amount of fluid being taken between meals. The three meals of the day should be evenly balanced, since a large meal at one time causes too great a variation in the vascular system, to which the heart does not readily adjust itself. The food should be nutritious, easily assimilable, and not likely to cause indigestion. A diet of carbohydrates is bulky, and is apt to cause flatulence and hyperchlorhydria, while a diet consisting of highly nitrogenous food increases the resistance in the peripheral circulation and is equally to be avoided. While, therefore, the diet should be a carefully mixed one, the albuminous element should predominate. Any article of diet which causes flatulent distension of the stomach or bowels should be avoided, since this, by direct pressure, embarrasses the heart and is one of the commonest causes of palpitation. If there is hypertension, see p. 1069.

In cases of ' severe ' cardiac failure, light solids form the best diet, and, as a rule, agree better than fluid food, being less likely to cause flatulence ; the necessary mastication is also an advantage. Care should be taken to ensure that the patient does not take a larger quantity of food than he can comfortably digest. When failure is ' extreme ' the amount of food should be considerably restricted, and only very small quantities at a time, at fairly frequent intervals, should be allowed. Biscuits, small thin sandwiches of potted meat, or small quantities of milk are not infrequently all that can be comfortably digested. Occasionally a pure milk diet is best.

The excessive use of tea, coffee and tobacco should be avoided. It is better for the patient to abstain from alcohol altogether ; but if he has been accustomed to its use and deprivation be a great hardship, a strictly moderate amount may be allowed. Strict attention to the condition of the bowels is advisable. If there is hypertension, a saline each morning and also some mercurial preparation at bedtime once or twice weekly are indicated.

The periodic administration of general tonics is sometimes helpful, especially during convalescence from any illness. Any existing anæmia, obesity, and bronchial catarrh should be treated without fail : the first on account of the myocardium and the tissues in general receiving an adequate supply by oxygen ; and the second because excessive weight involves more work on the part of the heart, and of the tendency to fatty infiltration.

The question of focal sepsis, especially in the teeth, the tonsils, the accessory nasal sinuses, the pharynx, the colon, the appendix, the gall bladder, and the genito-urinary tract, is an important one and should receive attention. Acute infections, especially in chronic valvular disease and congenital morbus cordis, should be guarded against.

Rest.—Rest is of cardinal importance in the treatment of cardiac failure, It is indeed, difficult to exaggerate its value. It is the objective of all therapeutic measures. Details regarding its application are dealt with on pp. 862, 863 and elsewhere.

Systematic Exercises and Massage.—Systematic and graduated exercises are sometimes useful in cardiac affections, provided they are judiciously employed and their effect watched. They are of special help in cases of slight cardiac failure due to the heart muscle being flabby and lacking in tone, as in fatty infiltration. Contra-indications for their use are acute affections of the heart, a severe degree of chronic valvular disease or of

chronic myocardial disease, 'severe' cardiac failure, and cases in which the heart failure is progressive. Simple movements, especially of the Swedish variety, are, in most cases, better than resistance exercises. In all cases such exercises should stop short of inducing any indications of cardiac distress or *maintained* increased frequency of the ventricular rate; and they should be followed by a period of rest. Massage is more often useful than is generally recognised. Vigorous massage may be useful in the case of those who have not the necessary time or opportunity for the usual forms of exercise to keep them in condition. Passive movements and light massage may be employed with advantage in the early stages of convalescence from a period of rest. The same considerations apply as in the case of systematic exercises.

Baths and Spa Treatment.—It is commonly known that immersion of the body in water may exercise a decided influence on the circulation. It is, further, believed by some that certain waters at Nauheim, on account of their ingredients, possess a specific therapeutic value in cardiac affections, but I am very sceptical with regard to this. Patients undoubtedly often derive very great benefit from a stay at Nauheim and at similar spas; but this appears to be due to the rest, the change of air, the regular mode of life and exercise, the careful dieting, and other factors. Given the same conditions of life, equally good results would be obtainable elsewhere. Spa treatment is particularly serviceable in patients who have indulged in excesses of various kinds.

The Digitalis Group of Drugs.—This includes digitalis, strophanthus, squills, convallaria majalis, and apocynum. They have a similar action on the heart, but as digitalis is the most reliable, only strophanthin, which is used for intravenous administration, need also be considered.

With regard to digitalis, the standardized tincture, the powdered leaf, the latter administered in the form of tablets or pills, and Nativelle's digitaline granules are reliable preparations. Fifteen minims (not drops) or 1 c.c. of the tincture is equivalent to 1½ gr. or ·1 gm. of the powdered leaf. The infusion is not advisable, as it is unstable. Digoxin, a pure crystallised glucoside, isolated from leaves of digitalis lanata, is more rapidly absorbed and excreted, and is more stable. Digoxin and strophanthin are extremely irritant if administered subcutaneously or intramuscularly. They are employed intravenously. The latter is a powerful poison in overdosage, and the best therapeutic dose is very near the toxic dose, which does not appear to apply in the case of digoxin. It follows, therefore, whether this preparation should be used or not and, if so, its precise dose, requires most careful consideration. I wish to say, however, that, with these qualifications I have never seen any untoward effects follow its use.

Digitalis is indicated in congestive heart failure—right-sided and in pulmonary venous congestion due to left ventricular failure; and in auricular fibrillation with a rapid ventricular rate and in auricular flutter (see p. 903), even in the absence of congestive failure; in all cases whatever the cardiac lesion may be. The drug is likely to prove far more effective when cardiac failure is associated with auricular fibrillation with a rapid ventricular rate, or auricular flutter with a rapid ventricular rate, than in cases with a rapid ventricular rate associated with normal rhythm. In the former cases the results of its administration in the majority of cases are very, and in some cases extraordinarily, good; it is followed by a rapid

fall in the ventricular rate (Fig. 23) and a concomitant improvement in the general symptoms. When auricular fibrillation, or auricular flutter, is not accompanied by a rapid ventricular rate, there is usually no marked effect. The drug is also likely to be far more beneficial when a lesion is the result of antecedent rheumatic infection. It is to be added that in all cases in which there is an acute infection or a thyrotoxic condition, there may be little or no response to digitalis.

Digitalis is more generally useful in mitral than in aortic cases; in all probability because both auricular fibrillation and congestive heart failure are much more common in mitral disease, and the latter is much more frequently of rheumatic origin than in the case of aortic disease. Formerly the question was often asked whether digitalis should be given in aortic incompetence. There is now general agreement that the answer is in the affirmative, provided the indications mentioned are present. Hypertension and arterial disease are not contra-indications. The drug is contra-indicated in persistent heart-block. Moreover, caution should be exercised and large doses avoided in acute lesions of the myocardium, such as rheumatic carditis, or cardiac infarction.

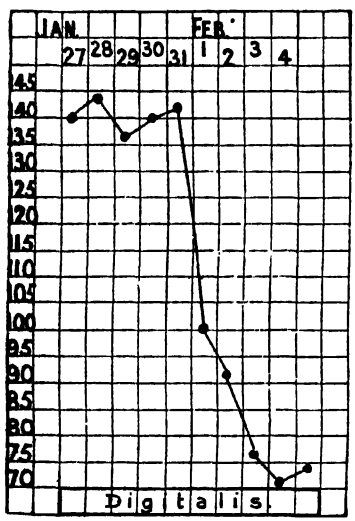


FIG. 23.—Chart showing typical result on the cardiac rate of the administration of digitalis in a case of auricular fibrillation with tachycardia. A drachm of the tincture per diem was commenced on 27th January.

In the great majority of cases the aim of digitalis medication is to accumulate in the body a sufficient quantity of the drug to produce a full therapeutic effect; and, in the majority of these, afterwards to maintain that quantity there. In order to obtain the first object, the intake of the drug should be greater than the amount excreted. Eggleston estimated that in man a total of 1·5 cat units, which equals about 25 minims of the tincture, per ten pounds is required. This amount, however, is too high. For the second purpose, the dosage should be reduced to such an extent as will balance the excretion, with consequent maintenance of digitalization.

In a certain proportion of cases, however, it is not necessary to proceed to full digitalization, a moderate dosage for a period being sufficient and, in the majority of these, improvement can afterwards be maintained without continuing the drug.

If the first method is adopted, with regard to the dosage to commence with, the larger it is the more rapidly is full digitalization produced. The choice of such in any individual case will depend upon the severity and urgency of the patient's condition. For average cases, a good method is to begin with 60 minims of the tincture, or 6 grains of digitalis leaf, and in severe (it should be noted that this word is not synonymous with 'severe' failure described on p. 857) cases, 90 minims of the tincture (or

its equivalent of the leaf) per diem, in each case divided into three or four doses.

In urgent cases, the employment of massive dosage of digitalis by the mouth and the intravenous injection of strophanthin or of digoxin, should be considered. In the first place, these methods are contra-indicated if the patient has already had any of the digitalis group of drugs during the preceding ten days; if the ventricular rate is below 140; unless the patient is in bed and under close observation; and reliable physiological standardized preparations are used.

As regards massive dosage by the mouth, for a patient weighing 10 stone, the following is advised: an initial dose of 1½ mgm. of digoxin, or 90 minims of the tincture, or 9 grains of the powdered leaf, and afterwards, provided there are no toxic symptoms at any time, 1 mgm. of digoxin, or 60 minims of the tincture, or 6 grains of the powdered leaf 6 hours later, and a half dose in another 6 hours. The first-named preparation is to be preferred. Respecting the intravenous method, as stated, I have never seen any untoward effects following strophanthin, but digoxin is preferable. The maximum dose of the former is $\frac{1}{60}$th gr., and of the latter 1 mgm. In the case of each, the drug should be injected very slowly and care must also be exercised to avoid leakage into the tissues outside the vein. In all cases in which either massive dosage by the mouth or intravenous injection has been employed, no more of the digitalis group of drugs should be administered for at least 24 hours, depending on the patient's condition, and when used the dosage should be smaller.

With regard to the respective merits of these two methods, the intravenous is indicated in very urgent cases and massive dosage by the mouth in urgent cases. If, however, there is vomiting, digitalis by the mouth is obviously impracticable. It may be added that the intravenous method may be employed also in urgent or even in merely severe cases, provided in each case the dose is proportionately diminished. But the reader is also referred to the next paragraph.

Digitalis can be absorbed from the rectum, and this method of administration may be used whenever there is vomiting, including in urgent cases when massive dosage by the mouth would otherwise be used and even in those in which it is not necessary to proceed to full digitalization. The dosage is the same as that by the mouth. A simple enema is given a few hours beforehand in order to prepare the bowel for absorption, and the tincture of digitalis should be diluted with warm saline to a bulk of 3 oz., and introduced slowly through a funnel.

With regard to the matter of maintenance dosage, the indication is to ascertain the optimum, *i.e.* the dosage sufficient to control the action of the heart, without at the same time giving rise to any toxic symptoms. This may require weeks or even months of careful observation. It is to be noted that sometimes a relatively small difference in the daily or even weekly dosage is of material moment to the patient's well-being. The patient's own sensations are often helpful and should be taken into consideration in addition to the ventricular rate, which should be counted by auscultation. The optimum dosage may exhibit a wide variation in different patients, but is usually 10 to 30 minims of the tincture, or its equivalent, per diem. In the course of time, variation in the dosage may be found to become necessary. The accumulative action of the drug is apparently not nearly so important

as was formerly believed. At the same time the patient should be watched for overdosage.

Among the indications of overdosage of digitalis are anorexia, headache, nausea, vomiting and diarrhœa. It should be observed that vomiting is not uncommon in cardiac failure apart from the administration of digitalis and, therefore, is not necessarily of toxic origin. The effect of overdosage on the heart may be to produce sinus bradycardia, occasional ventricular extra-systoles, *pulsus bigeminus* or *coupling of the beats* (Fig. 31), a rapid succession of extra-systoles, multifocal extra-systoles, sino-auricular block, auriculo-ventricular block, the ventricular variety of paroxysmal tachycardia, and even ventricular fibrillation. The occurrence of toxic symptoms is an indication to stop the drug until these have ceased and there is a rapid ventricular rate, after which the dosage should be diminished.

Digitalis has no effect upon auricular fibrillation itself; but it diminishes conductivity of the auriculo-ventricular junctional tissues, thereby interfering with the pathway of impulses from auricle to ventricle, and so cutting off some of the too numerous impulses reaching the ventricle, and thus leading to a reduction of the ventricular rate, as a result of which the cardiac contraction becomes stronger, with consequent improvement in the circulation and in the general symptoms.

In auricular flutter, the administration of full doses of digitalis at first usually induces partial heart-block, or an increase in the degree of block already existing, with a resulting diminution of the ventricular rate (Fig. 33). Later, the flutter may cease or auricular fibrillation may be induced. The latter is usually an advantage, because the ventricular rate can generally be more easily controlled by moderate doses of digitalis than in the case of auricular flutter. Auricular fibrillation may persist, or the physiological rhythm may be restored—either event occurring during the administration of the drug or after it has been discontinued. After the restoration of normal rhythm, recurrences of flutter are not uncommon. The same considerations regarding the dosage and method of administration of digitalis (or strophanthus) apply in auricular flutter as in auricular fibrillation with a rapid ventricular rate. For further details, see p. 903.

Cardiac Stimulants.—It is probable that no drug directly stimulates the heart. Nevertheless various drugs which stimulate the respiratory centre and the vasomotor centre are of value in circulatory failure, especially peripheral. Thus, cardiac failure is often accompanied by respiratory failure, resulting in anoxæmia. In such cases, drugs which stimulate the respiratory centre, by causing an increase in the rate and depth of respiration and so helping the venous return to the heart, increase the coronary circulation. Again, stimulation of the vasomotor centre causes an increase in the blood pressure, due mainly to the constriction of the arterioles of the splanchnic area.

Strychnine has a direct stimulant action upon the respiratory and vasomotor centres. But it and camphor—which acts reflexly on the two centres—have been mostly supplanted by nikethamide (coramine) and leptazol (cardiazol), which are powerful direct stimulants of both centres, and are valuable remedies in circulatory failure, particularly peripheral. Caffeine has less action on the respiratory and vasomotor centres than strychnine. Its chief action on the central nervous system is on the psychical areas of the

brain. Its principal peripheral effect is its diuretic action on the kidneys themselves, but as a diuretic it has been replaced by other xanthine drugs. Carbon dioxide is by far the most powerful respiratory stimulant, acting directly upon the respiratory centre, and is sometimes employed as a mixture of 5 per cent. CO_2 in 95 per cent. of oxygen.

Cardiac stimulants are of special value in peripheral circulatory failure.

Diffusible stimulants (ether, ammonia and alcohol) reflexly stimulate the respiratory and vasomotor centres, and are frequently useful in an acute emergency.

Dextrose is of value in conditions of circulatory collapse, such as may follow coronary thrombosis, and possibly in congestive heart failure. It is a form of nutriment which is rapidly absorbed and easily metabolised. It may be given by the mouth, by the bowel, or intravenously. One pound of dextrose dissolved in 2 pints of water and flavoured with orange or lemon juice forms a convenient concentrated solution, which may be given diluted to taste. For intravenous injection, a hypertonic solution is advocated, and 100 c.c. of a 30–50 per cent. solution may be administered.

Insulin, in conjunction with dextrose, is held by some to be of value in congestive heart failure and also in angina pectoris. With regard to the former, most benefit is to be expected when there is evidence that a defect of myocardial nutrition underlies or aggravates the condition. Five units of insulin subcutaneously, followed in 15 minutes by 50 g. of dextrose or lævulose by the mouth, is given once daily. This may be continued for a week, the dose of both being then doubled if no improvement results. This form of treatment may be employed concurrently with the administration of digitalis. Respecting angina pectoris, see page 989.

Diuretics.—If in congestive failure the response to rest, the digitalis group of drugs, and other methods of treatment is not quick or adequate, primary diuretics are, in addition, indicated. These include the xanthine group (theobromine, theophylline, and caffeine); the saline diuretics (potassium acetate and citrate, and sodium citrate); and the organic mercurial compounds.

At the outset I would point out and emphasise that it is advisable periodically to alternate the diuretics and also that a combination is sometimes more effective.

A combination formerly much used is pil. digitalis co., which consists of pulveris digitalis, pulveris scillæ and pilulæ hydrargyri, āā gr. 1.

Theobromine, gr. 5–10, is a powerful diuretic, but as it is very insoluble in water its absorption is slow so that it is not much employed. Theobromine and sodium salicylate (diuretin) is freely soluble, and is therefore used instead, the dose being gr. 10–20. Theophylline (theocine) is still more potent, but because of its lack of solubility is not used, theophylline and sodium acetate, gr. 2–5 being used instead. Both are apt to cause gastric disturbance. Aminophylline (euphyllin) is supposed to be as powerful as theophylline, and is more soluble and therefore more rapid. The dose is gr. 1½–3. It may also be employed by the rectum, intramuscularly, or intravenously. Caffeine is not much employed as a diuretic, having been largely supplanted by the other members of this group. It is used more as a stimulant.

Organic mercurial preparations are incomparably the most potent primary diuretics in the treatment of congestive cardiac failure, and their

discovery constitutes a striking advance in cardiological therapeutics. I would emphasise their very great value in suitable cases, for they are frequently successful when digitalis and other diuretics fail. They are especially indicated in severe cases, or when a rapid effect is desired. They are also of value in cases of chronic adhesive pericarditis with recurrent ascites. Digitalis may be given at the same time. It is necessary to point out that, owing to their high mercury content, they may give rise to symptoms of mercurial poisoning, such as stomatitis, severe colitis, with bloody diarrhœa, or hæmaturia. They should not be employed in acute nephritis, or severe impairment of kidney function, or hæmaturia, or enteritis, but a moderate degree of albuminuria, such as is common in heart disease, does not contra-indicate their use.

Novasurol is by far the most toxic, and its use has been abandoned in favour of the injection of mersalyl (salyrgan) which is safer and little, if at all, inferior in diuretic potency. It is administered either intravenously or intramuscularly. In either case a preliminary dose of 0·5–1 c.c. is given. If no toxic symptoms supervene, doses of 1½ or 2 c.c. may be repeated at intervals of 2 or 4 days. Or the drug may be administered once weekly for long periods to ambulant patients. Recently suppositories have been introduced, and are not far short as effective as the other two methods.

These diuretics are best administered the first thing in the morning in order to avoid the patient's sleep being disturbed. A profuse diuresis usually commences shortly afterwards and continues for 24 to 48 hours; and often 10 to 20 pints of urine may be passed within 48 hours. It is important to restrict the daily intake of fluid to within 40 oz. and occasionally even 30 oz. Moreover, the total amount of urine passed each 24 hours should be carefully measured, and it is also advisable to weigh the patient at the commencement of the treatment and at weekly intervals, a reduction in weight being a valuable criterion of the efficacy of the treatment. The diuretic effect of the drugs is increased by the administration of an acid-producing salt, such as ammonium chloride or nitrate. Thirty grains in solution by the mouth thrice daily for two or three days previously is the appropriate method.

QUINIDINE.—Quinidine is employed in the treatment of persistent auricular fibrillation and persistent auricular flutter, especially the former, with the object of arresting either condition—in other words, to restore the normal rhythm. It is also used in paroxysmal tachycardia, paroxysmal fibrillation and paroxysmal flutter, in the intervals between the attacks, to prevent their recurrence.

Quinidine is a cardiac depressant, and it acts directly on the auricular muscle and by depressing the vagus. It prolongs the refractory period of auricular muscle and slows the conduction rate. Prolongation of the refractory period tends to interrupt the circus movement in the auricles (see p. 897), while slowing of conduction favours its continuance. Where the action on the refractory period predominates, the circus movement is abruptly terminated and the normal rhythm is restored. The slowing of the rate of the circulating wave in the auricles tends to increase the frequency of the ventricular response, so that the ventricular rate rises during quinidine administration, before normal rhythm returns. This tachycardia may be prevented to a large extent by giving a preliminary course of digitalis before commencing quinidine. Extra-systoles may be observed after the auriculae

fibrillation has ceased, and may give rise to palpitation. They occur as a general rule only when the auricular rate has diminished considerably, generally to 250–300 per minute. Their appearance is an indication of poisoning. In successful cases of auricular fibrillation, the sequence of events is auricular flutter, transient arrest of the whole heart, and the restoration of the normal rhythm.

General toxic symptoms, cardiac failure, and embolism may occur during the administration of quinidine. Among the first are headache, giddiness, tinnitus, transitory visual disturbance, nausea, vomiting, abdominal pains, palpitation, præcordial pain, sweating, scarlatiniform or morbilliform rashes, urticaria, a mild degree of pyrexia, fainting attacks, and mental symptoms. Among the manifestations of cardiac failure are sudden collapse, sudden cessation of respiration, severe dyspnœa, cyanosis, and disappearance of the pulse—due to ventricular standstill during the transition stages. The risk of embolism occurs at the time when the auricle first commences to contract again after the restoration of the normal rhythm. Thrombi are expelled from the auricular cavity into the systemic or pulmonary circulation, and death may result. Death during the administration of the drug may be due to cardiac failure or to embolism.

In persistent auricular fibrillation the normal rhythm can be restored in at least half of suitable cases. Relapse occurs, sooner or later, perhaps in a majority of these. In my experience this can be avoided in a large proportion of cases by a gradual diminution of the total daily dosage and, later, the continuation of a small daily dosage for some time. Quinidine is less successful in restoring the normal rhythm in auricular flutter than in auricular fibrillation.

In persistent auricular fibrillation, or persistent auricular flutter, quinidine is most likely to be successful in those cases in which there is at the most only a moderate degree of valvular or myocardial disease, of cardiac enlargement, and of cardiac failure; in those in which the abnormal rhythm is the result of antecedent rheumatism or chorea; in cases in which there is an absence of acute endocarditis, or acute myocarditis; when the onset of the condition has occurred during an acute infection—such as influenza; when the abnormal rhythm has followed paroxysmal attacks; when of recent origin; and in the case of the young. It is particularly useful in hyperthyroidism. Contra-indications for the use of the drug are the presence of a severe grade of valvular disease, or of myocardial disease, great enlargement of the heart, a severe degree of cardiac failure—unless this is remedied by a course of rest and other therapeutic measures—heart-block, existing or recent acute or subacute endocarditis or myocarditis, a recent history of embolism, and in those cases when the patient cannot be confined to bed and be assiduously and carefully watched.

A preliminary course of rest in bed and of digitalis medication is advisable. It is the practice of some to stop the digitalis for a few days before commencing quinidine, while others continue its use during the administration of the latter, in order to control the rapid ventricular rate. The patient should invariably be confined to bed, absolute rest, physical and mental, should be enjoined, and he should be assiduously watched. Frequent electro-cardiographic examinations are very advisable. It is advisable to give a single dose of 5 grains, or two doses of 3 grains at an interval of 2 hours, to

test for possible idiosyncrasy, and if none is found to exist, to commence the routine treatment the following day. Five grains three times daily may be commenced with, and the total daily dosage increased by 5 grains each day up to 30 grains, not exceeding four divided doses in the 24 hours, which may be continued for a week, or until normal rhythm is restored, or symptoms of intolerance appear. The majority of successful cases follow the use of only small doses of the drug, and its use is rarely successful if more than 30 grains per diem are required. The drug should be stopped if severe toxic symptoms, severe cardiac failure, or embolism, occur, or if there is an auricular rate of 250 or 240 per minute—because of the risk of inducing 1 : 1 rhythm, or, as a rule, if there is a ventricular rate above 160. After the normal rhythm has been restored, the total daily dosage should be diminished by 5 grains each day to 5 grains twice, or even once, daily, and this continued for some months unless found to disagree with the patient. This method lessens the likelihood of relapse.

When quinidine is employed in paroxysmal tachycardia, paroxysmal fibrillation, or paroxysmal flutter, in the intervals between the attacks to prevent their recurrence, the dosage is 5 to 15 grains per diem.

Oxygen.—Oxygen is sometimes of value in cases of cardiac failure. The chief indications for its use are cyanosis and dyspnœa, but in the case of the former not if due to peripheral stasis. It should be administered continuously, it may be by means of a nasal catheter, an oxygen tent, or an oxygen mask. As a rule the last is uncomfortable, but recently (1938) a very efficient apparatus has been introduced in America by Boothby, Lovelace and Bulbulian, and may now be obtained in this country as the "B.L.B. inhalation apparatus."

Venesection.—This method of treatment is sometimes neglected when it might be employed to advantage and be even life-saving. It is indicated when there are manifestations of great distension of the right chambers of the heart—as, for example, cyanosis, turgescence of the veins of the neck, severe dyspnœa, an enlarged and tender liver, and increased area of impairment of the percussion note to the right, and also in acute pulmonary œdema, in either case especially if there is hypertension. As a rule it is contra-indicated in hypotension and anæmia of pronounced degree. Venesection may also be very useful when the blood pressure is much raised. The median basilic vein should be chosen, and 10–20 ounces withdrawn. If venesection is not practicable, 6–8 leeches over the right ventricle or liver may be of service.

Total Thyroidectomy in the Treatment of Congestive Heart Failure.—The number of cases with congestive heart failure in which total ablation of the thyroid has been performed is now sufficient to permit the evaluation of this procedure as a therapeutic measure in the treatment of heart disease. The results to hand already indicate that great discrimination should be exercised in the selection of cases, this requiring the most careful consideration respecting diagnosis and prognosis. It should at once be evident that this procedure should only be considered when the medical methods of treatment have been fully tried and have failed; if the operation is likely to result in improvement; and when the operative risks are not unreasonable. With regard to the last, results have established that the presence of renal impairment, chronic lung disease, and intractable œdema, add so materially to the risks connected with the operation as to contra-

indicate this form of treatment. On the other hand, the presence of hypertension does not appear to be a contra-indication, but in no instance has the operation brought about an appreciable lowering of the blood pressure. The therapeutic value of the operation corresponds with the lowering of the basal metabolism. When this is reduced to minus 30 per cent., myxœdema frequently develops, but this condition responds to small doses of thyroid without materially detracting from the improvement which has been obtained by the diminution of the basal metabolism. With a fuller and more widespread appreciation of the value of the organic mercurial diuretics, the question of this form of treatment does not arise as frequently as would otherwise be the case. Even so, it is now and again indicated in carefully selected cases.

Treatment of Symptoms

The indications for and the methods of treatment already described should be considered.

Sleeplessness.—The ventilation of the bedroom should receive attention, and, while the patient should be kept warm, the bedclothes should not be heavy. It should be remembered that insomnia may be due to dyspnœa, and in these cases the patient is sometimes troubled with 'night starts' as he is falling off to sleep; the dyspnœa should be treated on the lines to be laid down later. Sedatives (as described on p. 863) may be sufficient for sleeplessness. Failing these, or as an alternative to such, paraldehyde (suitably flavoured), chloral and bromide, or the quickly acting barbiturates (alone or in combination with bromide). The first is a valuable drug in many cases, especially when there is dyspnœa. If the patient is more restless or excited after taking the drug, it usually means that the dose has been too small. Chloral hydrate has the reputation of being a dangerous remedy in heart disease, especially in chronic myocardial disease, but I have used it very extensively and have never found this to be the case. It produces a refreshing sleep, and is especially useful when nocturnal dyspnœa or hypertension is present. It may be given in doses of 5 to 10 grains by the mouth, gradually increasing to 15 or even 20 grains if necessary, the dose being repeated in 2 hours if required, and the effects carefully watched. If these drugs fail, resort should be had to opium or one of its derivatives, which are especially useful when there are accompanying restlessness and dyspnœa, and are particularly necessary in cardiac asthma and coronary occlusion. In some cases a combination of bromide, chloral and tincture of opium suffices. The hypodermic administration of morphine is much more efficacious than when given orally. It is well to commence with small doses, for example, $\frac{1}{4}$th grain, and gradually to increase to $\frac{1}{2}$th grain, or even more, until relief is obtained, the effects being carefully watched. Cyanosis is not an absolute contra-indication to the administration of chloral, opium or morphine. Speaking generally, these drugs should not be administered in those cases in which there is much bronchial secretion, or œdema of the lungs, or in Bright's disease; but in individual cases they may be tried if the first dose be very small, and the dosage be subsequently increased with great caution. Further, when there is much bronchial secretion, or œdema of the lungs, a sharp look-out should be kept to see whether the administration

of the drug increases them; in such a contingency, atropine or strychnine should be administered in combination with the morphine.

CONGESTIVE FAILURE AND ŒDEMA.—The measures which are of particular value are the restriction of the daily amount of fluid, the digitalis group of drugs, and primary diuretics. If œdema of the lower extremities is slight, bandaging is often useful, and this may be combined with massage. If it is severe and does not respond satisfactorily to the measures mentioned, the mechanical removal of fluid by Southey's tubes or multiple punctures, preferably the former, should be considered. It should be performed under strict aseptic precautions, and the patient should be in the sitting position in order to obtain a full beneficial result. If pleural effusion or ascites, especially the former, does not yield to other treatment and causes embarrassment, the fluid should be withdrawn.

CARDIAC ASTHMA.—Sleeping in a more upright position may be of help as a prophylactic measure. If an attack occurs, the patient may be most comfortable when supported by high pillows or a bed-rest, or he may not be able to breathe with comfort even in bed, and may prefer to sit up supported in a large easy chair, perhaps leaning forward and supporting himself with his arms on the back of another chair. Diffusible stimulants, the nitrites—especially if there is hypertension, and oxygen are sometimes of value. Morphine (gr. $\frac{1}{6}$–$\frac{1}{4}$) with atropine (gr. $\frac{1}{100}$) hypodermically is the most effective measure. Adrenaline is recommended by some. If there are manifestations of great distension of the right side of the heart, or the blood pressure is much raised, venesection is indicated. If the condition persists, massive dosage of digitalis by the mouth, or the intravenous injection of digoxin or strophanthin should be considered (see p. 867).

PULMONARY ŒDEMA.—Dry cupping is sometimes beneficial in chronic pulmonary œdema. If an attack of acute pulmonary œdema occurs, a hypodermic of morphine, gr. $\frac{1}{4}$, with atropine gr. $\frac{1}{75}$–$\frac{1}{50}$th, should be administered immediately. Oxygen is often found to cause restlessness. The same considerations as regards venesection and digitalis therapy apply as in the case of cardiac asthma.

SYNCOPE.—It has been noted on p. 854, that this complication may be cardiac or peripheral in origin. The treatment of syncope is divided into prophylactic and immediate. With regard to the first, the ætiology should be reviewed. Heated rooms, crowds and prolonged standing should be avoided. If syncope occurs, the patient's head should be lowered and the clothes loosened at the neck. Plenty of fresh air is indicated. Diffusible stimulants (ether, ammonia or brandy) should be given by the mouth. Failing these, strychnine (gr. $\frac{1}{30}$–$\frac{1}{20}$th), or nikethamide administered subcutaneously or intramuscularly. See also Adams-Stokes Syndrome (p. 909), and Acute Peripheral Circulatory Failure (p. 875). In vasovagal attacks, atropine, failing which, adrenaline, should be injected subcutaneously.

PALPITATION.—This is a malady in which it is particularly important to investigate thoroughly and treat the cause; among these, digestive disturbances and toxic conditions are especially to be noted. Local applications, such as a belladonna plaster, or lin. bellad. c. chlorof., may be helpful. If these measures fail, sedatives (see p. 863) should be tried.

CARDIAC PAIN.—As in the case of palpitation, the ætiology should be reviewed. If there has been overstress, rest is indicated. A belladonna

plaster, or lin. bellad. c. chlorof., applied to the præcordium may be beneficial; while sometimes—especially in acute inflammatory conditions—the employment of hot fomentations or poultices, an ice-bag or Leiter's coil, a mustard leaf, or leeches may afford relief. If these measures fail, sedatives (see p. 863) may be administered, and in the event of their not being successful it may be necessary to resort to opiates.

VOMITING.—Milk is, in the majority of cases, the best food, to which sodium citrate (15 grains to each 10 ounces) may be added. If milk be not tolerated, peptonised milk, whey, albumin water, milk gruel, koumiss, or strong meat essences may be sipped, the patient not being allowed any solid food. A brisk purge should be administered, and bismuth with hydrocyanic acid may be given. Counter-irritation over the epigastrium is occasionally of some help for the relief of vomiting. If, in spite of these measures, the vomiting still continues, all food, and even water and drugs, by the mouth should be stopped, and resort be had to rectal feeding. The advantage in these cases of rectal feeding with milk pancreatised for at least 24 hours is not sufficiently recognised.

TREATMENT WHEN ACUTE PERIPHERAL CIRCULATORY FAILURE IS PRESENT

This comprises the following: Lowering of the patient's head, raising the foot of the bed to the extent of 1 or 2 feet, and the application of a tight binder to the abdomen. Diffusible stimulants. Saline and dextrose by the rectum, or intravenously. Strychnine, nikethamide (coramine), adrenaline, ephedrine, cardiazol-ephedrine, and pituitary (posterior lobe) extract ($\frac{1}{2}$–1 c.c.), or in the case of pregnancy, pitressin ($\frac{1}{2}$ c.c.).

Having discussed the various therapeutic measures which may be applicable to any form of cardiac disorder, these need not be again referred to when we come to consider the treatment of the individual cardiac affections: in this way much repetition will be saved.

FREDERICK W. PRICE.

FUNCTIONAL DISORDERS OF THE HEART

By functional disorders of the heart are meant those which occur independently of any structural change, whether of the valves, the myocardium, or the arteries; they are merely disorders of function, no organic lesion being necessarily present. It should be remembered, however, that any variety of functional disorder may be found in association with, though independent of, organic disease, especially if cardiac failure be present; and, further, that a persistent functional disorder may terminate in organic disease, although not necessarily so. Some writers deny the existence of functional disorder of the heart, being of opinion that in every case some structural change not only exists but accounts for the malady. Such a view is, in my opinion, untenable. I would, however, emphasise that not infrequently a diagnosis of functional disorder is erroneously made owing to the fact that the existence of organic disease has not been detected. As far as my experience goes, this applies especially to chronic myocardial disease unaccompanied by chronic

valvular disease, arterial disease, and perhaps slight mitral stenosis and chronic adhesive pericarditis. The first is referred to on page 949. With regard to the second, how often is arterial disease excluded as the result merely of the examination of the radial artery? Not only the radial, but at least the brachial, the temporal and the retinal arteries, and the aorta, should be examined.

Among functional disorders may be included palpitation, cardiac pain, irritable heart of soldiers, primary cardiac strain, sinus tachycardia, sinus bradycardia, and some cases of irregular action of the heart. No doubt some of these disorders may be either functional or due to organic disease. With regard to irregular action of the heart, it depends upon the type. It is almost universally agreed that sinus irregularity is always functional. Extra-systoles may or may not be due to some structural change in the myocardium. In the majority of cases, auricular flutter and auricular fibrillation are indicative of some myocardial change. It is true that cases of auriculo-ventricular block have been recorded in which there was an absence of any demonstrable lesion of the junctional tissue; but in some of these the vagus was found to be affected.

PALPITATION

By palpitation is meant the consciousness of the cardiac impact against the chest-wall, whether there is an increase in its rate or not, and whether the cardiac action is regular or not. I shall not deal here with those cases which are the result of extra-systoles, paroxysmal tachycardia, auricular flutter, auricular fibrillation, or heart-block.

Ætiology.—While palpitation may occur in organic disease of the heart, perhaps especially in aortic incompetence and cardiac hypertrophy from any cause, it is more frequently met with apart from this. It is more common in females. Among other causes are digestive disturbances—especially when attended with flatulent distension; the excessive indulgence of tea, coffee, tobacco or alcohol; neurasthenia and emotional states, the menopause, and the period of menstruation; during convalescence from any acute illness; thyrotoxicosis; and what is called disorderly action of the heart. The immediate cause of an attack is usually emotion, but it may be excessive physical exertion.

Symptoms.—The attack may last from a few seconds to a few hours. It is usually gradual in onset and passes off gradually. The subjective symptoms vary from a sensation of a gentle impact to the consciousness of a violent one against the chest-wall and actual pain in the præcordium in the severer forms. There may be flushing of the face, a sensation of throbbing in the head, and giddiness or faintness. The pulse is generally increased in rate, and its character may resemble that of the pulsus celer. The larger arteries, such as the carotid, may exhibit pulsation. The apex-beat is commonly diffuse, and its force increased, with a quickened outthrust. The heart is found to be not enlarged. The cardiac sounds are increased, and may be short and sharp. There may be a systolic murmur in the pulmonary area and less frequently at the apex. In dyspeptic patients, relief may coincide with the eructation of a large quantity of gas.

Treatment.—This is dealt with on p. 874.

CARDIAC PAIN

Discomfort or pain in the præcordium in the majority of cases is of extrinsic origin. This is especially so in females. It may be met with in neurasthenia and emotional states; digestive disorders, including of the gall-bladder, in all cases particularly if accompanied by flatulent distension of the stomach or colon; in general debility; during convalescence from an acute illness; toxic conditions; and in Irritable Heart.

Pain of extrinsic origin is more frequently related to emotion or mental effort, especially the former, than to physical exertion; it is in the great majority of cases situated in the præcordium, and usually over a smaller area of this than in the case of cardiac failure; it occasionally extends to near the angle of the left scapula or left armpit, or rarely to the left arm or over a larger area of the left front chest and even up to the neck; is either of a dull aching or of a sharp stabbing character; and is of shorter duration than in the case of cardiac failure. There may be hyperæsthesia and tenderness. Other symptoms, particularly connected with the nervous, vasomotor and alimentary systems are often present. Treatment has been discussed on p. 874.

Pain indicative of cardiac failure is referred to physical or, less frequently, mental effort, but it may not come on until some hours have elapsed; it also in the great majority is situated over the præcordium, and generally over the greater part or the whole of it; it is almost always confined to this area; is of a dull aching character; and is more or less continuous.

Treatment has been discussed previously.

The pain of angina pectoris is described on p. 987.

IRRITABLE HEART OF SOLDIERS

Synonyms.—Soldier's Heart; Disordered Action of the Heart (D.A.H.); Effort Syndrome; Neuro-circulatory Asthenia.

This is a condition which is characterized by a combination of symptoms due to a subnormal circulatory system—including, if not especially, the peripheral variety—and a subnormal nervous system.

The irritable heart of soldiers was first described by Myers (1870) and Da Costa (1871) in the United States of America. During and after the War of 1914–1918 much attention was paid to the subject in this country, owing to the large number of soldiers who were invalided home for so-called valvular disease of the heart and other cardiac disorders. The malady was first called irritable heart of soldiers, and, during the War of 1914–1918, soldier's heart, or disordered action of the heart (D.A.H.), and, later, by Lewis, effort syndrome. In the United States it is now termed neuro-circulatory asthenia. It is to be observed that the affection is not synonymous with athlete's heart or primary cardiac strain (see p. 880).

It is necessary to point out that what is called irritable heart of soldiers does not differ from that which is met with in civilian life.

Ætiology and Pathology.—The condition is more common during adolescence and up to early middle life, in poorly developed subjects, in those of a sedentary or light occupation and are out of training, and in urban life.

In the case of soldiers, it was formerly thought that the cause was either the accoutrements, such as tight belts and closely fitting uniforms, or over-exertion, such as "setting-up drill." It was found, however, that the correction of these did not obviate the malady.

It is now believed that a number of factors acting together, some more than others, constitute the cause. These include congenital or developmental weakness of the circulatory and nervous systems, a poor physique, a sedentary or light occupation, excessive physical exertion, an unsuitable kind of training, mental or emotional stress or strain, lack of sleep, infection, in a small percentage of cases hyperthyroidism, and, in my opinion, excessive smoking, especially of cigarettes.

An individual born with subnormal circulatory and nervous systems finds by experience that while he is able to engage in ordinary physical and mental effort he is incapable for those of a strenuous character. He arranges his manner of life accordingly, and consequently developmental weakness becomes superadded. Naturally such an individual does not stand the usual training so well as do those who were engaged in heavy or moderately heavy employments. Even with a slow and very carefully graduated training, he may never be able to engage in severe physical or mental effort. It is difficult to say how much physical stress or strain alone is an ætiological factor. Not infrequently there is a recent history of infection, either chronic, such as focal sepsis or pulmonary tuberculosis, or an acute infective disease.

Lastly, it is to be noted that the affection may be met with in those with organic disease of the heart.

Symptoms.—The onset is usually gradual. The commonest symptoms are breathlessness, palpitation, exhaustion, præcordial discomfort or pain, giddiness, and nervousness. Generally the shortness of breath, palpitation, and discomfort or pain are related to physical exertion or emotion; the sense of exhaustion to physical or mental effort; and the giddiness especially to change of posture. Breathlessness and palpitation may be very easily induced, and may also be present while at rest. The pain is commonly limited to the præcordium but sometimes radiates to near the angle of the left scapula, or rarely to the left arm or over a larger area of the left front chest or up to the neck. It is generally of a dull aching character but occasionally is sharp and stabbing. There may be hyperæsthesia and tenderness.

There may be faintness, and occasionally actual syncope, the latter probably being of the vasovagal type and more often in the young. Vasomotor symptoms, such as coldness and pallor or lividity of the extremities, and a tendency to sweating and flushing, are not infrequent. There may be lassitude, depression of spirits, irritability, loss of emotional control, insomnia, tremors of the hands, and headache, the last especially after exertion.

During sleep the cardiac and respiratory rates are normal. When the patient is awake but at rest they may be increased and there may be a slight increase in the blood pressure. There is frequently an abnormal response in the cardiac rate and the blood pressure with the assumption of the upright posture after lying down. The cardiac and respiratory rates and the blood pressure are unduly and it may be markedly increased by exertion, and, though perhaps to a less extent, by emotion, and their return to the former level after such is delayed. The apex-beat is often diffuse and its force increased, but the out-thrust is quicker and shorter than normal—which is

the opposite to that which obtains in hypertrophy. On X-ray examination, the heart is found not to be enlarged. The first sound may be increased in loudness, and may also be short and sharp. There may be cardio-respiratory murmurs (see p. 939), or a systolic murmur in the pulmonary area or at the apex, especially the former, in which case the murmur is generally harsh and may give the impression of being superficial. Reduplication of the second sound, it may be only after exertion or on lying down after such, is occasionally to be observed, and if present is indicative of cardiac strain (see p. 881).

Diagnosis.—It is necessary to diagnose the condition from chronic valvular disease, cardiac hypertrophy, focal sepsis, pulmonary tuberculosis, hyperthyroidism, and primary cardiac strain. This may be done by a consideration of the features described. In hypertrophy, the out-thrust of the apex-beat is slower and longer than normal; there is evidence of enlargement of the heart; and the first sound may be long, low in pitch and muffled. Primary cardiac strain is referred to on p. 881.

Prognosis.—As far as the duration of life is concerned, it is favourable. As to the course of the malady, this varies very considerably, and a period of observation is required to attempt a reliable opinion. The outlook is affected by the ætiological factors, the physical and, it may be especially, the mental make-up of the patient, probably most of all by the therapeutic measures adopted, the response thereto, and perhaps by the age of the individual. In the case of a chronic infection, it depends upon whether this can be removed. When the condition follows an acute infective disease, the prognosis is favourable provided convalescence is not hurried. This also applies when the affection is chiefly due to an anxiety condition, and suitable and competent psychological treatment is employed. The prognosis is probably better in the young.

Taking cases as a whole, the proportion of those who will not be able to engage in the physical and mental activities previously possible without experiencing some abnormal symptoms is by no means negligible.

Treatment.—PROPHYLACTIC.—In those of poor development, or of sedentary or light occupation, a slow and very carefully graduated training is of fundamental importance.

CURATIVE.—Reassurance and encouragement are of prime significance. In severe cases a preliminary rest in bed, of moderate duration, is usually helpful. If mental strain has been a factor, freedom from mental work until the patient has attained his optimum is advisable. Due attention to the cause of the malady, such as focal sepsis or an anxiety state, is obviously indicated. Psychotherapy has been spoken of under Prognosis. If there has been excessive indulgence in tobacco, smoking should be avoided altogether; and even if there has not, at the most it should be strictly moderate in amount. Alcohol is better avoided.

Efforts should be directed towards the restoration of the patient's general bodily and mental health. To this end careful attention to the matter of sleep, an ample amount of nutritious food, fresh air, slow and very carefully graduated exercise under wise supervision—preferably in the open air and, if the patient is fit for such, at first in the form of games—always stopping short of abnormal subjective symptoms, and breathing exercises are enjoined. Massage is not infrequently of help, and hydrotherapy is occasionally so. If the patient suffers from an unduly excitable nervous system, or is prone

to worry or be anxious, sedatives (see p. 863), in small daily dosage, are indicated for a time, and may be repeated occasionally if found to be required. Periodic courses of general tonics are worth a trial. Digitalis is of no avail and may even do harm.

PRIMARY CARDIAC STRAIN

By primary cardiac strain is meant a cardiac disorder which is the direct result of excessive physical exertion in an individual whose heart was previously sound.

It should be pointed out that most cardiologists are of opinion that physical exertion alone cannot cause such. They believe that in all cases the myocardium is weakened by toxins, either bacterial or chemical, or disease. Together with some cardiologists and general physicians, and pathologists of great authority, I do not share this view. At the same time I wish to make it clear that formerly physical exertion as an ætiological factor was very much exaggerated.

Ætiology and Pathology.—The affection is more likely to occur in middle or later life, and in those not in training. It may be due to sudden and violent physical exertion, such as boat-racing, and athletic and boxing contests; or the result of very severe, and either long continued or frequently repeated muscular effort, such as in heavy manual labour and in athletic training.

Regarding the first, when the heart is called upon for an increase of work by physical exertion, there is stretching of the muscular fibres and dilatation of the cavities together with an increased output of blood. Under normal conditions, the dilatation is temporary and physiological. In violent and sudden muscular exertion, however, it may persist, *i.e.* there is pathological acute dilatation. With rest in bed, the cavities usually gradually return to the normal, but functional disability may continue for some time.

Respecting the second, when the heart has to do continued extra work, cardiac hypertrophy takes place. If the physiological limits of the latter in any particular individual have been reached, any further demand on the organ will, sooner or later, have a permanent deleterious effect and pathological dilatation may take place. As regards this second group, it may be mentioned that those who do not believe that long continued very severe physical exertion alone can cause strain, quote the example of the horse. It seems to me that to compare, in this respect, man with an animal whose natural primary function and almost the whole of his activities have to do with physical exertion is hardly appropriate.

Symptoms.—When the malady is due to sudden and violent effort, there may be lividity or cyanosis of the face, giddiness, and vomiting; later, there may be collapse, quickened shallow breathing, coldness of the skin, præcordial uneasiness or actual pain, and a quickened, small and thready pulse; while later there may be indications of pronounced acute cardiac dilatation. The last involves both sides of the heart, but if the exertion has entailed severe fixation of the walls of the chest, the dilatation is chiefly right-sided, while if it has involved great contraction of the muscles, it is principally left-sided.

In the chronic forms of the affection, among the symptoms are shortness of breath, palpitation, giddiness or faintness, a feeling of weight or oppression, and discomfort or pain in the chest, the last sometimes extending to the left scapular region or arm. The pulse is usually small and weak, and its rate increased even while at rest. The area of cardiac impairment is not infrequently increased to the left and sometimes also to the right. The cardiac sounds may be feeble, or short and sharp, there may be a mitral or tricuspid murmur, and the second sound in the pulmonary area may be accentuated. Reduplication of the second sound, it may be only after exertion or on lying down after such, is sometimes present, particularly in the young, and is probably due to dilatation of the left ventricle.

Diagnosis.—This in large measure resolves itself into the question whether the case is one of primary cardiac strain, or whether the heart has been previously damaged; in the latter case, excessive physical exertion is merely the exciting cause of the malady. In considering this problem, a previous history of one of the causes of morbus cordis and evidence of myocardial or valvular disease are obviously of material importance.

Reduplication of the second sound, if present, is a valuable sign of primary cardiac strain.

There are certain fundamental distinctions between primary cardiac strain and irritable heart of soldiers. This is readily recognised by a comparison of the respective clinical features described (see pp. 878, 879).

Prognosis.—This exhibits a wide variation. In the young and robust, in the less severe cases, full recovery is the rule. This may occur in a few days or weeks, but on the other hand progress may be slow. Occasionally, however, recovery is not complete, the individual never being able to engage in physical exertion previously possible without experiencing some abnormal symptoms. In the more severe cases, the latter is not infrequent.

In middle or later life, even in the less severe cases, progress may be very slow, and full recovery is infrequent and perhaps only occasional; while in the more severe, even the duration of life may be shortened.

In all, a diminishing increase of pulse-rate is a favourable omen.

Treatment.—In the acute cases a very hot bath is to be commended, the patient being lifted out of it in a blanket, together with the administration of a few 15-grain doses of theobromine and sodium salicylate (diuretin). In the early stages, a strictly limited amount of food, both solid and liquid, is indicated. Oxygen may be required in some cases. When the patient is fit to get up, great caution should be exercised with regard to physical exertion. Warm baths, followed by a cold douche, may be tried provided there is a quick reaction.

In the chronic more severe cases, prolonged physical and even mental rest may be necessary. Massage, under certain conditions (see p. 864), may sometimes be of advantage, even in a comparatively early stage.

SINUS TACHYCARDIA

By the term tachycardia is meant an acceleration of the cardiac rate. There are two main varieties, namely: (1) sinus tachycardia; and (2) paroxysmal tachycardia. In addition, there is tachycardia in most cases of

auricular flutter and of auricular fibrillation. In the sinus variety the tachycardia is due to an increase in the function of rhythmicity in the sino-auricular node. In paroxysmal tachycardia, on the other hand, the tachycardia is the result of an abnormal rhythm, the impulses arising at some site other than the sino-auricular node. We shall here deal with sinus tachycardia. Paroxysmal tachycardia is discussed on p. 891.

Ætiology.—Sinus tachycardia may be physiological. In some healthy individuals the cardiac rate is persistently rapid. It is, therefore, difficult to decide when an increase of the cardiac rate in an individual is pathological; in this connection a record of the past history is of value. Transient sinus tachycardia may be a physiological reaction to emotional excitement, physical exertion, and the ingestion of food.

The pathological form of tachycardia may occur both during and after acute infective diseases, during convalescence from any acute illness, in pulmonary tuberculosis, focal sepsis, thyrotoxicosis, the excessive use of tea, coffee, tobacco or alcohol, and cardiac failure. It is also met with in irritable heart of soldiers, neurasthenia and emotional states, subnormal blood pressure, hæmorrhage, shock, cahectic conditions, certain organic diseases of the nervous system, and the use of certain drugs, such as atropine, adrenaline, and the nitrites.

Symptoms.—In tachycardia the patient may be conscious of the rapid action of the heart, and occasionally there is præcordial pain. The apex-beat may be diffuse and excited. There may be a systolic murmur at the apex, or base, or both. On the other hand, pre-existing murmurs may disappear.

A polygram and electro-cardiogram show merely an undue decrease of the diastolic interval (see p. 1003), that of the systolic being unaffected.

Diagnosis.—The differential diagnosis between sinus tachycardia and paroxysmal tachycardia is discussed on p. 893.

Treatment.—This resolves itself into dealing with the cause of the condition.

SINUS BRADYCARDIA

By the term bradycardia is meant a decreased cardiac rate. It must be distinguished from infrequency of the pulse-rate at the wrist, since the latter also includes ventricular extra-systole which is so feeble that the wave fails to reach the wrist. There are three varieties of bradycardia: (1) sinus bradycardia; (2) auriculo-ventricular block; and (3) some cases of auriculo-ventricular nodal rhythm. The last is a rare condition. We shall here deal with sinus bradycardia.

Sinus bradycardia is due to a decrease in the function of rhythmicity, the result of increased vagal tone or a direct action on the sino-auricular node. The cardiac rate is below 60 per minute, and is usually between 50 and 60, and rarely is as low as 40 and even less.

Ætiology.—Sinus bradycardia may be physiological, especially in males, advancing age, and athletes. Transient sinus bradycardia may be a physiological reaction to rest, sleep, and pressure on the carotid sinus, especially the right.

The pathological form of bradycardia is less common than is sinus tachycardia. It may occur (1) during the convalescence of acute infective diseases,

especially influenza, diphtheria, pneumonia, typhoid and typhus; (2) in certain toxic conditions, such as jaundice, diabetes and uræmia; (3) in hypothyroidism; (4) in some forms of cardiac disease—especially aortic stenosis and fatty degeneration of the myocardium; (5) in the use of certain drugs, such as digitalis, opium and, exceptionally, tobacco; and (6) during certain diseases of the nervous system.

In a polygram and an electro-cardiogram there is merely an undue prolongation of the diastolic interval (see p. 1003), that of the systolic being unaffected.

Diagnosis.—In sinus bradycardia the rate is only occasionally below 50. It is influenced by physical exertion, emotion, pyrexia, amyl nitrite, and atropine.

Sinus bradycardia should be diagnosed from extra-systoles, 2 : 1 and complete auriculo-ventricular block, and auriculo-ventricular nodal rhythm.

IRREGULAR ACTION OF THE HEART

The subject of irregular action of the heart is of great practical importance. Formerly it was notoriously a source of perplexity and difficulty to the clinician. It was known that irregularity might, on the one hand, signify even serious impairment or disease of the heart, or, on the other, that it might be of no practical consequence. It was not possible, however, to determine the significance of the irregularity in any given case, because there were no means of differentiating the types of irregularity, or what any particular type signified. By means of the electro-cardiograph and the clinical polygraph it is now possible to classify irregular action of the heart into types, and it is known what each type signifies. I would emphasize, however, that the work of elucidation having been accomplished, in a considerable majority of cases the use of a sphygmograph is sufficient, and in a fair proportion palpation and auscultation suffice.

Irregular action of the heart may be due to (1) sinus arrhythmia; (2) extra-systoles, or premature contractions; (3) paroxysmal tachycardia, (4) auriculo-ventricular nodal rhythm; (5) auricular fibrillation; (6) auricular flutter; (7) ventricular fibrillation; (8) heart-block; and (9) the pulsus alternans. The first two varieties are very common.

It may be advisable to describe here what is meant by the terms 'intermittent' pulse or a 'dropped beat,' 'pulsus bigeminus' or 'coupling of the beats,' and 'pulsus trigeminus.'

Intermission of the pulse is a form of irregularity which is not uncommon. By it is meant a condition in which the normal rhythm of the pulse is interrupted, either occasionally or more frequently, either at regular or irregular intervals, by an abnormally long pause during which no wave is felt at the wrist, a beat being missed. It is important to understand how intermission of the pulse is caused, especially from the point of view of prognosis. By far the commonest cause is a premature contraction of the ventricle ('extra-systole') which is so feeble that the wave fails to reach the wrist; the next most common cause is partial heart-block; while the condition is occasionally due to sinus irregularity, and very rarely to sino-auricular block. The differential diagnosis between extra-systole and partial heart-block is discussed under extra-systole. The differential diagnosis also between occasional

dropped beats due on the one hand to sinus irregularity and on the other to partial heart-block is discussed under heart-block.

By *pulsus bigeminus* or *coupling of the beats* is meant a condition in which the pulse-beats occur in pairs, for long or short periods. The paired beats may occur at regular intervals, or at irregular intervals, and some writers restrict the term *pulsus bigeminus* to the former, and that of *coupling of the beats* to the latter. When the paired beats fall at regular intervals, the commonest cause is the occurrence of extra-systoles, usually ventricular, in cases in which the fundamental or sinus rhythm is otherwise maintained;

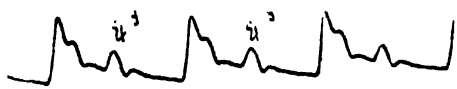


FIG. 24.—Pulsus bigeminus, due to a single extra-systole with its succeeding compensatory pause occurring regularly after each normal beat.

either a single extra-systole with its succeeding compensatory pause occurring regularly after each normal beat (Fig. 24), or such occurring after every two normal beats, the premature contraction in the latter case, however, being so feeble that no waves reaches the wrist. The next most common cause is partial heart-block, when the ventricle fails to respond to every third beat of the auricle (Fig. 25). A rare cause is sino-auricular block, in which the auricle fails to respond to every third impulse generated at the sinus. When the paired beats occur at irregular intervals, the cause is a ventricular extra-systole occurring regularly after each normal ventricular contraction in cases of auricular fibrillation; this is usually due to the action of digitalis (Fig. 31), but may occur independently of it.

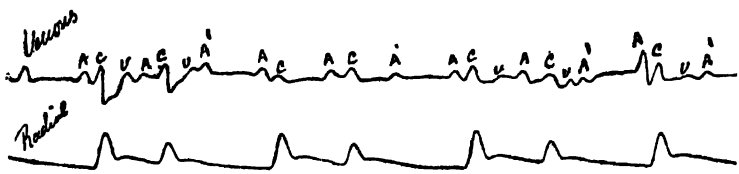


FIG. 25.—Pulsus bigeminus, due to partial heart-block, the ventricle failing to respond to the stimulus from the auricle at *A'*.

By *pulsus trigeminus* is meant a condition in which the pulse-beats are grouped in threes. The causes are: (1) extra-systoles—either a single extra-systole with its succeeding compensatory pause after every two normal beats, or such after every three normal beats and failing to send a wave to the wrist; (2) partial heart-block, when the ventricle fails to respond to every fourth beat of the auricle; and, rarely (3), sino-auricular block, in which the auricle fails to respond to every fourth impulse generated at the sinus.

The differential diagnosis between intermission of the pulse, pulsus bigeminus, and pulsus trigeminus due to the various causes mentioned is discussed elsewhere.

SINUS ARRHYTHMIA

This is a normal phenomenon, which is very frequent, both in health and disease. It is due to variation of vagal tone acting upon the sino-auricular node.

The chief characteristics of sinus irregularity is the variation in the length of the diastolic interval, the systolic being unaffected. The irregularity may be slight or even marked. In the great majority of cases it is related to respiration, the cardiac rate gradually increasing during inspiration and gradually diminishing during expiration. If not related to respiration, the irregularity may be only present during slow deep breathing. There is an abrupt slowing of a few beats and then a gradual increase.

Ætiology.—Sinus arrhythmia is much more frequent during childhood and adolescence, but may be found at all ages. It sometimes occurs after a febrile illness, and occasionally during the administration of digitalis, and even the act of swallowing may produce it—the heart-rate during the act being quickened for a few beats, followed by a reduction in the rate.

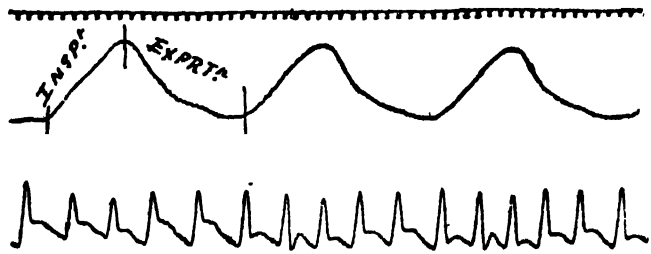


Fig. 26.—Simultaneous tracings of the respiration and the radial pulse, from a healthy boy aged 14, showing sinus irregularity.

Symptoms.—Usually there are no subjective symptoms, but rarely those of cerebral anæmia, such as giddiness, or faintness or even actual syncope, occur during an unusually long pause. On auscultation, the interval between the first and second sounds is found to be constant, while the varying length of the diastolic interval can be detected. If a tracing of the radial artery be taken, the intervals between the beats will be found to vary, while the pulse-beats are of equal or nearly equal size (Fig. 26). A polygram and an electrocardiogram (Figs. 58–60) show merely either of the two variations in the length of the diastolic periods just described.

The irregularity is diminished or abolished by an increase in the cardiac rate.

Diagnosis.—A diagnosis may be made from the features described. When irregularity of the cardiac action is found to be definitely related to respiration, it is in all probability of the sinus type.

Prognosis.—There is no reason to suppose that sinus irregularity is either indicative of an impaired heart, or that it adds to the gravity of any diseased cardiac condition which may be present. The condition, therefore, may be entirely disregarded.

Treatment.—No treatment is required.

THE EXTRA-SYSTOLE

Synonym.—Premature Contraction.

By extra-systole is meant a premature contraction the result of an impulse which is generated at some site other than the sino-auricular node.

It has been noted that if rhythmicity is more developed at any other portion of the primitive cardiac tube than the sinus, the impulse arises at that point (see p. 847).

There are three varieties of extra-systoles, according to whether the point of origin is situated in the auricle, or the auriculo-ventricular node or bundle above its division, or the ventricle. The first is called auricular extra-systole; the second, auriculo-ventricular nodal extra-systole; and the third, ventricular extra-systole.

In each case the sinus rhythm is otherwise maintained in most cases. Usually an extra-systole is followed by a long pause (compensatory pause). Rarely the premature contraction occurs between two normal beats (interpolated extra-systole).

Of the three varieties of extra-systoles, the ventricular is far the most



FIG. 27.—Simultaneous tracings of the jugular and radial pulses, showing a ventricular extra-systole at *Ex.s.* The usual rhythm of the auricle is maintained. The extra-systole in the jugular tracing is represented by the wave *c'*, immediately before the systole of the auricle. The compensatory pause is complete.

common, and the auricular the next frequent. The variety of extra-systoles in the same individual is usually constant, but the three varieties may occur in the same subject. Occasionally premature contractions arising from different foci are observed in one record—multiple extra-systoles.

Extra-systoles may occur at long intervals, or at frequent, irregular intervals; or regularly after each beat, or after every second, or third, or more, normal beats; or there may be a rapid succession of extra-systoles—usually persisting for a few cycles only (Fig. 62), but rarely even for a few minutes.

THE VENTRICULAR VARIETY OF EXTRA-SYSTOLE.—We may take this variety for the purpose of illustration. While the chambers of the heart are contracting in the normal fashion, a premature contraction of the ventricle takes place, this arising independently of a stimulus from the auricle, which maintains its usual rhythm and contracts as the result of the normal stimulus from the sinus. The exact time at which the premature contraction of the ventricle takes place is either immediately before the systole of the auricle (Fig. 27), or—as is usually the case—synchronously with it, or

after it, but prior to that point of time at which it would have occurred if this had been in response to a stimulus received from the auricle in the normal way. In most cases the succeeding impulse from the auricle fails to cause a contraction of the ventricle; for this reason the pause which follows the premature contraction is abnormally long, being called the *compensatory pause*. When this prolonged diastole and the preceding shortened diastole together equal in time two normal cardiac cycles, the compensatory pause is said to be *complete*. Since during the prolonged pause the ventricle has had an unusually long period in which to fill and recuperate, the pulse-beat immediately following a compensatory pause has often a greater amplitude than on other occasions. Sometimes, more especially when the cardiac rate is slow, a ventricular extra-systole occurs so early in the cardiac cycle that the ventricle does contract in response to the normal stimulus which is transmitted from the auricle immediately after the premature contraction; in this way a premature contraction is interpolated between two normal beats. This form of the extra-systole is called *interpolated* (Fig. 28).

On auscultation, in the vast majority of cases, two heart-sounds are



FIG. 28.—Simultaneous tracings of the jugular and radial pulses, showing an interpolated ventricular extra-systole (c' and r'), represented in the diagram by the downstroke +. The downstrokes in the space *As* represent the auricular waves (a) in the jugular, and the downstrokes in the space *Vs* represent the carotid waves c, and the slanting lines connecting them represent the a–c interval (Mackenzie).

synchronous with each extra-systole, these forming with those of the preceding normal contraction a group of four sounds. Sometimes, however, the extra-systole occurs early in diastole, and before the cardiac muscle has had sufficient time to recover fully from the preceding systole, in which event the premature contraction is so feeble as to fail to open the aortic valves, and only the first sound is heard; in this way a group of three sounds becomes audible. Very rarely the premature contraction is so feeble as not to produce any cardiac sounds whatever.

The amplitude of the pulse-wave of an extra-systole is not so great as that of a contraction occurring at a normal interval, because the heart muscle has not had time to recover from its previous effort. The earlier an extra-systole occurs in the diastole, the more feeble it is; it may be so feeble that no wave is felt at the wrist, so that there is simply an abnormally long pause, resulting in what is called a "dropped beat" or an "intermittent" pulse; as has been already noted, an extra-systole which fails to reach the wrist is, indeed, the most usual cause of an intermittent pulse. If a single extra-systole with its succeeding compensatory pause occurs regularly after each normal beat, then the beats at the cardiac apex occur in pairs, as also do the pulse-beats, the condition being called *pulsus bigeminus* (Fig. 24). Simi-

larly, if a single extra-systole with its succeeding compensatory pause occurs after every two normal beats, then the apex-beat occurs in threes, as also do the pulse-beats, the condition being known as *pulsus trigeminus*; but if the premature contraction is so feeble that no wave reaches the wrist, the pulse-beats are paired.

If a polygraphic record of a case of ventricular extra-systole (Fig. 27) be analysed, it will be found that, as the normal rhythm proceeds as usual, the *a* wave appears at regular intervals; each *a* wave is followed by a *c* wave, except when an extra-systole occurs, when the *c* wave either precedes the *a* wave, or—as is more commonly the case—occurs synchronously with it, in which case the amplitude of the wave is correspondingly increased.

Auricular Variety of Extra-Systole.—In this variety there is a premature contraction of the auricle, the stimulus arising in the wall of the auricle prior to the normal stimulus from the sinus. The premature contraction of the auricle is usually followed by a premature contraction of the ventricle, following the usual transmission of the stimulus from the auricle along the auriculo-ventricular bundle. Not infrequently, in the case of extra-systole the stimulus from auricle to ventricle travels slowly, so that the *As–Vs* interval is lengthened, and the prematurity of the ventricular systole is consequently not so great as that of the auricle; in this way the compensatory pause is shortened. In some instances the contraction which immediately follows the extra-systole takes place rather earlier than the normal interval, this being probably due to the unusual length of the rest period; in this way there is further encroachment upon the compensatory pause. This is less marked in the case of the second contraction, and it disappears within a few cycles. Sometimes there are variations in the rate of transmission of these auricular premature contractions to the ventricle.

Occasionally the stimulus from the auricle does not reach the ventricle at all, and no premature contraction of this chamber takes place, in which event the premature contraction of the auricle is not followed by a premature contraction of the ventricle, the condition being known as 'blocked auricular extra-systoles (Fig. 63). In these cases a long pause is to be noted in the sphygmogram. As in the case of the ventricular variety, an auricular extra-systole is followed by a lengthened pause; but, with rare exceptions, this compensatory pause is not complete. In some cases, however, the compensatory pause is complete.

In a polygraphic record of a case of auricular extra-systole, each *c* wave is preceded by an *a* wave, while there is a premature *a* wave and a premature *c* wave, sometimes with an increased *a–c* interval, and an alteration of the relative position of the beats following the extra-systole.

Auriculo-Ventricular Nodal Variety of Extra-Systole.—In this variety the stimulus for premature contraction originates in the auriculo-ventricular node or bundle above its division, travelling upwards into the auricle and downwards into the ventricle, and giving rise to a premature and simultaneous contraction of both auricle and ventricle. The premature ventricular contraction more or less coincides with that of the auricle, but this is by no means absolute; the contraction of both chambers may be absolutely synchronous, or the ventricular systole may begin after or before that of the auricle. When the auricular contraction occurs before that of the ventricle, the period of time between the contraction of the upper and

lower chambers is shortened. The compensatory pause may or may not be complete.

In a tracing of the jugular vein from a case of auriculo-ventricular nodal extra-systole, there is prematurity of the *a* wave, and also of the *c* wave; when the premature contraction of the chambers is synchronous, both waves are combined, in which case the amplitude of the wave is increased; when the auricular contraction occurs before that of the ventricle, the *a* wave precedes the *c* wave, but the *a–c* interval is diminished to about 0·10 sec.

In the ventricular and auriculo-ventricular nodal varieties of extra-systoles, in contrast with the 'double' venous pulsation in the jugular vein which may be visible in the case of the auricular variety, there is usually an unduly large 'single' pulsation coincident with the premature contraction; this is due to the contraction of the upper and lower chambers of the heart occurring synchronously, the result being that the auricle, instead of discharging its contents into the ventricle, does so into the venæ cavæ.

Ætiology and Pathology.—Extra-systoles may be met with at any age, but are much more frequent in the elderly and middle-aged, especially the former, than in the young, and are rare during the first decade of life, and are more common in men than in women. They are more frequent in the subjects of organic disease of the heart than in those who are not, and in myocardial than in valvular affections. They are to be found in digestive disturbances, especially when attended with flatulent distension, acute infections, hypertension, arterial disease, focal sepsis, thyrotoxicosis, the excessive consumption of tea, coffee, tobacco and alcohol, emotional states, and as the result of the administration of certain drugs, such as digitalis, barium, aconite and chloroform. In a considerable proportion of cases there is no ascertainable cause. Extra-systoles are especially apt to occur during rest following physical exertion, soon after getting into bed, change of posture, after a big meal and during cardiac dilatation with failure.

Extra-systoles indicate that at the time of the premature contraction some portion of the myocardium below the sinus is more excitable than the sinus. This may or may not be due to some structural change in the myocardium; it may, for example, be caused by poisoning of the heart wall without structural damage.

Subjective Symptoms.—An individual in whom extra-systoles occur may be unconscious of their presence. On the other hand, he may experience a sensation of fluttering in the chest when a premature beat occurs: or he may be conscious of the long pause and complain of intermission of the pulse, or that the 'heart stops'; or the contraction of the heart following the pause may be accompanied by the consciousness of a thud or shock in the region of the heart, sometimes followed by a feeling of exhaustion. The patient may complain of a sensation of a 'catch in the breath,' or of 'gripping in the throat.' Very rarely, during a prolonged pause, giddiness, faintness, or even actual syncope may take place.

Diagnosis.—Extra-systoles may be recognised with certainty by means of the electro-cardiograph or the clinical polygraph. But it is important to recognise that in the majority of cases a correct diagnosis can be made simply by palpation and auscultation. The normal rhythm of the heart is disturbed by the occurrence of a premature beat in the radial pulse and at the cardiac apex, followed by an abnormally long pause. The auscultatory signs have

already been noted; they are of much diagnostic value. When, on palpation of the radial artery, an apparently otherwise regular pulse is sometimes interrupted by an unusually long pause, it should suggest either an extra-systole which is so feeble that no wave is felt at the wrist, or partial heart-block. When the former is responsible, a premature beat can be detected at the cardiac apex and on auscultation one or two heart-sounds will, in the great majority of cases, be audible during the early part of the pause, because the ventricle has contracted; whereas in the case of partial heart-block there will be absence of an apex-thrust and of heart-sounds during the pause, because the ventricle has failed to contract. Further, in the case of extra-systole, a wave is usually present in a sphygmographic tracing, and a premature contraction is always visible in a tracing of the apex-beat. These three features are almost invariably sufficient to distinguish between an intermittent pulse due to an extra-systole which fails to reach the wrist and that due to partial heart-block. An electro-cardiogram or a polygram will place the matter beyond doubt. It may be here noted that it is necessary to exclude sinus irregularity and also sino-auricular block, in cases of an unusually long pause in the radial pulse. The differential diagnosis between pulsus bigeminus, pulsus trigeminus, and infrequency, including halving, of the pulse rate, due on the one hand to extra-systoles, and on the other to partial heart-block, can also readily be made, as a rule, by means of palpation and auscultation.

It is sometimes very difficult, if not impossible, by palpation and auscultation alone, to diagnose extra-systoles, occurring frequently and at irregular intervals, especially if of auricular origin, from auricular fibrillation. Extra-systoles are diminished or abolished by an increase in the cardiac rate, while the opposite obtains in auricular fibrillation. Again, a sphygmographic tracing is almost invariably sufficient. It is also necessary to exclude auricular flutter when the response of the ventricle to auricular contraction is at irregular intervals (p. 902, and Fig. 76).

Prognosis.—The question of prognosis of extra-systoles is of some consequence. Unfortunately the lay mind has come to attach an unnecessary significance to them. Furthermore, the medical practitioner should understand that extra-systoles constitute one of the most frequent causes of irregularity of the pulse, and that an extra-systole which fails to reach the wrist is the commonest cause of an 'intermittent' pulse. Apart from rare exceptions (see below), when extra-systoles are considered by themselves—that is, without reference to the conditions with which they may be associated—there is so far no evidence for supposing that they are either indicative of an impaired heart, or that they add to the gravity of any existing morbid condition. While it is true that extra-systoles may precede the occurrence of other forms of cardiac irregularity, such as the complete irregularity associated with auricular fibrillation, it should be borne in mind that these might have arisen independently. The prognosis, therefore, should be based entirely upon the causal or associated condition.

The significance of a rapid succession of extra-systoles has some relation to that of paroxysmal tachycardia. Multiple extra-systoles of ventricular origin are usually of very serious significance, and are generally a presage of ventricular fibrillation.

Treatment.—Our first duty is to reassure the patient; this may be done

with confidence. The ætiology of extra-systole should be thoroughly reviewed, the general health should receive attention, and if cardiac failure be present it should be treated on the lines laid down elsewhere. Some writers speak well of quinidine, 5 to 15 grains per diem, for the irregularity itself, but this does not accord with my experience. Neither have I found digitalis of any value. Sedatives (see p. 863) are frequently of benefit for the associated symptoms, especially when there is irritability of the nervous system or insomnia.

PAROXYSMAL TACHYCARDIA

By the term paroxysmal tachycardia is meant a condition in which a marked acceleration of the cardiac rate occurs, which commences abruptly and usually without apparent cause, lasts for a varying period, ceases abruptly, and is due to an abnormal rhythm, the stimulus for contraction arising at some site other than the sino-auricular node. The return of the cardiac rate to what it was prior to the paroxysm is due to the reversion of the cardiac rhythm to the normal.

It is necessary to point out that under this term some writers include paroxysmal auricular flutter with marked acceleration of the ventricular rate, and paroxysmal auricular fibrillation with marked acceleration of the ventricular rate, using the term " simple " paroxysmal tachycardia for the other cases. I shall not include these two conditions.

The first beat of the paroxysm is premature, and usually the paroxysm is followed by a long pause, as in the case of extra-systole, before the normal rhythm is restored. The individual beats of the paroxysm are essentially the same as those of isolated extra-systoles. Between the attacks there may be single extra-systoles. The site of origin of these is usually the same as of the beats of the paroxysm.

There are three varieties of paroxysmal tachycardia, according to whether the point of origin of the new rhythm is situated in the auricle, the auriculo-ventricular node, or the ventricle—in that order of frequency. The first is called auricular paroxysmal tachycardia ; the second, auriculo-ventricular nodal paroxysmal tachycardia ; and the third, ventricular tachycardia. The first two varieties together constitute supraventricular paroxysmal tachycardia. In the auriculo-ventricular nodal variety there is a simultaneous contraction of both auricle and ventricle ; the contraction of both chambers may be absolutely synchronous, or the ventricular systole may begin after, or before, that of the auricle. The variety of the paroxysms in the same individual is almost invariably constant.

The paroxysms may last only for a few beats, or up to a few days, or, rarely, even a few weeks or more. The patient may experience one attack and never have another ; or he may have many in the course of 24 hours ; or the attacks may occur at varying intervals, frequent or long, for many years.

Ætiology.—The ætiology of paroxysmal tachycardia is obscure. The malady may occur at any age, but usually is first met with during middle life, and appears to be more common in males. A history of previous infection by rheumatism is not infrequent, and a fair proportion of cases are the subjects of chronic valvular disease, particularly mitral stenosis, or of myo-

cardial disease. Paroxysmal tachycardia is occasionally met with in coronary occlusion, when it is most likely to be of the ventricular type, focal sepsis, thyrotoxicosis, and the excessive use of tea, coffee, tobacco or alcohol.

Usually there is no exciting cause of the attacks, but among such are physical exertion, emotional excitement, digestive disorders, especially with flatulent distension, and very rarely the adoption of a certain posture.

The ventricular variety is most frequently met with in later life, and in the vast majority of cases is associated with serious organic disease of the heart, especially coronary occlusion, and very rarely in fatal cases of digitalis poisoning.

Symptoms.—In some cases the patient is able to recognise both the onset and termination of the attack. If the attack be brief, he may be unconscious of the tachycardia. If it persists for a time, however, he is usually conscious of it, and generally complains of rapid action of the heart, or of a fluttering sensation in the chest, or palpitation; and occasionally of throbbing or pulsation in the neck, the head, or some other part of the body. The face is generally pale and has an anxious expression. The patient may complain of a sense of exhaustion, and of oppression or discomfort or even pain in the chest. There may be abdominal distension, or nausea, or vomiting. Quickened or even distressed breathing may be present. There may be giddiness, faintness, or even loss of consciousness, and rarely convulsions. The usual symptoms of cardiac failure, commonly both left- and right-sided, generally supervene; or, if these were present before the attack, they increase in severity. The degree of failure depends upon the cardiac rate, the duration of the paroxysm, its variety, any associated morbid condition, and the integrity of the myocardium. In long-continued paroxysms, and even in some cases in which they last for only a few hours, it may be severe or even extreme. It is usually more severe in the ventricular variety. In a small proportion of cases, anginal pain occurs.

The cardiac rate may range from 120 to 250. In the majority of cases it is between 160 and 200, being usually more rapid in the ventricular variety. The effect of posture, physical exertion and pressure on the carotid sinus on the pulse-rate is described under Diagnosis. The pulse is of smaller volume than normal. Not infrequently the pulsus alternans is present. In the auriculo-ventricular nodal and the ventricular varieties, the rhythm may be irregular, but the irregularity is so slight that it is detected only by graphic methods. The blood pressure is generally lowered during an attack. The cardiac sounds may be shorter and sharper and feeble. If murmurs were present prior to the onset of the attack, they may become faint or even disappear; this applies particularly in the case of a mitral presystolic bruit. The jugular veins may be distended, and there may be the ventricular form of the jugular pulse. The results of X-ray examination show that the heart often becomes actually smaller during short attacks, but in cases in which the attacks are of long duration or the organ is seriously diseased, considerable and rapid—often within a few hours—cardiac dilatation may occur, in which case the physical signs thereof, described on p. 956, may be noted.

Analysis of polygraphic tracings gives different results according to the nature of the abnormal rhythm.

A remarkable feature of the condition is that with the sudden reversion of the rhythm to normal there is usually an extraordinarily rapid recovery to

the state in which the patient was prior to the paroxysm. In some cases the cessation of the attack is accompanied by the passage of large quantities of wind and excessive eructations, while a large quantity of urine may be voided.

Diagnosis.—We should think of the possibility of paroxysmal tachycardia (or of auricular flutter), whenever an individual complains of attacks of palpitation, or is conscious of a marked increase in the cardiac rate, in either case occurring suddenly and without apparent cause, or suffers from indications of cardiac failure coming on rapidly, if the rhythm of the pulse be regular.

Paroxysmal tachycardia should be distinguished from sinus tachycardia, and auricular flutter with continuous 2 : 1 auriculo-ventricular block.

The most important factors in the diagnosis of the condition are: (1) Usually there is no exciting cause of the paroxysm, unlike sinus tachycardia. (2) The commencement and termination of the attack of tachycardia are sudden—the maximum rate is attained within a few beats, and the return of the cardiac rate to what it was prior to the attack or, as in some cases, to near this, occurs equally suddenly; whereas in tachycardia associated with the normal rhythm the onset and termination are gradual. (3) A persistent rate of over 160 is almost always due to an abnormal rhythm, and of over 140 usually so. If the rhythm is regular, the condition is either paroxysmal tachycardia, or 2 : 1 auricular flutter; while if completely irregular, auricular fibrillation. (4) In normal rhythm the cardiac rate is influenced by posture, physical exertion and pressure on the carotid sinus, especially the right. In paroxysmal tachycardia the rate is not affected by these—excepting that carotid pressure may cause the paroxysm to cease. In all cases electrocardiographic examination will put the diagnosis beyond doubt (see pp. 1012–1014).

The differential diagnosis between paroxysmal tachycardia and 2 : 1 auricular flutter is discussed on p. 902.

For the differential diagnosis of the varieties of paroxysmal tachycardia, see pp. 1012–1014.

Prognosis.—The prognosis in any case of paroxysmal tachycardia is difficult. It may be considered from two points of view: (1) That of a particular paroxysm; and (2) the question of recurrence of the attacks.

With regard to the former, the points which should be taken into account are the nature and degree of any associated morbid condition, the variety of the paroxysm, the ventricular rate, the duration of the attack, the integrity of the myocardium, and the history of any previous attacks. In the vast majority of cases the ventricular variety is associated with serious organic disease. The question of cardio-vascular organic disease is of much greater moment than the cardiac rate. When the ventricular rate is not very high, and there is an absence of œdema of the lungs, hepatic enlargement and systemic œdema, and there is little or no cardiac dilatation, the outlook is good as far as the risk to life is concerned; while, on the other hand, if the clinical picture is the reverse, it is uncertain—but it should be remembered that the paroxysm may cease at any time, in which event the patient may improve with surprising rapidity. Death during an attack is of rare occurrence, although it may happen, especially if the tachycardia is of ventricular origin.

With regard to the question of the recurrence of the attacks, it is impossible to give an answer. The patient may never suffer from a subsequent attack; while, on the other hand, they may recur even several times in the course of 24 hours, or at frequent intervals for many years. There is, however, a tendency to a recurrence.

Treatment.—This resolves itself into two parts: (1) Treatment during an attack; and (2) the prevention, if possible, of the recurrence of the attacks.

With regard to the first of these, the results of treatment are in the majority of cases unsatisfactory. It is true that the paroxysm not infrequently ceases when various remedies are applied, but it should be remembered that the nature of the disorder is to stop suddenly and, therefore, the question of *post hoc* and *propter hoc* arises.

The patient should rest, either in the recumbent position or sitting in an easy-chair, and keep as quiet as possible.

The following methods of treatment may be tried in the auricular and nodal varieties: The adoption of certain postures, such as bending the body, with, it may be, the head between the knees; various movements of the body; rapid deep breathing; holding the breath as long as possible, including after a deep inspiration or a deep expiration; local applications, such as hot fomentations, or poultices, an ice-bag, or a mustard-leaf, to the præcordium; firm compression to the abdomen; a carminative, or a diffusible stimulant, or drinking ice-cold water; the induction of vomiting; moderately firm pressure on either eyeball, with the eye closed; and firm pressure with the tips of the fingers on the carotid sinus in the right or left side of the neck for a quarter to a half minute or more, stopping short of pain, repeated several times if necessary. The last is the most likely to be successful. Failing these measures, a stiff dose of bromide and chloral, without or with opium, by the mouth. Morphine ($\frac{1}{2}$ grain suppository, or $\frac{1}{4}$ grain hypodermically), provided there is an absence of a reasonable fear of the patient becoming an addict to the drug. Quinidine may be tried, if the patient can be assiduously watched and there is an absence of idiosyncrasy to the drug (see p. 871). Six grains may be given every two or three hours for four or five doses. Recently the drug has been administered intravenously, but this is not recommended. If the foregoing measures are unsuccessful, massive doses of digitalis by the mouth, or digoxin or strophanthin intravenously, are rarely effective.

In the ventricular variety, quinidine may be tried. Massive dosage of digitalis is even contra-indicated.

Respecting the prevention of the recurrence of the attacks, a searching inquiry should be made for both the underlying and exciting causes, with the object of treating them. Sedatives (see p. 863) are often used. Quinidine, 5 to 15 grains per diem, is not infrequently successful. Digitalis, in moderate dosage, is occasionally so.

AURICULO-VENTRICULAR NODAL RHYTHM

This is a rare condition, in which the impulse is generated in the auriculo-ventricular node, and travels upwards into the auricles and downwards into the ventricles, giving rise to a simultaneous contraction of both auricles and

ventricles. There is generally depression of the function of rhythmicity at the sino-auricular node due to the action of the vagus.

The condition is believed to occur more often in the young, and may be met with in digitalis and acute infections. The new rhythm is usually temporary, and generally recurs. It may last for a few beats up to a few days or even longer. It is frequently abolished by physical exertion and atropine. If only an isolated beat is involved, there is a ' nodal escape.'

The rate varies between 30 and 50 and rarely more, being usually about 40. In some cases a large pulsation in the jugular vein, the result of the simultaneous contraction of the auricles and ventricles, is to be observed.

The contraction of the upper and lower chambers may be absolutely synchronous, or the ventricular systole may begin after, or before, that of the auricle, the last being the most common. In the first instance, the *a* and *c* waves of a polygraphic tracing are superimposed, in which case the amplitude of the *a* wave is increased; while in the second, the *a* wave precedes the *c* wave, but the *a*–*c* interval is diminished to about 0·10 sec.

Auriculo-ventricular nodal rhythm should be diagnosed from auriculo-ventricular block and sinus bradycardia.

The condition is of no clinical importance.

AURICULAR FIBRILLATION

It is of great practical importance that auricular fibrillation should be recognised, owing to its bearing on the diagnosis, prognosis and treatment of cardiac affections. It is a specific clinical condition, which can be recognised with certainty. It is characterized by an absence of all signs of the normal contraction of the auricles, and in the vast majority of cases by complete irregularity of the arterial pulse. It accounts for approximately 50 per cent. of all cases of persistent irregularity of the heart, and it is found in from 60 to 70 per cent. of all cases of serious cardiac failure with dropsy. The condition has been known variously as ' delirium cordis,' ' pulsus irregularis perpetuus,' and the ' mitral ' pulse.

By auricular fibrillation is meant a condition in which co-ordinate contraction in the auricle is replaced by inco-ordinate contraction, the individual fibres, or groups of fibres, instead of contracting in an orderly and simultaneous manner, doing so rapidly and independently of each other, with the result that systole of the chamber as a whole never takes place. When auricular fibrillation has once set in, in the great majority of cases it is permanent. But, instead of this, it may be paroxysmal (Fig. 29). The tendency to occurrence increases, however, until finally the condition usually becomes persistent or established.

Effect of Auricular Fibrillation on the Heart.—The effect of auricular fibrillation on the cardiac action is mainly threefold: (1) The forcible contraction of the auricles driving the blood through the open auriculo-ventricular valves into the ventricles during the latter part of ventricular diastole is lost. This results in the ventricle being less filled. (2) Instead of the ventricle receiving impulses from the auricle at regular intervals, it receives them at completely irregular intervals. (3) In the great majority of cases there is an increase in the ventricular rate. The result of these three factors combined is that some of the ventricular contractions are

so feeble as to fail to open the aortic valves, and the pulse is diminished in volume and its rhythm is irregularly irregular. The third factor is the most important.

Ætiology.—The majority of cases of auricular fibrillation fall within two groups, especially the first: (1) those with a history of rheumatism; and (2) patients suffering from chronic myocardial disease, coronary disease, or hypertension. In the case of the former, the condition occurs more commonly in early middle age and in females, and the patients frequently have chronic valvular disease, much more often mitral, especially stenosis, than aortic, in which it is comparatively rare. In the second group of cases, it is more common in the elderly and in males. The next most frequent cause is thyrotoxic conditions (see pp. 486, 491, and 996), and the next is syphilis. Auricular fibrillation has been also found occasionally in acute infective diseases, such as pneumonia, infective endocarditis, and diphtheria, in coronary occlusion, and in the terminal stages of various exhausting diseases. Occasionally there is no apparent cause.

The onset of the disorder can now and again be traced to bodily effort,

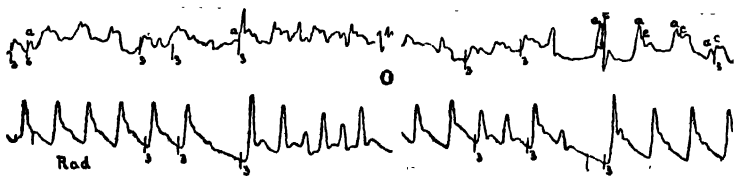


FIG. 29.—Simultaneous tracings of the jugular and radial pulses, showing the commencement and termination of a short attack of paroxysmal auricular fibrillation. The first six beats and the last three in the sphygmogram are regular and due to a normal contraction of the heart. The beats between occur during a period of auricular fibrillation. At *O* a period of 15 seconds has been cut out. (Mackenzie.)

especially in the middle-aged or elderly, perhaps to trauma, and rarely to the administration of fatal doses of digitalis.

Pathology.—Auricular fibrillation is, in the majority of cases, indicative of some myocardial change, usually fibrosis.

It was observed by Mackenzie that, in cases of complete irregularity of the pulse, the pre-existing auricular wave in the phlebogram had disappeared. From this he inferred first, that the auricles were paralysed and, later, instead of this, that auriculo-ventricular nodal rhythm was present. Some time afterwards, Rothberger and Winterberg, and Lewis attributed the absence of auricular contractions to auricular fibrillation, a condition which had been produced experimentally in animals.

The exact mechanism of auricular fibrillation and auricular flutter has been further elucidated by Lewis and his co-workers, and it is now generally but not universally accepted that a *circus movement* is responsible. Mines and Garrey had demonstrated that in a circular ring of muscle, under certain conditions, a wave of contraction can be made to circulate continuously. This is only possible if the crest of the circulating wave encounters muscle which is responsive, *i.e.* which has recovered from the refractory state that immediately follows contraction. Thus, the refractory period at a given point

on the circuit must be less than the time taken by the wave to make a full circuit. If we consider a wave of contraction circulating in such a simple muscular ring, at any given moment, the crest of the wave has in its wake a zone of muscle which is refractory, and between the tail of the refractory zone and the crest of the wave is a zone of muscle which is responsive, known as the gap. The length of this gap is influenced by three factors, namely: (1) The length of the circular path; (2) the rate at which the wave circulates; and (3) the refractory period of the muscle. Lengthening of the path, slowing of the conduction rate, and shortening of the refractory period tend to increase the gap; while shortening of the path, increase of the conduction rate, and lengthening of the refractory period tend to decrease or abolish the gap.

It has been shown that in both auricular fibrillation and auricular flutter a circus movement is present in the auricles, which no longer respond to the regular stimuli from the sino-auricular node. In auricular flutter the pathway of the main circulating wave probably encircles the orifices of the two venæ cavæ. The wave circulates at a rate of 180 to 360 per minute, and constantly traverses the same path. In auricular fibrillation the circulating wave is faster, being between 300 and 600 per minute, and the path is shorter,

FIG. 30.—Tracing of the radial pulse, from a case of auricular fibrillation, showing complete irregularity of the pulse.

more sinuous and variable. The gap is very short, so that the crest and the wake of the circulating wave are almost fused, and the crest is advancing through irregular channels. In both flutter and fibrillation the auricular muscle is responding to stimuli from a central circulating wave, from which offshoots or subsidiary waves pass in all directions towards the periphery. Intermediate between pure flutter and fibrillation is a condition termed impure flutter, in which the rate of the circulating wave is 350 to 400, and the path traversed is not absolutely constant, as in the case of pure flutter.

Prolongation of the refractory period in auricular fibrillation and in auricular flutter will help to close the gap between the crest of the oncoming wave and its receding wake, since this gap is necessary for the maintenance of the circulating wave, whether in flutter or fibrillation.

Symptoms.—Patients with auricular fibrillation frequently complain of a sensation of fluttering in the præcordium, or of irregular action of the heart, or of both, possibly only on exertion. Apart from this, occasionally there is an absence of subjective symptoms. In the great majority of cases, however, ever, symptoms of heart failure, generally involving both ventricles, are present. It would appear, however, that paroxysmal dyspnœa and acute pulmonary œdema rarely if ever occur. The subjects of auricular fibrillation also rarely suffer from typical attacks of angina pectoris. Embolism is occasionally met with.

The degree of failure may vary from slight to even extreme. As a rule, the onset of symptoms is gradual, but may ensue rapidly, and the patient may become very ill within a few weeks, or days, or, rarely, even a few hours. Both depend upon the ventricular rate, the cause and any associated morbid condition, and the integrity of the myocardium, perhaps chiefly the first.

There is a wide variation in the ventricular rate, according as the pathway for impulses to the ventricle is free or interfered with, this ranging from 140 or even 180 to 40, or, very rarely, even 30 per minute in complete auri-

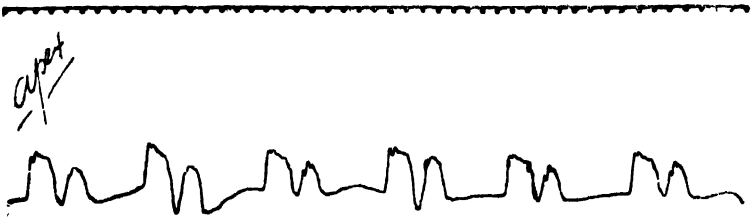


Fig. 31.—Tracing of the apex-beat, from a case of auricular fibrillation, fully under the influence of digitalis, showing coupled beats.

culo-ventricular heart-block. In the great majority of cases the rate is increased, being usually between 90 and 140. The rate of the radial pulse does not necessarily represent the ventricular rate, for many beats of the heart may not be transmitted to the wrist, especially, when the ventricle is beating rapidly; the ventricular rate, therefore, should be counted at the apex, by auscultation. Apart from the very rare cases of complete auriculo-ventricular block, in which case the pulse is regular, the pulse is completely irregular. In a sphygmogram (Fig. 30) it will be found that two



Fig. 32.—Simultaneous tracings of the jugular and radial pulses, from a case of auricular fibrillation, showing multiple undulations (marked Fibl.) in the phlebogram, caused by the fibrillating auricle.

beats of the same length or amplitude rarely follow each other. There is often no relation also between the length of a pause and the amplitude of the beat which follows it—*i.e.* a short pause may be followed by a strong beat, and a long pause by a weak beat. There may be superadded ventricular extra-systoles. Their presence is usually observed during the administration of one of the digitalis group of drugs (see page 868). When the ventricular rate is slow, or very rapid, the irregularity may be only slight, and we may have to adopt careful measurements of the sphygmogram to detect it. In cases of mitral stenosis in which a presystolic bruit, *due to auricular systole,*

is present, this disappears with the onset of auricular fibrillation; while if a diastolic bruit be present, it persists.

The jugular veins may be so distended that there is no visible pulsation in them. When pulsation is visible, however, it is of the positive type, only one wave being visible, this occurring during ventricular systole. In a tracing of the jugular vein, apart from the very rare cases of complete auriculo-ventricular block, when the rhythm is regular, the rhythm is completely irregular. There is an absence of the *a* wave. There may be the ventricular form of venous pulse. In cases in which there is infrequent cardiac action, multiple undulations, caused by the fibrillating auricle, may be present during diastole. There is also an absence of the normal *a* wave in a cardiogram and in a tracing of the liver pulse.

Diagnosis.—Auricular fibrillation can be diagnosed with certainty on electro-cardiographic examination; or when complete irregularity of the arterial pulse, the ventricular form of venous pulse, and multiple undulations in the jugular pulse are present, together with an absence of all signs of an auricular wave in a tracing of the apex-beat and of the liver pulse; or when there is complete irregularity of the pulse in conjunction with the ventricular form of venous pulse; the first being the most reliable. We may be reasonably certain from the mere presence of complete irregularity of the pulse. It is possible to determine complete irregularity of the pulse in a large proportion of cases by palpation and auscultation alone. When, however, the ventricular rate is slow, or very rapid, it may be necessary to adopt careful measurements of a sphygmogram to detect it.

Auricular fibrillation should be distinguished from sinus arrhythmia (p. 885), extra-systole (p. 889), and auricular flutter (p. 902).

Prognosis.—Auricular fibrillation is in the majority of cases indicative of some myocardial change. Furthermore, the condition usually has a considerable effect on the cardiac efficiency. Put briefly, the prognosis depends upon the ventricular rate, the cause, the nature and degree of any associated morbid condition, the integrity of the myocardium, and the response to the administration of the digitalis group of drugs, or, less frequently, to quinidine. If there is an absence of tachycardia, or the tachycardia is only of moderate grade or of more severe grade, but well controlled by digitalis, and if the integrity of the myocardium be relatively good, the patient may live even for many years. In the great majority of cases this is not the case. A persistent ventricular rate of 120 or over is usually of serious omen. Occasionally, with the inception of auricular fibrillation, grave cardiac failure may supervene with surprising rapidity, and death may follow within a few weeks, or even within a briefer period.

As has been pointed out, paroxysmal auricular fibrillation has a tendency to become more frequent, and ultimately the condition usually becomes permanent.

Auricular fibrillation associated with thyrotoxicosis is dealt with on p. 997.

Treatment.—The ætiology should be reviewed, with the object of treating any associated condition, and the various therapeutic measures applicable to any form of cardiac disorder should be considered in detail.

Apart from these, treatment of persistent auricular fibrillation resolves itself into the consideration of the employment of the digitalis group of

drugs, or of quinidine. The ultimate object of the employment of either is the same, namely, to regain the degree of cardiac efficiency which existed prior to the onset of the abnormal rhythm. This in the main depends upon the restoration of the pre-existing ventricular rate. The functions of digitalis and of quinidine differ. The primary object of administering digitalis in auricular fibrillation accompanied by a rapid ventricular rate is to reduce and, later, control the ventricular rate within normal limits; the drug has no effect upon the auricular fibrillation itself. The primary object of administering quinidine, on the other hand, is to arrest the auricular fibrillation; in other words, to restore the normal rhythm, and any beneficial effect of the drug is due to this.

In considering which drug should be employed, as well as the methods of their administration, the reader is referred to pages 865–868 and 870–872. With regard to the former, the following may be added: The degree of response to digitalis is an important consideration, a manifestation on the part of the patient of a particular intolerance to this drug being a point in favour of quinidine. The absence of indications of cardiac failure does not necessarily mean that this drug should not be tried, as cardiac failure may supervene later on. Other considerations are the risk—amounting to a possible fatal issue—attending the administration of the drug, the degree of probability of restoration of the normal rhythm, the probable degree of success resulting from this, and the degree of probability of relapse. In a small proportion of cases after the restoration of the normal rhythm, the general health of the patient is even worse. Cases for the administration of the drug should be selected with great care. We are justified in taking a comparatively small risk, while in doubtful cases we should clearly put the pros and cons of this method of treatment to the patient or his friends. Lastly, it should be remembered that if quinidine fails, digitalis medication is still open to us. In conclusion, the digitalis group of drugs is indicated in the great majority of cases of auricular fibrillation, quinidine being reserved for special cases.

The treatment of paroxysmal auricular fibrillation is that of paroxysmal tachycardia.

The treatment of auricular fibrillation associated with thyrotoxicosis is discussed on p. 998.

AURICULAR FLUTTER

Auricular flutter is a specific clinical condition, comparatively rare, in which a marked acceleration of the rhythmic co-ordinate contraction of the auricles occurs. It was first demonstrated clinically by Ritchie in 1905.

The rate of the contractions of the auricle may vary from 180 to 360, the usual rate being about 300, per minute. The ventricular rate varies considerably in different cases, this depending upon the auricular rate and the ability of the auriculo-ventricular junctional tissues to receive and transmit the impulse from the auricle. Very rarely the ventricle responds to each auricular contraction, resulting in 1 : 1 rhythm. In the vast majority of cases, however, there is partial heart-block or, very rarely, complete heart-block. In the former case there is usually a constant and uniform ratio between the auricular and ventricular rates, this varying from 2 : 1 to 5 : 1, the former being the

most frequent. In some cases, on the other hand, the response of the ventricle to auricular contraction is at irregular intervals, giving rise to irregularity of the pulse rhythm, which may be very irregular.

The commencement of auricular flutter is sudden. The condition may be paroxysmal or permanent. In the case of the former the paroxysm may last only for a few beats, or up to a few days, a few weeks, or, rarely, even months. The termination of a paroxysm is sudden. The patient may never have another attack; or attacks may recur at varying intervals, frequent or long. When once a patient has suffered from an attack of auricular flutter, there is a tendency to its recurrence from time to time. Paroxysmal auricular flutter may be succeeded by the normal rhythm, or sometimes by auricular fibrillation, the latter occurring during the administration of digitalis or apart from the use of the drug. There may be alternation of auricular flutter, the normal rhythm and auricular fibrillation, the changes taking place suddenly, and occurring from day to day or even for a few moments. Either auricular flutter or auricular fibrillation may ultimately become permanently established.

In persistent auricular flutter, the ventricular rate may diminish as the result of the occurrence of partial heart-block, and this may take place during the administration of digitalis or apart from the use of this drug.

Ætiology.—The ætiology of auricular flutter is similar to that of auricular fibrillation (see p. 896). It would appear however that, taking cases as a whole, it occurs at a somewhat later age; males are more often affected; rheumatic heart disease is less frequent and chronic myocardial disease more common; and thyrotoxicosis is a somewhat less common cause.

Pathology.—See pp. 896, 897.

Symptoms.—The symptoms of auricular flutter depend upon the ventricular rate, the duration of the condition, and the degree of integrity of the myocardium.

When there is marked tachycardia, the symptoms are similar to those of paroxysmal tachycardia (see pp. 892, 893). In the rare cases of 1 : 1 rhythm, the onset may be ushered in by giddiness, faintness, or even loss of consciousness. In those in which there is a material degree of, but not marked, tachycardia, usually the patient is conscious of the action of the heart; and after some time, in the great majority of cases, indications of cardiac failure supervene, or, if these were present before the onset, they increase in severity. In those in which there is an absence of a material degree of tachycardia, very frequently the patient is unconscious of the action of the heart; and there may be only slight, if any limitation of the field of cardiac response.

The rate and rhythm of the arterial pulse vary in different cases and, it may be, at different times in the same case. If the ventricle responds to each auricular contraction, the ventricular rate is exceedingly rapid, and graphic methods are usually necessary to determine it. In the vast majority of cases, however, partial heart-block is present, and as 2 : 1 rhythm is the most usual, a ventricular rate of 120 to 150 is frequently found. In other cases of partial heart-block, the ventricular rate may not be much increased, and, indeed, there may be even bradycardia, as in 4 : 1, or more partial heart-block, as well as in complete heart-block. When there is a constant and uniform ratio between the auricular and ventricular rates, the rhythm of the arterial pulse

is regular; in these cases, however, if the ventricular rate be above 150, pulsus alternans may be present. When, as is not infrequently the case, the response of the ventricle to auricular contraction is at irregular intervals, there is irregularity of the pulse rhythm; indeed, in some of these cases the sphygmogram may somewhat resemble that from a case of auricular fibrillation, detailed measurements being necessary for the purpose of differential diagnosis. An irregular pulse often becomes regular and more rapid as the result of exertion, due to the occurrence of 2 : 1 rhythm. On inspection of the neck, the jugular veins may be distended, and no pulsation visible; or very rapid movements may be evident.

A tracing of the jugular pulse differs in outline according to whether the ventricle responds to each auricular contraction, or to the degree of heart-block which may be present. In the former case there is usually a single wave. When the ventricle responds alternately to the auricle, there are two *a* waves to each ventricular beat, and these usually fall within the limits of ventricular systole. In 3 : 1 rhythm the character of the jugular pulse may be seemingly that of normal cardiac action, and it is particularly in these cases that an electro-cardiographic examination is required to establish the diagnosis. As has been already noted, complete heart-block is rarely found.

Diagnosis.—The diagnosis of the condition rests on the detection of the extremely rapid contractions of the auricle, and not infrequently this is impossible without the employment of the electro-cardiograph.

We should consider the possibility of auricular flutter (or of paroxysmal tachycardia) whenever an individual complains of attacks of palpitation, or is conscious of a marked increase in the cardiac rate, in either case occurring suddenly and without apparent cause, or suffers from indications of cardiac failure coming on rapidly, if the rhythm of the pulse be regular.

Auricular flutter with continuous 2 : 1 auriculo-ventricular block should be distinguished from sinus tachycardia and paroxysmal tachycardia. In the case of the first, the same considerations apply as in paroxysmal tachycardia (see p. 893). In the differential diagnosis between flutter and paroxysmal tachycardia, the following should be noted: If the cardiac rate is above 160, the condition is more likely to be paroxysmal tachycardia. In flutter, pressure on the carotid sinus often causes transient slowing of the cardiac rate, or even long pauses, especially if digitalis is being administered; strenuous physical exertion may convert the 2 : 1 into 1 : 1 rhythm, with resultant precise doubling of the rate; the condition is usually of longer duration; and the response to the digitalis group of drugs is notable.

If the rhythm be irregular, it is necessary to consider whether the case may not be one of auricular fibrillation. In this connection, *if a sphygmogram from a case of auricular flutter be carefully studied, it will be found that even though the ventricular rhythm is very irregular the pulse-beats measure out into groups of equal length, whereas this is never the case in auricular fibrillation.* The polygraph and electro-cardiograph are of notable assistance in the differential diagnosis. The diagnosis of auricular fibrillation with a markedly exaggerated ventricular rate in which the irregularity is only slight from auricular flutter should also be considered. Irregularity due to the presence of extra-systoles should also be excluded. Cases of auricular flutter in which the auriculo-ventricular ratio is constantly 3 : 1 to 4 : 1, so that the ventricular rate is not much, if any, increased, and in which the ventricular rhythm is

regular, are easily missed. The use of the electro-cardiograph is necessary in such cases.

Prognosis. — **The prognosis of auricular flutter resembles that of paroxysmal tachycardia. It is, however, more responsive to treatment.**

Treatment.—The ætiology should be reviewed, with the object of treating any associated condition, and the various therapeutic measures applicable for any form of cardiac disorder should be considered.

Apart from this, the treatment of persistent auricular flutter consists of the administration of digitalis, or of quinidine. The former should be tried first (see pp. 865, 868). I generally advise digitalis medication until almost full digitalization has been obtained. If the disorder persists, the dosage should be gradually diminished to a moderate or even small one, and this continued for a time, in the hope that the flutter may cease. If unsuccessful, this method may be repeated after a short interval. If the flutter still continues, the question of quinidine, with the object of terminating the condition, should be considered. This subject is dealt with on pp. 870–872. If,

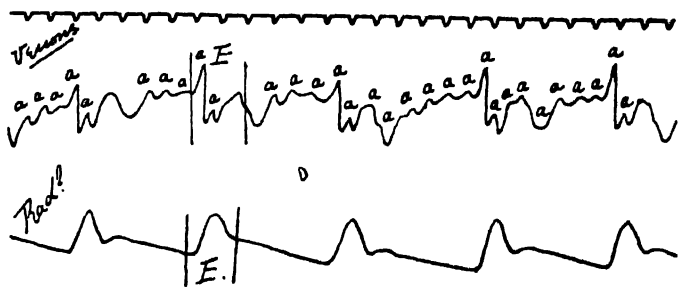


Fig. 33.—Simultaneous tracings of the jugular and radial pulses from a patient with auricular flutter fully under the influence of digitalis. The auricular rate is 382, and the ventricular rate is 50, per minute.

on the other hand, almost full digitalization induces auricular fibrillation, digitalis may be discontinued for some days, in the hope of a return to the normal rhythm. If this does not occur, treatment resolves itself into the consideration of the employment of digitalis, or of quinidine.

The treatment for the prevention of the recurrence of the attacks is the same as in the case of paroxysmal tachycardia.

The treatment of auricular flutter associated with thyrotoxicosis is discussed on p. 998.

VENTRICULAR FIBRILLATION

In ventricular fibrillation co-ordinate contraction of the ventricles is replaced by inco-ordinate contraction. It is a frequent cause of sudden death.

The condition may be induced experimentally by electric and other kinds of stimuli, by ligature of a coronary artery or one of its main branches, and by massive doses of digitalis, strophanthus, quinidine, or of adrenaline.

It is very rarely met with clinically, but may occur in coronary occlusion and angina pectoris; as the result of poisonous doses of the drugs mentioned; following auricular fibrillation, multiple extra-systoles, or ventricular paroxysmal tachycardia, and in complete auriculo-ventricular block; in certain acute infective diseases, particularly diphtheria; and in chloroform anæsthesia.

In ventricular fibrillation there is sudden loss of consciousness, and death almost invariably takes place.

It is believed that the tendency to the condition is lessened by the administration of quinidine, in moderate dosage; and that if the condition does occur, massage of the heart, if practicable, is sometimes effective.

HEART-BLOCK

By heart-block is meant defective conductivity or conduction of the heart. It may be divided into: (1) Sino-auricular block; (2) auriculo-ventricular block; (3) bundle-branch block; and (4) arborization or intra-ventricular block.

It should be pointed out that some writers use the term intraventricular block to include bundle-branch block and arborization block.

Sino-auricular Block

Sino-auricular block is a rare condition, in which the whole heart, *i.e.* both the auricle and the ventricle, fails to beat, due to an impulse in the sino-auricular node not being generated, or possibly the auricle failing to respond to such.

The condition may be met with in digitalis poisoning, and during the administration of quinidine. It is chiefly of vagal origin, and is abolished by atropine and exercise. It is occasionally associated with auriculo-ventricular block.

The interruption may occur occasionally or more frequently; or regularly after each normal beat; or, rarely, involving a succession of two, three, or more cycles. The first gives rise to an intermission of the pulse or a 'dropped' beat. The length of the long pause is usually rather less than the duration of two normal cardiac cycles, because a few cycles preceding it are rather quicker and a few after it are rather slower, resembling 'dropped beats' in the second degree of auriculo-ventricular block (see p. 903). The second results in halving of the cardiac rate. The third gives rise to a very long pause.

Rarely the condition gives rise to symptoms of cerebral anæmia, such as giddiness, faintness, or even actual syncope. When two, three, or more cycles are implicated, Adams-Stokes syndrome may occur.

In a polygram and an electro-cardiogram there is an absence of evidence of auricular and ventricular contraction during the long pause.

Sino-auricular block should be distinguished from sinus arrhythmia, extra-systoles, and partial auriculo-ventricular block.

Auriculo-ventricular Block

In auriculo-ventricular block, there is defective conductivity or conduction of the auriculo-ventricular node, or bundle above its division, or both.

There are three grades of auriculo-ventricular block: (1) In the first, the transmission of the wave of excitation from the auricle to the ventricle is merely delayed, resulting in a prolongation of the interval which separates the commencement of the contraction of the auricle and that of the ventricle, each impulse from the auricle reaching the ventricle, which duly responds. (2) The excitation wave from the auricle does not always reach the ventricle. (3) No impulses reach the ventricle from the auricle, so that the auricles and ventricles beat independently of each other, the former in response to impulses arising in the sino-auricular node at an approximate rate of 72 per minute; and the latter as the result of impulses arising in the auriculo-ventricular junctional tissues, generally in the auriculo-ventricular bundle between the site of the lesion and the division of the bundle into two branches, at a rate of about 30 per minute, which is the normal ventricular rate.

According to some writers, the first and second grades together constitute partial or incomplete heart-block, the first being called depressed conductivity; while other writers limit the former term to the second grade. The third grade is called complete auriculo-ventricular block.

First Degree of Heart-Block.—This grade of heart-block may give rise to irregularity of the pulse on account of variations in the length of the *As–Vs* interval. Some writers believe that contraction of the auricle produces a faint muffled sound, and that consequently when there is a slight delay between the auricular and ventricular contractions there may be a reduplication of the first sound, while if the delay be considerable, so that the contraction of the auricles falls in early diastole, there may be a reduplication of the second sound. In cases of mitral stenosis unaccompanied by auricular fibrillation a slight interval between the systolic murmur and the next first sound, is sometimes to be noted. In a polygram and an electro-cardiogram (leads I and III of Fig. 78) there is merely an increase in the *As–Vs* interval, this exceeding $\frac{1}{5}$th of a second.

Second Degree of Heart-Block.—In this condition what are called 'dropped beats' occur. These may be only occasional, or they may be more frequent. Or each third or fourth impulse may fail to reach the ventricle; in the former case the ventricular beats are grouped in twos, and in the latter they are grouped in threes, and in this way a bigeminal or trigeminal pulse results. Or every other impulse may fail to reach the ventricle, giving rise to halving of the ventricular rate, the condition being spoken of as 2 : 1 rhythm (lead II of Fig. 78); or only each third or fourth auricular impulse may be transmitted to the ventricle, resulting in 3 : 1 or 4 : 1 heart-block. In some cases certain ratios alternate.

It might naturally be supposed that the length of the prolonged pause during a dropped beat would be equal to two regular pulse-beats; such, however, is usually not the case for the following reason. There are variations in the *As–Vs* interval in association with dropped beats, there being a progressive increase of the *As–Vs* interval preceding and a progressive shortening of the interval following each dropped beat; the former is due to the increasing difficulty the impulses from the auricle have in reaching

the ventricle, and the latter to the rest which the ventricle has experienced during the pause. The result of the progressive increase of the *As–Vs* interval prior to, and of the progressive shortening of the *As* to *Vs* interval after, the dropped beat is that the long pause becomes shortened. When, however, there are no variations in the *As–Vs* interval in association with a dropped beat, the length of the prolonged pause is equal to two regular pulse-beats.

2 : 1 heart-block gives rise to infrequency of the pulse-rate, the rhythm being regular. This grade of heart-block is sometimes continuous, but usually the ventricle responds from time to time to successive stimuli received from the auricle, the pulse-rate, therefore, being usually above 36 per minute.

On analysis of a polygraphic tracing it will be found that the *a* wave is present at uniform intervals, and is of more frequent occurrence than the *c* or *v* waves—it may be even twice, three, or more times as frequent, according to the degree of block; but, unlike complete heart-block, each *c* wave is preceded by an *a* wave.

Complete Heart-Block.—Here the pulse-rate is slow, usually not more than 36, and not infrequently between 20 and 30 per minute, though some cases have been recorded in which the rate has been up to 60 or more beats per minute; it is little influenced by physical exertion, emotion, pyrexia, or

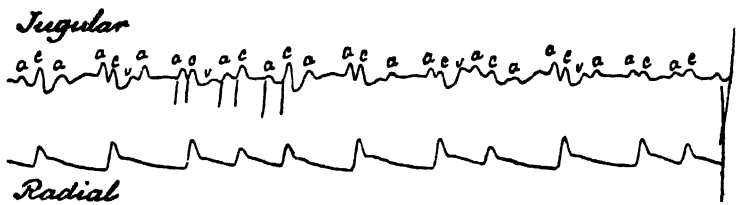


Fig. 34.—Simultaneous tracings of the jugular and radial pulses, showing partial heart-block. Note the progressive increase in the *a–c* interval of three successive rhythmic beats.

amyl nitrite, or, as a rule, by atropine. The beats are usually full and strong, and, as a rule, the rhythm is regular, the pulse being irregular, however, when extra-systoles are present. In a tracing of the radial artery, small waves occurring at regular intervals on the descending limb of the pulse-beat, probably due to auricular systole, may sometimes be noted. The systolic blood pressure is generally high, and the diastolic may be considerably diminished. There is usually evidence of hypertrophy of the left ventricle. On inspection of the neck, regular pulsations in the jugular veins, at considerably more frequent intervals than, and having a constantly varying time-relation to, those of the radial and carotid arteries and the apex-beat, due to auricular systole, may sometimes be noted; and in some instances a large pulsation in the jugular vein is seen from time to time when the auricular and ventricular contractions happen to coincide. On auscultation a first and second sound are found accompanying each contraction of the ventricle, and, in the opinion of most, faint muffled sounds may occasionally be heard over the præcordium during the long pauses, due to the contractions of the auricle. Some writers, too, have noted an accentuation of the first sound, synchronous with the

large pulsation in the jugular vein, when the auricular and ventricular contractions coincide.

If a polygraphic tracing be analysed, the disassociation of the auricular and ventricular rhythms is manifest. The *a* waves occur at regular intervals, and are more numerous than the *c* or *v* waves, and the time-relation of the *a* and *c* waves is a constantly varying one—the *a* waves at one time preceding, at another following, and at other times again coinciding with the *c* waves. When an *a* wave falls during the limits of ventricular systole its amplitude is increased. Extra-systoles may be present.

Ætiology and Pathology.—Auriculo-ventricular block is more frequent in males than in females. Taking cases as a whole, the most common causes are: (1) During the administration of full doses of digitalis; (2) fibrosis of the myocardium (see p. 949), more frequent in late middle and elderly life, and in males; and (3) in acute infective diseases, such as acute rheumatism, diphtheria, influenza, and pneumonia. In the case of the first and third, the lesser grades are more frequent; while in the second, the more severe degrees. In the first, the condition is temporary; in the third, usually so; and in the

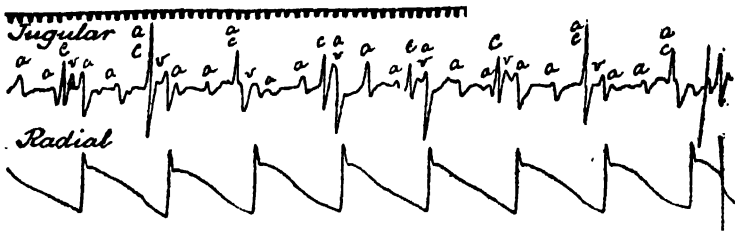


FIG. 35.—Simultaneous tracings of the jugular and radial pulses, from a woman aged 25, with severe heart failure, showing complete auriculo-ventricular block. The auricular rate is 88, and the ventricular rate 30, per minute.

second, it is generally persistent. Rarely complete heart-block is congenital, being associated with a defect in the auriculo-ventricular septum.

The most common pathological findings in heart-block are fibrosis of the myocardium and atheroma of the coronary arteries. Usually involvement of the auriculo-ventricular node or bundle is part of a widespread myocardial fibrosis, but occasionally the special artery to the bundle, a branch of the right coronary artery, is narrowed or occluded and the lesion is more limited. Syphilitic lesions are not common, and even in syphilitic patients atheroma of the coronary arteries may be the cause of heart-block. Acute inflammatory or degenerative changes are found when heart-block occurs during an acute infective disease.

Cases have been recorded in which no lesion could be demonstrated in the auriculo-ventricular node or bundle, and excessive vagal stimulation has been held responsible.

Symptoms.—There may be symptoms due to the associated cardiac lesion, whether myocardial or valvular, which are almost invariably present.

With regard to the block itself, in the case of 'dropped beats' the patient may be conscious of the long pause and of a thud following it, as in the case of extra-systoles. In the severe grades of partial and in complete block, he may complain of the forcible action of the heart. There may be

some degree, usually mild, of cardiac insufficiency, such as a sense of weakness, and early fatigue and shortness of breath on exertion, but the question arises whether this is due partly, or even wholly, to the associated morbid affection. Not infrequently Adams-Stokes syndrome occurs.

ADAMS-STOKES SYNDROME.—This, as originally described, is characterized by attacks of loss of consciousness and convulsions, both tonic and clonic, associated with marked infrequency of the ventricular rate. But the term may now be applied to various grades—from merely transient giddiness and faintness to the most grave condition of loss of consciousness due to cerebral anæmia the result of ventricular failure, which is not necessarily associated with marked infrequency of the ventricular rate, for very rarely it is due to sino-auricular block, ventricular fibrillation, or paroxysmal tachycardia.

The syndrome may be met with in one of the following conditions: (1) Partial heart-block, in which there occurs either an intermittent period of complete heart-block, resulting in a temporary standstill of the ventricles; or, rarely, merely a temporary increase in the grade of the partial heart-block, resulting in a temporary increase in the degree of the bradycardia. (2) Complete heart-block, in which the condition has become permanently established, especially if the ventricular rate is below 30 per minute. In these cases pauses of unusual length, due to temporary standstill of the ventricles, the result of diminished irritability of the ventricles, may occur. (3) Suddenly developed transient complete auriculo-ventricular block. Several cases of this kind have been reported. The conduction of the stimulus for contraction along the auriculo-ventricular junctional tissues is normal except that there is a liability to transient interruptions. (4) Very rarely in sino-auricular block, ventricular fibrillation, and paroxysmal tachycardia, especially the ventricular variety. Taking cases as a whole, Adams-Stokes syndrome is most commonly met with in patients with a severe grade of partial heart-block in whom complete block is developing. When complete heart-block has become permanently established, the ventricles apparently tend to become accustomed to the condition, and the pauses of unusual length referred to are not so likely to take place.

The severity of the symptoms depends principally upon the duration of the cerebral anæmia. It is generally believed that if this lasts two or three seconds, there is merely giddiness and faintness; if double that time, there is likely to be loss of consciousness; and if over about twelve seconds, there will probably be convulsions. There may be repeated seizures. There may or may not be a warning. In grave cases there is marked pallor or cyanosis, widely dilated pupils, and deep or even sterterous breathing. Usually the convulsions are confined to the face and upper limbs, the tongue is not bitten, and urine and fæces are not passed involuntarily. Within a few seconds of the cessation of the cerebral anæmia the colour and consciousness return.

Diagnosis.—The various grades of auriculo-ventricular heart-block are readily determined by means of the polygraph or electro-cardiograph, since these instruments afford separate records of the movements of both the upper and lower chambers of the heart. The first grade can only be recognised by means of either of these instruments, excepting that in cases of mitral stenosis unaccompanied by auricular fibrillation a slight interval between the auriculo-systolic murmur and the next first sound is sometimes to be noted. Fortunately they are not necessary in a considerable proportion of the other

cases. Thus, a diagnosis between occasional dropped beats, pulsus bigeminus, pulsus trigeminus, and infrequency, including halving, of the pulse rate—due on the one hand to extra-systoles and on the other to heart-block can almost invariably be made apart from them (see p. 890). It should be borne in mind that sinus irregularity and sino-auricular block may closely simulate occasional dropped beats due to partial heart-block. Lastly, auriculo-ventricular block should be distinguished from sinus bradycardia and auriculo-ventricular rhythm.

It is sometimes difficult to distinguish between partial and complete heart-block without the aid of the polygraph or electro-cardiograph. Most cases with a ventricular rate of 36 or under, however, are cases of complete heart-block. Moreover, the presence of more rapid pulsations in the jugular veins and of small waves occurring at regular intervals on the descending limb of a sphygmogram, and auscultatory phenomena afford help in differential diagnosis.

Adams-Stokes syndrome is easily recognised from the features described. It should be distinguished from the other causes of loss of consciousness and convulsions.

Prognosis.—Much depends upon the cause and any associated morbid affection. The occurrence of partial heart-block during the course of an acute infective disease is a sign, and may be the only sign, of myocardial involvement. Persistent heart-block of mild degree also is indicative of myocardial damage. With regard to persistent heart-block of severe degree, there are two questions of importance in considering the prognosis, namely—(1) Whether there is involvement of the heart muscle as a whole, and if so it is progressive; and (2) is the patient subject to syncopal attacks, and, if so, what is their severity and frequency? In the absence of both, and when also the patient does not suffer from syncopal attacks, the span of life may be prolonged for many years, and he may be able to live a fairly active life without inconvenience. But when the opposite is the case, especially if the syncopal attacks are severe and frequent, life is always in danger; and, apart from the risk of a fatal termination during an attack, death may occur with the usual clinical picture of cardiac failure. A number of syphilitic cases have been recorded in which energetic anti-syphilitic treatment appears to have been rewarded with recovery.

Treatment.—The ætiology and any associated morbid condition should be thoroughly reviewed.

When heart-block occurs during the course of an acute infective disease, rest in bed is indicated. When there is reason to suspect that syphilis is the cause, appropriate and energetic treatment should be employed. Persistent heart-block of mild degree requires no treatment in itself. In persistent heart-block of severe grade it is of particular importance that the patient should live within the limits of his strength. Digitalis is contra-indicated in partial heart-block. It may be cautiously tried in complete block in which there is congestive failure.

Adams-Stokes Syndrome.—The patient should be warned to avoid anything known to predispose to the attacks, and, as far as possible, should be protected from the risks of falling.

For the prevention of the occurrence of the attacks, adrenaline and ephedrine are the most successful remedies. The first should be admin-

istered either subcutaneously or intramuscularly, from 5 to 10 minims of a 1 : 1000 solution thrice daily, failing which, every few hours. Ephedrine differs from adrenaline in that its effect persists for several hours, and, moreover, it has the advantage of being effective when administered orally. I have found barium chloride, administered by the mouth, apparently undoubtedly effective in three cases, one of which was extremely severe. The drug increases the irritability of the heart muscle. It may be given in pill form, at first in doses of $\frac{1}{2}$ gr. twice daily and, if necessary, cautiously increased to 1 gr. thrice daily but stopping short of toxic symptoms. If unsuccessful alone, it may be tried in combination with adrenaline. Thyroid appears to be sometimes of value and may even be completely successful. Potassium iodide, by its depressing effect on the ventricular muscle, may even aggravate the condition when the cause is other than syphilis. Atropine is indicated in cases of partial heart-block in which there is vagal over-activity.

If an attack occurs, adrenaline is the only potent therapeutic measure at our disposal, but is contra-indicated in the very rare cases of ventricular fibrillation. It is necessary to point out that when—as in the vast majority of cases—the attack is due to a temporary standstill of the ventricles, with consequent temporary cessation of the circulation, intracardiac injection is necessary, because the beneficial effect of the drug is due to its action in stimulating the sympathetic nerve endings in the heart muscle. The dose should be 0·5 to 1 c.c. of 1 : 1000 solution. In the rare cases in which the attacks are due to merely a temporary increase in the grade of an existing partial heart-block, the drug may be effective even if given subcutaneously or intramuscularly.

Bundle-Branch Block

Bundle-branch block is relatively uncommon. If complete, there is a complete interruption of the wave of excitation along either of the two main branches of the auriculo-ventricular bundle. The excitation wave is transmitted to the two ventricles along the branch which is unaffected. There is slight asynchronism of the contraction of the two chambers. The condition may be persistent or temporary. According to the new nomenclature, the left branch is much more frequently affected.

Auriculo-ventricular block, and less frequently auricular fibrillation (Fig. 81), may co-exist.

The ætiology and pathology of bundle-branch block are the same as those of complete auriculo-ventricular block, excepting that perhaps the former condition is more common in the elderly and in males; is more frequently associated with hypertension, chronic myocardial disease, and atheroma of the coronary arteries; occasionally is associated with coronary occlusion; and is also more often organic.

The subjective symptoms are not distinctive. There may be a visible and palpable bifid apex-beat, and reduplication of the first sound at the cardiac apex, or between this point and the left border of the sternum, so that three sounds are audible. In the opinion of most, the third sound is presystolic in time, but in that of some, it is systolic. Reduplication is still present when there is complete auriculo-ventricular block, or auricular fibrillation. There is sometimes pulsus alternans.

Bundle-branch block should be thought of whenever the foregoing physical signs are present. It is to be noted, however, that these may be met with in other conditions. A diagnosis may be made with certainty by means of the electro-cardiograph.

In persistent left bundle-branch block, apart from relatively few exceptions, the prognosis is very serious, a fatal termination occurring within at the most two years in the majority of cases. In right bundle-branch block, the outlook is very much less unfavourable. In the case of both, much depends upon the degree of cardiac failure.

With regard to incomplete or partial bundle-branch block, see p. 1021.

Functional Bundle-Branch Block

This is a rare condition in which there is increased duration of the Q. R, S group of deflections together with a diminished P–R interval. It is met with in young healthy individuals who tend to have paroxysmal tachycardia. It is considered highly probable that the abnormal electro-cardiogram is really not due to functional bundle-branch block, and it is thought that there is a special path of conduction from the sino-auricular node or its neighbourhood to either of the ventricles, and that in the same individual sometimes the wave of excitation travels along this channel and at other times along the normal one. So far, however, there is an absence of post-mortem findings. The electro-cardiographic features may sometimes suddenly cease, either spontaneously, or with physical exertion or the administration of atropine.

Arborization or Intraventricular Block

In this, there is diminished conductivity of the subendothelial arborizations of the Purkinje system. The ætiology and pathology are similar to those of bundle-branch block. In the vast majority of cases the condition is associated with widespread chronic myocardial disease. It is believed by some that the affection may be recognised by means of the electro-cardiograph (see p. 1021).

The prognosis is even more serious than that of bundle-branch block, being almost always grave.

PULSUS ALTERNANS

Definition.—By pulsus alternans is meant a condition of the pulse in which a larger beat and a smaller beat alternate. Sometimes the smaller beats are slightly delayed, but they are never premature.

Ætiology.—The condition is usually transient, but may persist for some minutes, hours, days, or weeks. The former generally occurs for a few cycles immediately following an extra-systole, but it may be with an increase in the cardiac rate brought on by physical exertion, in both instances being usually slight or moderate. Persistent pulsus alternans occurs in two sets of circumstances, namely: (1) a marked acceleration of the cardiac rate in auricular flutter or paroxysmal tachycardia; and (2) in failure of the left ventricle, in the great majority of cases in those over middle age and due to the causes mentioned on p. 853, but sometimes in younger people

with post-rheumatic valvular disease, and occasionally in pneumonia and other acute illnesses.

Pulsus alternans is increased or may be induced by an acceleration of the cardiac rate, and may be diminished or disappear with the decreased rate.

The condition is indicative of depressed contractility.

Symptoms.—The pulsus alternans in itself causes no subjective symptoms, but when associated with left ventricular failure manifestations of the latter are present (see p. 857). Sometimes the smaller beats are so feeble that no waves are transmitted to the wrist, resulting in infrequency of the pulse.

Diagnosis.—Gross alternation of the pulse can usually be recognised by the finger. Lesser grades can be readily detected by the sphygmomanometer, preferably by the auscultatory method. The pressure in the armlet is raised until the pulse below it disappears, and then lowered very gradually. The larger beats reappear at a higher pressure than the smaller beats, so that just below the systolic level the pulse-rate is halved. In extreme cases the difference in pressure between the larger and smaller beats may be 20 to 30 mm., but usually it is only 1 to 5 mm. A radial tracing is valuable in distinguishing

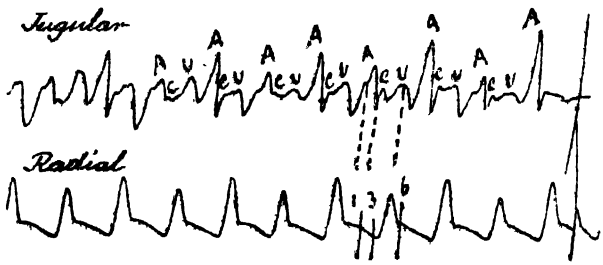


FIG. 36.—Simultaneous tracings of the jugular and radial pulses, showing continuous pulsus alternans.

pulsus alternans from extra-systoles. In the former the beats are evenly spaced, excepting that sometimes they are slightly delayed; whereas in the latter they are premature and the pause following the smaller beat is longer than that after the larger one.

The condition is sometimes but not usually evident in an electro-cardiogram.

Prognosis.—When the pulsus alternans occurs apart from a marked acceleration of the cardiac rate, it is an indication of severe or even extreme exhaustion of the heart muscle. When the condition is persistent, death may follow within a few months, or at most a few years. When transient, the exhaustion may be only temporary but even in these cases the prognosis should be guarded. When the condition is associated with marked tachycardia, it appears to be of relatively minor significance in itself.

Treatment.—When unassociated with marked tachycardia, complete rest, physical and mental, is urgently indicated, and if the condition is persistent this should be long-continued. The left ventricular failure should be treated on the lines discussed elsewhere. It is to be noted that digitalis is not contra-indicated.

FREDERICK W. PRICE.

CARDITIS: THE RHEUMATIC INFECTION OF THE HEART IN CHILDHOOD

Definition.—By carditis is meant inflammation involving the endocardium, the myocardium, or the pericardium, or the three simultaneously.

Before dealing with endocarditis, myocarditis and pericarditis individually, it may be advisable to discuss the rheumatic infection of the heart in childhood. This is a subject of great importance, for by far the larger proportion of cases of heart disease under 30 years of age, and a considerable proportion of those of later life, are the direct result of this infection.

It is necessary to point out that even yet rheumatic infection of the heart in childhood is very frequently overlooked. The two chief reasons are: (1) the clinical picture of acute and subacute rheumatism was originally drawn from the disease as it appears in adult life, whereas in childhood it presents many and important points of difference; and (2) even when a rheumatic infection has been diagnosed, it is sometimes exceedingly difficult to come to a definite decision as to whether the heart is involved or not.

It is important to bear in mind the following facts: In adult life arthritis is the chief manifestation of the rheumatic infection, and is looked upon as constituting a typical attack, while cardiac involvement is regarded as a complication. In children, on the other hand, arthritis is often vague in character, and may be entirely absent, while affections of other parts are more frequent, and constitute a more conspicuous feature in the disease. Thus, sometimes the affection is confined to the tendons or the fascia in the neighbourhood of the joints. What are called 'growing-pains' are frequently of rheumatic origin. Subcutaneous nodules, various erythemata and purpura rheumatica are more frequent manifestations of the rheumatic infection. Chorea is a common indication. Tonsillitis is perhaps more commonly rheumatic than in adult life. There may be unexplained pyrexia. Lastly, cardiac involvement is a much more frequent manifestation of the rheumatic infection in childhood than in adults; it is at least as frequent an indication as any other, and should not be regarded as a 'complication'; and it may occur in association with any of the foregoing, or with an indeterminate febrile attack, or alone—that is, it may be the only manifestation of rheumatism. Another point to bear in mind is that while rheumatic carditis may occur acutely in children, it often does so in a subacute and insidious form. Not rarely there is a total absence of subjective symptoms. Or, if such be present, they are often masked by other manifestations of the rheumatic infection. Pallor, fatigue, loss of appetite and wasting may be the first symptoms. Sometimes the onset is accompanied by a rise of temperature above that already existing, this increased pyrexia occurring without any increase in the arthritic symptoms. The usual cardiac symptoms may be present (see Endocarditis, Myocarditis and Pericarditis). The diagnosis rests mainly on physical signs, together with the results of electro-cardiographic examination, and the existence of the condition is frequently unsuspected until the heart is examined. The physical signs, however, are not infrequently slight and vague in character, and the diagnosis is consequently often attended with extreme difficulty.

In view of the foregoing, it is clear that when in a child there is even a suspicion of rheumatic infection, he should at once be put to bed, and a most careful clinical examination of the heart made daily and an electro-cardiogram be taken every few days, and if there be any doubt whether the organ is involved or not, he should be kept in bed until this has been set at rest.

In cases in which a definite diagnosis of carditis has been made, a most difficult question which may have to be decided later on is whether *active* carditis still persists or not. In this connection the sleeping pulse-rate is of value. If there is active carditis, the sleeping pulse-rate remains raised and may even equal the pulse-rate when the child is awake, while in the tachycardia of nervous origin, the sleeping pulse-rate is normal. The sedimentation rate of the red blood cells is also used for this purpose. It is increased in the active stages of the disease, and falls to normal when activity ceases.

ENDOCARDITIS

Definition.—By endocarditis is meant inflammation of the lining membrane of the heart. In the great majority of cases the inflammation involves chiefly the endocardium of the valves, and is not infrequently so limited. The term valvulitis is applied to endocarditis of the valves, while inflammation of the endocardium lining the cavities of the heart is referred to as mural endocarditis. The surface of the valves next the blood stream, namely, the ventricular surface of the semilunar valves and the auricular surface of the auriculo-ventricular valves, is affected. In adults the left side of the heart is far more commonly affected than the right, the mitral valve being more frequently attacked than the aortic; while, on the other hand, during fœtal life the opposite is the case. Some degree of myocarditis is probably always present with endocarditis.

A satisfactory classification of endocarditis is not easy, that most commonly adopted being as follows: (1) Acute, (*a*) simple, and (*b*) septic, infective, ulcerative or malignant; and (2) chronic or sclerotic. It should be noted that it is impossible to draw a sharp line of distinction between these varieties on grounds of ætiology, pathology, or morbid anatomy. Clinically, however, the distinctive features of each are fairly marked, although even in this case the distinction is not absolute. More recently a subacute variety, ulcerative in character, has been described (see Septic Endocarditis).

Acute Simple Endocarditis

Ætiology.—Acute simple endocarditis occurs most commonly in childhood and adolescence. It is rarely, if ever, a primary disease. Acute and subacute rheumatism, in one of its forms (see p. 913), account for the great majority of cases. Scarlet fever is occasionally the cause, while pneumonia, typhoid fever, small-pox, and wasting diseases are responsible for a certain number of cases.

Pathology.—The mitral valve is the most commonly affected, the next in frequency being the aortic, and the third both the aortic and mitral valves. In this form of endocarditis the parts affected become swollen, as the result of œdema and connective tissue proliferation, and cauliflower-like or warty

excrescences, varying in size from that of a pinhead to a bean, called vegetations, make their appearance on the segments of the valve or on the mural endocardium. The valvular vegetations are usually not situated at the extreme margins of the cusps, but at those parts which come into apposition during closure, namely, a short distance from their margins. The vegetations consist of blood platelets, leucocytes and fibrin. In rheumatic endocarditis *Aschoff's nodes* (see p. 289) are sometimes found in the inflamed valves. Various micro-organisms have been described in association with the vegetations, but they are not present in large numbers and may be absent, and even if present it is not certain that they are the cause in this form of endocarditis. Fragments may become detached from the affected valves, be carried by the blood to remote parts, and ultimately become impacted in a vessel; this process is known as embolism, and the impacted fragment as an embolus. This may result in obstruction of the circulation, and (1) necrosis, or hæmorrhage, or both, within the area of distribution of the occluded vessel, and the formation of infarcts; or (2) gangrene of the area supplied in the case of one of the larger arteries of the limbs. Infarction most generally occurs in the spleen or kidneys, although it is not infrequently found in the brain or its membranes, the retina, lungs (in right-sided endocarditis), intestines and skin.

The myocardium is involved, in varying degree, in at least most cases and perhaps in the great majority, but the involvement is permanent only in a certain proportion.

An attack of acute simple endocarditis is in the great majority of cases followed by the formation of fibrous tissue; in a certain proportion of cases by septic endocarditis; or possibly, in rare instances, by resolution. In the case of the first, the fibrous tissue tends to contract as time advances, giving rise to various deformities of the valves and ultimately to permanent stenosis, or incompetence, or both combined.

Symptoms.—In the first place, the reader is referred to the remarks on p. 913.

The patient may suffer from shortness of breath, palpitation, and discomfort or pain in the præcordium; and if there is involvement of the myocardium there may be manifestations of pronounced cardiac failure.

The onset is sometimes accompanied by a further rise of temperature without any increase in the symptoms of the causative disease. The degree of the pyrexia due to the cardiac affection is usually not marked, but occasionally there is a sharp rise of temperature. The cardiac rate is generally increased. There may be irregularity of rhythm (see p. 916), the result of implication of the myocardium.

In the early stages the apex-beat may be rather excited in character. Later, however, and in some cases even quite early, there may be physical signs of dilatation of the heart, generally both-sided (see p. 857). The first sound in the mitral area may become slightly prolonged, or roughened, or may exhibit a lack of clearness; and within 24 hours it may be accompanied by a distinct murmur, soft in character. Later, the second sound in the pulmonary area may become accentuated and even reduplicated. In the case of the aortic valve, the second sound may become altered; and—later, a soft-blowing murmur may accompany it, usually either along the left border of the sternum from the level of the second to the fourth intercostal spaces, or over the sternum between the level of the second rib to the fourth

space. A short and accentuated first sound at the apex, and an accentuation and it may be reduplication of the second sound in the pulmonary area are believed by some to be early signs of mitral stenosis, but excitation of the cardiac action should be excluded. A presystolic murmur at the apex usually does not make its appearance until some time after the onset of the rheumatic infection, the mitral orifice having become permanently stenosed. If there is considerable dilatation of the left ventricle due to myocarditis there may be a soft-blowing diastolic murmur in the mitral area—the so-called relative or functional mitral stenosis (see p. 938).

If there is severe carditis there may be even severe cardiac failure, usually both-sided, with considerable and rapid dilatation, even early in the disease.

There is usually a moderate leucocytosis and sometimes a slight secondary anæmia. Embolism may occur.

Diagnosis.—The diagnosis of acute simple endocarditis is often a matter of great difficulty. We should suspect its existence when there is an increase in the cardiac rate and in the degree of pyrexia without any aggravation of symptoms of the causative affection; or when tachycardia and pyrexia persist without an apparent cause; or when there are subjective symptoms together with acceleration of the cardiac rate and the existence of a murmur not previously present. The occurrence of auriculo-ventricular block during the course of an acute infective disease indicates involvement of the myocardium, and auricular fibrillation and extra-systoles are suggestive.

Evidence of dilatation of the heart and a recently developed apical systolic murmur do not necessarily signify acute endocarditis, for these may be found in any acute febrile disease, and in acute myocarditis. The character of a systolic murmur is of some diagnostic value, a soft-blowing one being in favour of endocarditis. Accentuation of the second sound in the pulmonary area later in the illness is also suggestive of mitral incompetence. An aortic systolic murmur is not so suggestive of acute endocarditis as is a mitral, while a pulmonary systolic may be almost disregarded. The reader is also referred to the other physical signs described above.

It is necessary to distinguish the murmur of acute endocarditis from that due to previously existing valvular disease. The existence of subcutaneous nodules or pericarditis, the sudden appearance of partial heart-block (indicative of coincident acute myocarditis), or the appearance of new murmurs or the disappearance of old ones, is in favour of a fresh attack of acute endocarditis, whether simple or infective. Embolism is not pathognomonic of acute endocarditis, as it may occur in chronic valvular disease, especially in mitral stenosis. In acute endocarditis, however, it is not infrequently multiple and recurrent, and is of more usual occurrence in the systemic than in the pulmonary circulation.

If acute endocarditis occur in an individual already the subject of valvular disease, the murmur is not of recent development, it is often loud or harsh, audible over a considerable area, and evidence of cardiac enlargement is usually present.

Prognosis.—The immediate prognosis of acute simple endocarditis is, as a rule, favourable, death being of rare occurrence; this may happen, however, if there be accompanying pericarditis or severe myocarditis. With regard to the ultimate prognosis, it has been pointed out that complete

resolution in all probability rarely occurs. Organisation is the usual sequel, ultimately giving rise to permanent stenosis, or incompetence, or both; in a certain percentage of these cases, the early murmur may disappear, and a permanent murmur may not become established until much later on, even several years. It should be noted that the future prognosis of a case of acute simple endocarditis largely depends upon whether convalescence is sufficiently prolonged. In a certain number of cases, ulceration of the valve results.

Treatment.—The treatment of a case of acute simple endocarditis is of great consequence, especially with regard to the future of the patient.

The indications are to endeavour to arrest the morbid process as early as possible, and to give the heart the best chance of the fullest possible repair.

The treatment of the causative disease should be adopted. For that of rheumatic fever, the reader is referred to pp. 293–296.

In all cases, after the manifestations of active disease have ceased, rest in bed is indicated for *at least* three months; this to be followed by an equal period of partial rest; and games should not be indulged in for another year.

During the first two months that he is confined to bed, the patient should keep as quiet as possible, physically and mentally, and should not be allowed to sit upright. Afterwards an extra pillow may be allowed, and a week or so later the back may be gradually more raised. After the period in bed, the patient should be moved to a couch, to which he should be confined for four weeks. During the latter half of this, passive movements, or gentle massage, or both, may be tried. Then slight walking exercises may gradually be attempted. If during any of these or later stages exertion be accompanied or followed by any abnormal subjective symptoms, or succeeded by maintained increased frequency of the pulse, the amount of exertion has been too much and should be proportionately reduced.

During the active stage of the disease small blisters applied frequently to the præcordium are advocated by some; and during the later stages the internal administration of sodium iodide is recommended. The results of the administration of digitalis are, as a rule, very disappointing, whether auricular fibrillation (or flutter) is present or not. If it is employed, caution should be exercised and large doses avoided.

Otherwise, the reader is referred to the various therapeutic measures described on pp. 861–873.

Convalescent Home Treatment.—Prolonged convalescence in special country homes devoted exclusively to children recovering from active rheumatic carditis is now advocated. The advantage of this form of treatment is that a return to normal life is made gradually, under skilled supervision, so that any indications of persistent activity of the disease or relapse may be quickly detected, and further complete rest promptly instituted. At some of these homes, facilities also for education are available, and this overcomes one of the greatest drawbacks of prolonged rest in children, namely, interference with education. Though this line of treatment is still on trial, considerable success has been reported in this country and America. A dry and elevated site is important. At some homes, treatment on the same lines as in the treatment of pulmonary tuberculosis is employed, the wards being so constructed that one side can be opened up.

It is well to examine a patient who has suffered from acute endocarditis

at regular intervals after the attack, and careful inquiry should be made as to his mode of life. In children, we should be especially on the look out for any rheumatic manifestation, and, as soon as detected, the condition should be immediately and adequately treated.

FREDERICK W. PRICE.

SEPTIC ENDOCARDITIS

Synonyms.—Infective Endocarditis; Ulcerative Endocarditis; Malignant Endocarditis.

Objections have been raised against each of these synonyms: that all endocarditis is infective, that ulceration is not invariable, and that some cases recover. But that some distinctive name is necessary to mark off a disease-process which is quite different from "simple" or "rheumatic" endocarditis is generally recognised. The assertion frequently made, that no sharp line of demarcation can be drawn between simple and ulcerative endocarditis, though true, does not dispose of the fact that in the great majority of cases the distinction is of fundamental importance and not very difficult of recognition.

The disease has an importance somewhat out of proportion to its frequency, partly on account of its great gravity and partly on account of the difficulties which often beset the diagnosis. The incidence of the disease in the wards of a large general hospital is about 1 in 170 cases.

Ætiology.—*Relation to rheumatism and other diseases.*—In more than half of all cases of the disease there is a clear history of acute or subacute rheumatism or of chorea. In the majority of these cases the patient has suffered from rheumatic endocarditis some time previous to his present illness, and has been left with definite and recognised valvular disease; in a few the condition of rheumatic endocarditis has passed directly, but often imperceptibly, into that of the septic condition. Usually the interval between the occurrence of the rheumatic fever and the onset of septic endocarditis is measured by several years, and these have been for the most part years of good general health. To those few cases in which the transition between the rheumatic endocarditis and septic endocarditis is a gradual one the term "malignant rheumatism" has been applied by some authorities. But the term introduced confusion in respect of the bacteriological questions involved, and is perhaps on this account to be avoided. Next in frequency to the rheumatic group of diseases in the patient's history, but insignificant in comparison, are scarlet fever, gonorrhœa, influenza, typhoid fever, malaria, syphilis, Graves's disease, dysentery and pneumonia.

Influence of congenital defects.—A congenital defect in the heart predisposes it to infection, apparently through the medium of that chronic thickening of the endocardium which is often found in connection with these defects. This factor has been definitely established in regard to the aortic valve.

Other ætiological factors.—Strain is present in some cases as a definite causative factor. This was seen in a series of cases which occurred in soldiers during the War of 1914–1918; these cases were aortic in the main, and in several of them there was no evidence of pre-existing valve lesions of an acquired nature.

Age.—The chief incidence is between the ages of 15 and 50. Out of 150 cases collected by the writer 122 occurred between these ages. One-half of all the cases occurred between 20 and 40, no doubt on account of the predisposition created by the presence of sclerosis of the heart valves after acute rheumatism, the chief age incidence of which is a decade earlier than this. The youngest case of the series was that of a child aged 2½ years, the subject of congenital heart defects. The oldest cases were those of a woman aged 64, and of a man aged 63, both of whom developed pneumococcus endocarditis with lobar pneumonia.

Sex.—This does not appear to be a determining factor.

Pathology.—The essential pathology in septic endocarditis is a progressive microbic infection of one or more of the heart valves, or of the mural endocardium. *The infecting micro-organisms*, as judged by positive blood cultures during life rather than by post-mortem investigations, are very variable. An analysis of 40 cases of the disease in which positive blood cultures were made during life showed streptococci in 26, pneumococci and Pfeiffer's bacillus in 5 each, gonococcus in 2, *Staphylococcus albus* in 1, and an unclassified micro-organism of bacillary form in 1. The *gonococcus* accounts for the infection in a few cases. If post-mortem results are taken, *Staphylococcus aureus* bulks largely in the analysis and the pneumococcus is represented more frequently. A few other organisms, relatively unimportant, also appear—*B. typhosus*, *B. coli* and *C. diphtheriæ*. Streptococci are certainly the most common organisms concerned, and the characters of those members of the group found in this disease deserve special attention. If we except acute cases due to *S. pyogenes* (*S. hæmolyticus*), the types of streptococcus most often found are not highly pathogenic, but of low virulence, such as are found in normal fæces and in normal saliva (*S. viridans*). They are for the most part short-chained cocci, not lethal for mice, and they yield a set of biochemical reactions that mark them off quite sharply from *S. pyogenes*. These facts harmonise with certain broad clinical and pathological observations and serve to explain them: the chronicity of many of the cases, and the latency of others; the scanty leucocytosis often seen; the apyrexial periods not infrequently present; the absence of suppuration in the embolic infarcts which is such a feature of the disease; the absence of any visible focus of infection in the great majority of the cases; the enormous number of living micro organisms that may be present in the blood stream at a time, it may be, when the patient is not acutely ill. The writer has shown that it is not difficult to set up a condition of septic endocarditis in the rabbit by the intravenous injection of "saprophytic" streptococci from healthy human saliva and fæces.

The condition of infection once established in the endocardium, a state of "arterial pyæmia" results, the circulation being fed by micro-organisms from the infected area. Minute vessels become plugged by masses of these microbes. Larger emboli, formed of pieces of the fungating vegetations, and of various sizes, add to the pyæmic process. Destructive and vegetative processes proceed together at the site of infection, which spreads to adjacent structures in the heart, both by contact and by direct extension. It has been shown that the micro-organisms in the blood stream are destroyed *in vitro* in 24 hours when citrated blood is incubated without culture media. This fact suggests that they are paid out into the blood stream from the

heart lesion, but that their duration of life in the former is short. It also explains the fact that blood cultures are not infrequently sterile.

Symptoms and Course.—The disease may be *latent*, and only discovered post mortem. It may be *fulminating*, in which case it may be suspected, but rarely diagnosed. In the fulminating cases the infection is usually by *S. aureus*, and the ulcerating endocarditis is only one part of the *S. aureus* pyæmia. Such is the endocarditis complicating acute osteomyelitis, and that seen in very acute pyæmia resulting from *S. aureus* infections of the skin. The more important types are the *acute* and *subacute*.

The acute form.—The onset is usually abrupt, often with a rigor, and the symptoms are those of an acute specific fever. Pain in, and swelling of, joints is common, with acid sweats, often leading to a disgnosis of rheumatic fever and calling for the use of salicylates. Not infrequently the failure of response to full doses of salicylates is the first observation to throw doubt upon the diagnosis. The pneumococcus cases are generally of this type, pneumonia or pleurisy with effusion being usually present; the patient remains very ill after the eighth day of his disease, infection of the endocardium being perhaps the most serious cause of absence of crisis. Gonococcus infection is also usually of this form; the temperature chart may show two "spikes" in the 24 hours. The duration of the acute cases is from 7 to 30 days. A very few cases undoubtedly recover.

The subacute type ("Subacute bacterial endocarditis").—This is probably the most common type of the disease. Attention has been drawn to it by Osler, Horder, Libman and others. The onset is gradual, often insidious, so that it may not be possible to determine with accuracy when the disease began; it seems certain that in many of the cases the process of endocardial infection has existed much longer than is suspected. The initial symptoms are general weakness with sweats and anæmia, or a condition somewhat resembling subacute rheumatism, or fever which is unexplained by the physical signs. The duration of these cases is very variable; from 2 to 6 months includes the majority of them; but a few may last for 12 months or even longer. The infecting micro-organisms are streptococci of the fæcal and salivary type (*Streptococcus viridans*, *Streptococcus endocarditidis*), Pfeiffer's bacillus and occasionally the pneumococcus. In some of these cases the pre-existing valve lesion is very slight, although its presence is generally known if the patient is of the private class.

The heart.—In the great majority of cases signs of valvular disease or congenital defect are present at the outset. In a few cases, signs of valvular defect appear during the course of the disease. Rarely, there may be no evidence of valvular disease at any time: this experience is almost confined to cases in which the infection is of a terminal kind, occurring in patients who are too ill to admit of thorough examination, or in whom there is early and considerable dilatation of the heart. As the disease progresses it is common to get evidence of the involvement of other valves than the one originally infected, such as the appearance of signs of aortic regurgitation in a case originally one of mitral disease. Undue importance is perhaps attached to changes heard in the character of the murmurs from day to day. When the heart symptoms are prominent, the case is said to be of the "cardiac type," and such a clinical picture does quite commonly present itself: in which event the patient has in most instances been a heart invalid for some time previ-

ously. But in a considerable proportion of the subacute cases it is a striking thing that the heart shows little recognisable defect, at least for a considerable time. For the greater part of its course it may be said that subacute septic endocarditis is very largely destitute of cardiac symptoms. Arrhythmia, signs of restriction of the field of cardiac response to effort, and the results of so-called congestive failure—not only may all of these be conspicuous by their absence; it is unusual to see them.

When the infection (often pneumococcal) involves the right side of the heart only, evidence of valvular disease is generally lacking, the symptoms and signs being mainly those of recurrent pleurisy, consequent upon pulmonary infarction, with or without liquid effusion.

Arterial embolism.—This event is extremely common and constitutes one of the cardinal signs of the disease. *The importance of the search for emboli and their effects in a suspected case cannot be overestimated.* But to obtain an adequate conception of the disease-process here considered it is necessary to enlarge considerably the earlier notions of the embolic process in two directions: the diffuseness of the embolic site and the minuteness of the embolic fragment. The skin shows two distinct lesions, both highly characteristic of the disease—(*a*) Petechiæ, varying greatly as to their number in different cases—there may be no more than two or three, and only discovered after careful search at the root of the neck, in the nail bed or beneath the conjunctiva, or there may be a great number, presenting an appearance as though the patient has been flea-bitten. (*b*) Discoloured areas, usually tender, and most often affecting the pads of the fingers or toes, coming and going in the course of a few hours or days. The appearance of one of these red areas is often accompanied by sudden pain or acute tenderness on pressure. These lesions are of considerable diagnostic importance. They do not occur in rheumatism.

In the kidney there may be gross embolic events leading to infarction and hæmaturia. Of equal if not of greater importance is the occurrence of very minute microbic embolisms in the glomeruli, leading to the appearance of red blood cells and traces of albumin in the urine, and ultimately to a state of embolic focal nephritis, demonstrable under the microscope post mortem (Bæhr; Gaskell). The earliest symptoms of the disease may be those of renal failure. The retina may be affected, exploration of the fundus revealing hæmorrhages. One of the most common seats of emboli of the massive kind is the spleen, leading to enlargement and usually a palpable organ. Acute and severe pain may occur with the event, and friction, due to perisplenitis, may be heard. Apart from embolus the spleen may be enlarged; a palpable spleen is of considerable diagnostic importance. The brain may suffer, the most common result being hemiplegia. The embolus may lead to infective arteritis, with subsequent aneurysm formation and hæmorrhage which may be abruptly fatal. The mesenteric vessels and those of the limbs are frequently involved, either the main artery, or, more often, its branches, and especially the radial and posterior tibial. Here, again, aneurysms may develop, and gangrene occasionally.

Pyrexia.—Fever is present in nearly all the cases, perhaps in all at some time or other in the course of the disease; but occasional afebrile periods may occur, lasting from 2 or 3 days up to a fortnight, in the subacute cases. In the acute cases a high continued fever is not uncommon, and when this

is so the patient is highly toxic and asthenic and the heart symptoms are apt to be in abeyance ('typhoid type'). Irregular remittent fever is the most common form, both in the acute and in the subacute types. A high and regular quotidian intermittent fever is not uncommon—the gonococcus cases are particularly prone to this variety of fever. Rigors are common in the fulminating and acute cases; they also occur in subacute cases when embolism is rife. Whatever the form of the fever the temperature is apt to take a lower range shortly before death. *A fall in the temperature, the patient remaining very ill, is of no service and must not be taken for a good prognostic.* Such a fall of temperature may occur when signs of renal inadequacy supervene.

The blood shows a progressive and ultimately severe anæmia. The degree of leucocytosis varies with the type of the disease. In acute cases it is generally high (20,000 to 40,000), though this, again, varies with the degree of the patient's response to the infection. In the subacute cases the leucocytosis is rather remarkably constant about the figures 9000 to 12,000. In a few cases there is leucopenia. Blood cultures are extremely important in the matter of diagnosis. And yet it not uncommonly happens in the subacute cases that the diagnosis is certain and no growth of micro-organisms is obtained. In the great majority of cases, however, positive blood cultures are obtained, given proper technique.

General state.—Loss of flesh is invariable, but rarely a marked feature. Pains are common, and are usually arthralgic in character; they are prone to develop suddenly, are rarely accompanied by effusions, and when severe, are most often due to embolic events. The complexion in the subacute cases tends to a *café-au-lait* tint, which is a point of diagnostic value to the trained eye. Clubbing of the fingers is very common, quite apart from the influence of possible old-standing valvular disease. The patients are often singularly optimistic concerning themselves. Libman lays stress upon areas of deep tenderness about the lower end of the sternum and the sterno-costal junctions. Albuminuria is very common, tending to increase with the progress of the disease, and doubtless associated with the focal glomerular nephritis to which reference has already been made.

Modes of Termination.—1. *Recovery.*—A rare event, yet one which certainly occurs at times, even when the diagnosis is beyond doubt.

2. *Death.*—Out of 149 cases studied by the writer, the recorded terminal events occurred in the following order of frequency: heart failure (66), coma (23), sudden death (19), uræmia (18), exhaustion (8), hyperpyrexia (2). Cases dying in coma were for the most part those in which cerebral embolism, with or without hæmorrhage, had taken place. Sudden death was due to perforation of a valve cusp, rupture of aneurysms in the sinus of Valsalva, perforation of the interventricular septum and cerebral hæmorrhage.

Diagnosis.—Evidence of endocarditis, the occurrence of multiple arterial embolism, and the isolation of micro-organisms from the blood stream: the co-existence of these three facts makes the diagnosis of septic endocarditis indubitable. But, as has already been remarked, the diagnosis may sometimes be made quite confidently in the absence of a positive blood culture in certain of the subacute cases. The most important point to establish is the presence of multiple arterial embolism. Seeing that the prognosis is so serious, it follows that a diagnosis of septic endocarditis should never

be made unless convincing evidence be forthcoming. In the differential diagnosis the following diseases call for consideration:

1. *Pneumonia.*—There may be considerable difficulty here, seeing that consolidation of the lung is usually present in pneumococcus infection of the endocardium. Care must be exercised, because hæmaturia and splenic enlargement in a case of pneumonia do not necessarily imply infarction. Nor does a positive blood culture in pneumonia necessarily mean endocarditis. But petechiæ, and the presence of emboli in arteries, in a case in which signs of valvular disease and a positive blood culture are present, justify a diagnosis of septic endocarditis.

2. *Typhoid fever.*—A positive Widal test with a leucopenia in a patient who has not previously suffered from the disease, or has not had prophylactic inoculation may be regarded as almost decisive in favour of typhoid fever; especially is this so if the agglutination titre is found to rise when the test is repeated after a few days. Typhoid infection of the endocardium is very rare.

3. *Rheumatic fever.*—The recurrence of acute rheumatism in a patient who has previously developed valvular disease often gives rise to considerable anxiety on account of the similarity which may exist between the symptoms present and those of septic infection of the endocardium. The rheumatic process may spread itself over several months, salicylates notwithstanding. These difficult cases usually occur in children between the ages of 10 to 16 years. Endocarditis is always present, and often there is pericarditis, or pleurisy, or both; though pericarditis is a common complication in rheumatic infection, it is very rare in septic endocarditis, resulting only from infarction or an aneurysm leaking into the pericardial sac. There may be considerable loss of flesh and marked anæmia. The form of the temperature chart rarely affords help. The facts which help to exclude septic endocarditis are the presence of nodules, or of chorea, and the absence of petechiæ, of hæmaturia, of enlarged spleen, and especially of micro-organisms in the blood stream.

4. *Peliosis rheumatica* may cause even greater difficulty, but the condition is uncommon. The association of fever, purpura, anæmia, albuminuria and joint pains in a case of old-standing aortic regurgitation under the writer's care naturally raised fear of infection of the damaged valve cusp. But the purpuric spots and the joint pains were bilateral and symmetrical, there were ecchymoses in addition to the petechiæ, there were effusions into the joints, and blood cultures yielded no growth.

5. *Malaria.*—The resemblance is but superficial, owing to the fact that in some cases of septic endocarditis the fever may be markedly intermittent, and rigors with heavy sweats may occur. The absence of malarial parasites in the blood and the absence of leucopenia are much against a diagnosis of malaria.

6. *Tuberculosis.*—General tuberculosis may be closely simulated by acute septic endocarditis with continued fever when the heart signs are equivocal. But there is leucopenia in general tuberculosis, a sterile blood stream (on repeated culture), and signs of embolism do not occur. Sometimes cases of septic endocarditis find their way into sanatoria for the treatment of phthisis, on the ground that they are cases of "phthisis without physical signs."

Prognosis.—As has already been stated, recovery occasionally takes place in the acute, and still less frequently in the subacute form of the disease. All the same, the diagnosis once definitely established, the outlook is of the gravest, treatment notwithstanding. That the patient is very little affected in general health, that he is extremely hopeful concerning his condition, that the state of the heart in itself gives no cause for concern, and that the number of micro-organisms per c.mm. of blood has fallen very considerably—none of these things should tempt the physician to abate anything from the serious view he takes of the case. Periods of improvement often occur, with or without special lines of treatment, but the fatal issue seems only to be delayed. It is very difficult to surmise the length of time the patient will live after the diagnosis is made. If there are already present the signs either of renal or of cardiac failure the end is not far off; weeks measure it. Otherwise, developments may proceed quite slowly, and the patient may live some months. But there remain to be reckoned with the various accidents attending upon the dissemination of the endocardial vegetations, or the ulceration of the valves, either of which accidents may bring about a speedy termination. Not seldom, when it seems certain that the course of the disease has been checked, death, more or less sudden, and due to some purely mechanical cause, cheats the physician and those who watch his efforts.

Treatment.—PROPHYLACTIC.—Reference has been made to the undoubted fact that the source of the infecting agent in most cases is the mouth or intestine. This suggests that special attention should be directed to these regions in all persons who are the subjects of valvular disease. Oral sepsis of all sorts should receive treatment. Dead teeth, crowned, or not, should be sacrificed. Septic tonsils should be removed. The condition of the intestinal tract should be investigated, and measures adopted to lower the content of streptococci if this appears high.

CURATIVE.—The general (non-specific) measures adopted in the treatment of all cases of septicæmia are applicable here: plenty of fresh air and light, good food frequently administered, and hæmatinic drugs for the anæmia. The writers consider that open-air treatment, as for cases of pulmonary tuberculosis, should be adopted whenever possible. The various measures that have from time to time been tried in order to inhibit the bacterial factor in the disease are the following:

Chemical antidotes.—"Blood antiseptics" have, as a rule, proved very disappointing in the history of the treatment of the disease. Quinine, mercury, arsenic (including salvarsan), carbolic acid, formalin, the sulphocarbolates and many others, whether administered by mouth, subcutaneously or intravenously, lead to no results worth recording. On the other hand, efforts at "sterilisatio magna" of the blood stream are not without immediate danger. The introduction of sulphonamides in the treatment of coccal infections naturally led to their use in this disease. The results have been disappointing; this is to be attributed to the fact that these drugs are not helpful in *S. viridans* infections. The supplementary use of heparin is still under trial.

Anti-sera.—As most cases of septic endocarditis are of streptococcal origin, it was hoped that the use of anti-streptococcus serum might lead to cure. The result of a good many trials has been very disappointing. The

experience of vaccine therapy in this disease is no more cheering than that of serum therapy.

X-rays have been employed and radium, both alone and in conjunction with chemotherapy. Results have been encouraging only in a few cases where the infection was grafted upon a congenital defect.

HORDER.
A. E. GOW.

CHRONIC OR SCLEROTIC ENDOCARDITIS

Chronic or sclerotic endocarditis is characterized by an increase of the connective tissue of the valve-segments and other parts, which subsequently contracts.

Ætiology and Pathology.—Chronic endocarditis may be (1) a sequel to the acute simple variety, and, in the opinion of some, occasionally to subacute bacterial endocarditis; or (2) primary, that is, of a slowly progressive nature from the outset.

The first, *i.e.* secondary chronic endocarditis, is the more common. It is more apt to occur in early life, most frequently between the ages of 10 and 20. The mitral valve is more often affected. The connective tissue tends to contract as time advances, leading to thickening and shortening of the valve-segments, resulting in incompetence; or to adhesions between the cusps, with consequent stenosis; or to incompetence and stenosis combined. In the case of the mitral valve, there may also be shortening and thickening of the chordæ tendineæ and apices of the papillary muscles. In the case of aortic incompetence, the affection may be due to rupture of a valve-segment or to perforation. There may be a deposition of lime-salts. Recurrent attacks of acute endocarditis are not uncommon.

Primary chronic endocarditis is more frequent in males, and in later life. There are two varieties. The first is of much the same nature as atheroma—primary chronic degenerative endocarditis. It is more often met with in the elderly. The causes are much the same as in the case of atheroma (see p. 1038). The aortic valve is much more commonly affected, where it is relatively frequent, but it is not rare in the case of the mitral valve. There are patches of thickening and degeneration, and there may be calcification of the valves. There may be atheroma of the aorta, or of the coronary arteries, or general atheroma. The second variety is the result of syphilis, and generally commences in middle-life. The disease-process extends to the cusps of the aortic valve, resulting in incompetence, or, in the opinion of a few, rarely to absolute stenosis; and in the opinion of some, rarely to the base of the aortic cusp of the mitral valve, with consequent incompetence.

It may here be noted that fœtal endocarditis is usually of the chronic or sclerotic form.

Symptoms. Chronic or sclerotic endocarditis produces no symptoms until such structural changes have taken place in a valve as to cause stenosis, or incompetence, or both combined.

CHRONIC VALVULAR DISEASE

Definition.—By chronic valvular disease is meant a chronic affection of the cusps of the cardiac valves, or of the orifices, or both. Not only may

the orifices and cusps be affected, however, but also the chordæ tendineæ and the musculi papillares. Whatever the nature and form of the valvular affection, it gives rise to stenosis or narrowing, which results in obstruction to the flow of blood; or to incompetence, which allows of regurgitation; or frequently to both of these together. Along with organic valvular disease there are often coincident changes in the cardiac musculature, the coronary arteries, or the aorta.

The Relative Proportion and the Combinations of the Different Valvular Diseases.—It should be noted that not infrequently more than one valve is involved at the same time, especially in the case of rheumatic valvular disease.

The mitral is the valve most commonly affected, and incompetence of this valve is more frequent than stenosis. When mitral incompetence results from a previous attack of acute endocarditis, there is usually some degree of stenosis as well; when it is of the *relative* variety, it is often associated with tricuspid incompetence. Pure mitral stenosis is nearly always infrequent; in the process of thickening and contraction there is some degree of incompetence. Aortic regurgitation is very common; a greater or less degree of stenosis, however, not infrequently accompanies the incompetence. Pure aortic stenosis, on the other hand, is one of the rarest of valvular affections. There is usually also incompetence of the valve, generally at most of moderate degree. Disease of the pulmonary valve is comparatively rare, and is usually of congenital origin. Pulmonary stenosis is one of the most frequent forms of congenital heart disease; as an acquired condition, it is very rare. Pulmonary incompetence is the rarest of valvular diseases. Tricuspid incompetence is the most common form of right-sided valvular affections. In the vast majority of cases it is of the *relative* variety, in which case it is a common result of mitral disease. Tricuspid incompetence is rarely primary, and then stenosis is usually present with it and it may also be mitral or aortic disease. When tricuspid incompetence occurs alone it is in all probability congenital. Tricuspid stenosis is comparatively rare, but not so rare as was formerly supposed; the acquired form is usually associated with mitral stenosis, and there may also be aortic valvular disease.

In chronic valvular disease due to acute or subacute rheumatism, the following is the order of frequency: mitral disease alone; mitral and aortic disease; aortic disease alone; mitral and tricuspid disease.

Ætiology.—Chronic valvular disease may be of congenital origin (*vide* Congenital Heart Disease); or the result of a previous attack of acute simple endocarditis and, in the opinion of some, of subacute bacterial endocarditis; or of primary chronic degenerative endocarditis; or, in the case of the aortic valve and, in the opinion of some, rarely of the mitral valve, of syphilis; or new-growths; or traumatism; or functional. This does not include *relative* incompetence of a valve.

When chronic valvular disease is the result of a previous attack of acute endocarditis, it is more apt to occur in early life; when due to primary chronic endocarditis of a degenerative nature, in later life; while, in the case of syphilis, the morbid affection usually commences in middle life. Neoplasms may arise from the walls of the heart or from the valves. They rarely cause obstruction. A traumatic lesion of a cusp or of the chordæ tendineæ, the result of excessive physical exertion, may cause incompetence, or stenosis of

a valve, and is of much more common occurrence in the case of the aortic than the mitral valve. It rarely takes place, however, in the absence of pre-existing disease of the valve.

In *relative* incompetence of a valve the cusps themselves are healthy. This is more common on the right than on the left side of the heart, and is not nearly so frequent in aortic as in mitral disease. In the case of the auriculo-ventricular valves the condition may be brought about by: (1) Dilatation of the cavity of the ventricle; (2) enlargement of the orifice on account of relaxation of the surrounding muscular structures; the tonicity of the muscular ring is impaired, and the cusps do not completely come together; (3) both combined; (4) shrinkage or stretching of the musculi papillares or chordæ tendineæ as a result of disease. In the case of the semilunar valves, it is the result of dilatation of the aortic ring, or of the pulmonary orifice, as the case may be.

Pathology.—See Chronic or Sclerotic Endocarditis, and Syphilitic Mesaortitis.

Effects of Valvular Disease upon the Walls of the Heart and other Organs.—It can be readily understood that a valvular lesion is a mechanical impediment to the heart muscle in its work. The heart, however, possesses the faculty of adapting itself to this and thus maintaining an efficient circulation; that is, what is called *compensation* is established. This is brought about by an increase in the thickness of the muscular walls and, in some cases, also by an increase in the capacity of the cavity of one or more of the chambers of the heart, *i.e.* compensatory hypertrophy and compensatory dilatation respectively. It should be clearly understood that compensatory dilatation is different from the dilatation which is the result of cardiac, *i.e.* muscular failure.

When compensation is such that the heart is fully up to the normal, there is what is termed complete compensation. Comparatively rarely is this the case, *i.e.* there is usually a diminution in the reserve force and, it may be, of the rest force of the heart; and in any case such is apt to occur sooner or later. This is called 'decompensation,' or failure or loss of compensation. Some, however, limit at least the latter term to cardiac failure of 'moderate' or more severe degree (see p. 857).

In the case of stenosis of a valve, as the process of narrowing of the orifice is usually slow, the muscular wall of the chamber immediately behind the orifice hypertrophies, which enables it to overcome the obstruction; in other words, compensatory hypertrophy takes place. If this is complete, a normal amount of blood is propelled through the smaller valve aperture.

In the case of valvular incompetence, the cavity immediately behind the orifice has to accommodate the regurgitant stream of blood in addition to that which arrives in the normal manner, so that an increase in the capacity of the chamber is necessary, *i.e.* compensatory dilatation occurs. Again, a larger amount of blood than normal must be propelled with each systole of the chamber in order to make up for that which regurgitates, with resultant hypertrophy of the muscular wall, *i.e.* compensatory hypertrophy takes place. If this is complete, the circulation receives the normal supply of blood.

The muscular power of a hypertrophied chamber tends to fail sooner or later, *i.e.* cardiac failure and secondary dilatation occur. In this event, there is a diminished blood supply in front of the orifice and an increase in the

amount of blood behind it. A cavity dilated in this manner is placed at a disadvantage in contraction. In the case of a ventricle, there may be stretching of the mitral or tricuspid orifice, with *relative* or functional incompetence of either valve.

Passing to the consideration of the different valvular lesions:

In aortic valvular disease, the strain falls on the left ventricle. In stenosis, the chamber hypertrophies, it may be to a considerable degree. A normal amount of blood may be propelled into the aorta. Cardiac failure and consequent dilatation of the left ventricle and, it may be, *relative* mitral incompetence may supervene, in which case there may be the same subsequent events as in mitral disease. In aortic incompetence, there is both compensatory dilatation and hypertrophy of the left ventricle (Fig. 37), which may be even very marked—the so-called *cor bovinum*—especially if there is also mitral incompetence. If compensation is complete, the latter is propor-

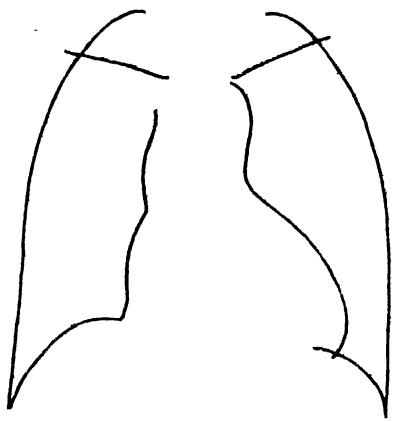


FIG. 37.—Orthodiagram from a case of aortic incompetence, of rheumatic origin, showing enlargement of the left ventricle.

tionate to the former. Secondary dilatation may supervene, with, it may be, *relative* or functional mitral incompetence and its subsequent events.

In mitral stenosis, the strain falls mainly on the left auricle and, still more so, on the right ventricle. The former chamber dilates and, to a certain extent, hypertrophies. The right ventricle hypertrophies, it may be markedly so. The pressure in the pulmonary circulation is raised, there is apt to be chronic venous congestion and œdema of the lungs, and the pulmonary artery and its branches may become dilated and even atheromatous. Later, the right ventricle dilates, and *relative* or functional tricuspid incompetence, dilatation and hypertrophy of the right auricle, and systemic chronic venous congestion may supervene. Occasionally when the wall of the left auricle is diseased, that chamber dilates to aneurysmal proportions, extending to the right as far as the chest-wall. On X-ray examination, enlargement of the left auricle, the pulmonary artery and the right ventricle can usually be made out. The left auricle projects backwards and to the right, and the

infundibular part of the right ventricle and the pulmonary artery project above the left ventricle on the left border of the heart (Fig. 38). In cases in which auricular fibrillation with cardiac failure is present, the right auricle

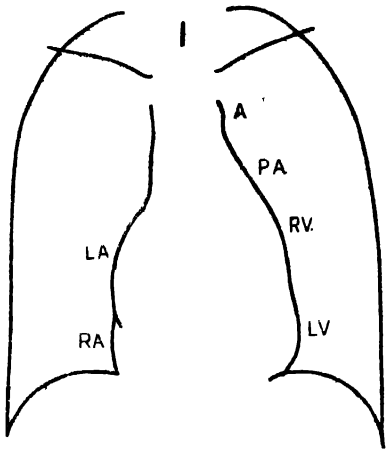


FIG. 38.—Orthodiagram from a case of mitral stenosis, showing enlargement of the left auricle, which projects to the right, and enlargement of the pulmonary artery and infundibular part of the right ventricle on the left border of the heart. A., aorta; P.A., pulmonary artery; R.V., infundibular part of the right ventricle; L.V., left ventricle; L.A., left auricle; R.A., right auricle.

becomes increasingly enlarged (Fig. 39). In uncomplicated stenosis, the left ventricle does not hypertrophy; indeed, the quantity of blood passing from the left auricle to the left ventricle may be less than normal, and the chamber

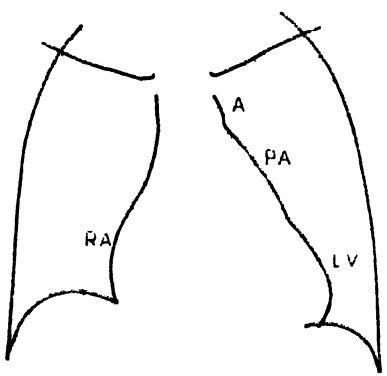


FIG. 39.—Orthodiagram from a case of mitral stenosis and auricular fibrillation with cardiac failure.

may be rather atrophied. If, however, there is also mitral incompetence, there is left ventricular dilatation and hypertrophy. In mitral incompetence, in accordance with the principles explained above, the left ventricle under-

goes both compensatory dilatation and hypertrophy. Secondary dilatation may occur. There may be dilatation and hypertrophy of the left auricle, and the subsequent events resemble those in mitral stenosis.

Lesions of the right side of the heart produce corresponding results to those of the left. In pulmonary stenosis, the right ventricle hypertrophies, it may be in a marked degree, and later may dilate. In pulmonary incompetence, compensatory dilatation and hypertrophy of the right ventricle occur, and it may be secondary dilatation. In tricuspid stenosis, there is dilatation and, to a certain extent, hypertrophy of the right auricle; while in tricuspid incompetence, compensatory dilatation and hypertrophy of the right ventricle take place, and secondary dilatation may occur.

Valvular disease of the right side of the heart is apt to cause systemic venous congestion.

Symptoms. See cardiac failure; the different valvular diseases; and syphilitic aortitis.

Aortic Stenosis

Aortic stenosis may be absolute or relative. In absolute stenosis the orifice is less than its normal size, while in relative stenosis the size is normal, but dilatation of the aorta just above the valve is present.

Ætiology.—Absolute stenosis is almost always the result of an antecedent attack of acute endocarditis, in which case there is usually incompetence, generally, at the most, of moderate degree, and not rarely the mitral valve is also affected; or primary chronic degenerative endocarditis. The first is the commonest cause in young adults, and the second in the elderly. It is rarely of congenital origin and, in the opinion of a few, due to syphilis.

Relative stenosis due to general dilatation of the aorta just above the valve may be caused by atheroma or syphilis.

Symptoms.—The symptoms are usually very delayed and, indeed, the condition may be latent all through life—even more than in the case of mitral incompetence, but when they do occur they appear more rapidly. They are those of aortic incompetence excepting that a sensation of beating or throbbing in the head or elsewhere is uncommon; those of cerebral anæmia are, in my opinion, less frequent; anæmia is rare; pain and angina occur less often; and sudden death is not so likely.

In uncomplicated stenosis, the pulse may not show any appreciable abnormal features. If, however, of considerable or more degree, it is of smaller amplitude, the upstroke is slow, and gradual and oblique, and the pulse is well sustained. It may be anacrotic, or of the bisferiens type. In the case of the former, the tidal wave may be more forcible than the percussion wave, and as a result the latter part appears merely as an indentation in a slow slanting upstroke, the apex of which is formed by the tidal wave. In the latter the tidal wave may be felt separately from the primary impact—that is to say, the summit is bifurcate due to the predicrotic fall being followed by a rise equal to or above that of the percussion wave. The blood pressure tends to be rather subnormal, with the diastolic relatively high. When the lesion is due to primary chronic degenerative endocarditis, hypertension may be present; and the vessel wall may be thickened and

tortuous. Almost always there are evidence of hypertrophy of the left ventricle (see p. 955), it may be of considerable degree; and the outthrust of the apex-beat may be even slower and longer than in the case of hypertrophy—a 'slow heave,' which is sustained. The area of cardiac impairment is correspondingly increased.

A thrill, systolic in time, is usually palpable at the base, generally best felt in the aortic area, and as a rule rough. There is a systolic murmur at the base, with its point of maximum intensity usually in the aortic area, usually harsh but it may be musical or blowing. The murmur is often loud and, indeed, cases have been recorded in which it was heard even several feet away from the patient. The direction of selective conduction is upwards along the vessels of the neck, but if the murmur is loud it may be audible all over the front of the chest and even at the back, in which case it is most evident at the level of the fourth vertebra, close to the left border of the spinal column. The second sound in the aortic area varies considerably in loudness, largely due to the nature of the lesion and the presence or absence of arterial disease. Thus, the fusion of the cusps may be such as not to allow the necessary apposition, so that the second sound is diminished or practically absent. In hypertension and atheroma, on the other hand, the sound is apt to be increased.

Signs of dilatation of the aorta are sometimes also present.

The physical signs of *relative* mitral incompetence may supervene.

Diagnosis.—For the diagnosis of syphilitic aortitis, see pp. 978, 979.

It is necessary to point out that it is not justifiable to make a diagnosis of aortic stenosis from the mere presence of a systolic murmur over the aortic area, additional evidence being required.

A diagnosis of aortic stenosis can readily be made when the characteristic pulse, evidence of left ventricular hypertrophy, an aortic systolic thrill and murmur, especially if the latter is loud and harsh, with the direction of selective propagation upwards along the vessels of the neck, and a diminished or absent second sound are present. When, however, only one or few of these features are present, difficulty with regard to the diagnosis may easily arise. An anacrotic pulse is characteristic, but not pathognomonic; nevertheless, it is of greater diagnostic value than pulsus bisferiens. While the presence of a thrill is a valuable diagnostic sign, it may also be found in circumscribed aneurysm of the aorta. A systolic murmur with the direction of selective propagation upwards along the vessels of the neck is at least strongly presumptive, and, in the opinion of some, is almost sufficient evidence. Before arriving at a diagnosis of absolute stenosis, unless a typical pulse is present, X-ray examination for dilatation of the aorta is necessary.

Certain conditions must be excluded in considering the diagnosis of aortic stenosis. Among these are bruits due to anæmia; cardio-respiratory or cardio-pulmonary murmurs; those due to excitation of the cardiac action, for example, in thyrotoxicosis; mere roughness or stiffness of the aortic cusps; general dilatation (diffuse aneurysm) of the aorta just above the valve; circumscribed aneurysm; pulmonary stenosis; patency of the interventricular septum; and pressure upon the aorta by a mediastinal tumour in which no definite pulsation can be detected.

The distinguishing features of cardio-respiratory murmurs are discussed on p. 939. In general dilatation of the aorta just above the valve, the murmur

may sometimes be heard over the vessels of the neck, but occasionally the area of impairment at the level of the second and third intercostal cartilages extends farther to the right than the normal limit, the second sound is usually accentuated and may also be ringing, and audible over a much wider area, and there may be pulsation in the supra-manubrial notch. In a circumscribed aneurysm there may be a systolic murmur and thrill, but as a rule there is little difficulty in diagnosis. It is unnecessary to point out the value of X-ray examination in the diagnosis of both forms of dilatation of the aorta. The differential diagnosis from pulmonary stenosis is dealt with on p. 941.

Prognosis.—The prognosis of aortic stenosis depends mainly on the ætiology, the degree of the lesion, whether it is stationary or progressive, and the condition of the myocardium, the aorta and the coronary arteries. Some authorities are of opinion that when the affection is due to antecedent acute endocarditis, the outlook is even more favourable than in mitral regurgitation. When it is the result of primary chronic endocarditis, the prognosis is less favourable, as the lesion is more likely to be progressive, and to be associated with chronic myocardial disease, and atheroma of the aorta and even of the coronary arteries. If syphilis is responsible for the lesion, the outlook is much worse.

Treatment.—See p. 944.

Aortic Incompetence

Ætiology.—Aortic incompetence is more commonly found in middle or later life, and in males. There are three main causes: (1) A previous attack of acute endocarditis, in which case some degree of stenosis is not uncommon, and the mitral valve is often affected. This is the commonest cause of the condition in young adults. (2) Syphilitic mesaortitis. This usually commences in middle life. The valvular incompetence may be due to the disease-process spreading to the cusps; or to dilatation of the aortic ring—relative incompetence; or to both. (3) Primary chronic degenerative endocarditis, more particularly when the affection occurs in the elderly. Relative incompetence is sometimes also the result of atheroma, persistent hypertension, and, in the opinion of some, rarely in severe anæmia. Aortic incompetence is the most frequent chronic valvular affection due to injury, and may follow sudden physical overstrain, causing a rupture of a valve-segment. The condition is extremely rarely of congenital origin.

Symptoms.—The reader is also referred to Syphilitic Aortitis.

In not a small proportion of cases the malady is latent for many years. When symptoms do occur they tend to do so less gradually than in the case of mitral disease unless in the latter there is associated auricular fibrillation. Shortness of breath is possibly the most common symptom. The patient may complain of consciousness of the action of the heart, or of a sensation of beating or throbbing in the head, the neck, or elsewhere. Symptoms due to cerebral anæmia, including giddiness and faintness with change of posture, are relatively frequent, and probably more so than in any other form of heart disease. Not uncommonly the patient is pallid, and he may have an anxious expression; later, when relative incompetence of the mitral valve has become established, the facies may resemble that which is characteristic of mitral cases. In some there is pronounced anæmia. Præcordial pain and angina

pectoris occur more often than in mitral disease, especially if the coronary arteries are implicated. Left ventricular failure may develop (see p. 857). Right-sided failure (see p. 857) may supervene, but œdema is less frequent than in mitral and chronic myocardial disease, and widespread œdema is relatively exceptional.

Embolism and auricular fibrillation are less frequent than in mitral disease, while sudden death occurs more often than in any other form of valvular disease.

In uncomplicated aortic incompetence, the typical pulse is very characteristic, and is called the collapsing, the water-hammer, or Corrigan's pulse. Its character may be intensified by grasping the wrist and raising the arm above the head, and this method of examination should always be employed



FIG. 40.—Sphygmogram from a case of aortic incompetence.

in suspected aortic regurgitation. The typical pulse is of great amplitude, the upstroke is rapid and more vertical, and the fall is sudden. The tidal wave may be considerable, but is maintained only for a short period, the dicrotic notch falls low on the downstroke, while the dicrotic wave may be well marked, small, or altogether absent (Fig. 40). The artery is empty between the beats. The systolic blood pressure is variable but is usually increased, while the diastolic is diminished and may be very low, with resultant increase in the pulse-pressure, which may be great. The systolic blood pressure in the femoral artery is higher than in the brachial. When, in addition to incompetence, absolute stenosis is present, the characteristic pulse and blood pressure of the former will be modified by the latter condi-

FIG. 41.—Sphygmogram from a case of aortic stenosis and incompetence. The characteristic pulse of the latter condition is modified by the presence of stenosis.

tion (Fig. 41); this is of great diagnostic importance. A characteristic feature of aortic incompetence is exaggerated pulsation of the arteries. This may be especially noted in the carotid, temporal and brachial arteries, and may be evident in the abdominal aorta, in the suprasternal notch, and elsewhere. Increased pulsation of the retinal arteries is sometimes to be noted with the ophthalmoscope. With light pressure of the stethoscope over the larger arteries, *e.g.* the femoral, the brachial and the carotid, a sharp clear sound during systole—the so-called pistol shot sound—may be audible, while with moderate pressure, a double murmur is sometimes to be noted—the Duroziez's sign. The phenomenon of the capillary pulse may be observed, and visible pulsation in the superficial veins, especially in the veins of the back of the hand, when hanging down, is rarely to be noted. In the opinion of some writers, pulsation over the upper part of the præcordium, and in the

second and third right intercostal spaces, is occasionally to be noted, even in the absence of dilatation of the aorta.

There is evidence of hypertrophy of the left ventricle, which may even be very marked—the so-called *cor bovinum*, especially if there is also mitral incompetence (see p. 955).

A diastolic murmur is audible. It usually commences with the second sound, which it may replace or merely accompany, or sometimes immediately after it, and continues for a variable period, generally the greater part, during the long pause. Its point of maximum intensity is variable. While typically over the inner end of the second right intercostal cartilage, in the majority of cases it is elsewhere: often over the sternum, usually anywhere between the level of the second rib to the fourth space, but occasionally somewhat below this; or, probably less frequently, along the left border of the sternum, from the level of the second to the fourth intercostal spaces, but generally in the third and fourth. Rarely it is loudest in the neighbourhood of the xiphisternum or the apex. The murmur is often heard over a wide area. Its selective propagation is downwards. It is diminuendo, and usually blowing but occasionally musical. There is occasionally a diastolic thrill, its point of maximum intensity being the same as that of the murmur. An aortic systolic murmur is often, if not usually, present, due either to dilatation of the aorta or to absolute stenosis. Not infrequently a murmur during diastole is audible at the apex (Flint's murmur), and in a certain proportion of these also a presystolic thrill.

In *relative* incompetence, the second sound is usually accentuated and this may sometimes be determined.

For the results of X-ray examination, see p. 928 and Fig. 37, and pp. 977, 978 and Fig. 44.

Later, the physical signs of relative mitral incompetence may be present.

Diagnosis.—For the diagnosis of syphilitic aortitis see pp. 978, 979.

There is little or no difficulty in recognising aortic incompetence in the great majority of cases. The character of the pulse and blood pressure, exaggerated pulsation of the arteries and the phenomenon of the capillary pulse, signs of hypertrophy of the left ventricle, a diastolic murmur and, it may be, a thrill, presenting the features described, furnish a clinical picture with regard to the diagnosis of which there should be no mistake. It is to be noted that the arterial signs, in varying number, are sometimes met with in other conditions, for example, thyrotoxicosis. In slight incompetence, none of these signs may be present, there may be little or no evidence of left ventricular hypertrophy, and a diastolic murmur may be difficult to hear and inconstant. It is, therefore, very advisable that auscultation should be conducted under the quietest conditions possible, with the patient in various postures, and including during holding the breath after a full expiration.

In the differential diagnosis from *relative* incompetence the results of X-ray examination are valuable. When in aortic incompetence there is also a systolic bruit, if such is due to stenosis, the characteristic pulse of the former will be modified by the latter condition.

When the point of maximum intensity of the murmur is in the pulmonary area the condition may be mistaken for pulmonary incompetence. In the latter, the symptoms are principally those of right-sided failure; there is an

absence of the characteristic pulse and blood pressure, of exaggerated pulsation of the arteries, and of capillary pulsation; and there is evidence of hypertrophy of the right, and not of the left, ventricle. In addition, pulmonary incompetence is generally due to dilatation of the pulmonary artery, *i.e.* *relative* incompetence, in which event there is evidence of the causal condition.

When in mitral stenosis there is a diastolic murmur in the pulmonary area, it may be difficult to determine whether this is indicative of slight aortic incompetence or is a Graham Steele's murmur, but it may be noted that the latter is relatively rare.

In cases in which there is a diastolic bruit with its point of maximum intensity at or near the apex-beat, the differential diagnosis between aortic incompetence and mitral stenosis arises. This is discussed on p. 938.

A venous hum in the neck transmitted downwards to over the sternum, even its lower part, a patent ductus arteriosus, and an arterio-venous aneurysm may be mistaken for aortic incompetence. In the case of each, there is a continuous murmur during systole and diastole, frequently with a systolic accentuation. The differential diagnosis is not difficult.

When in addition to aortic incompetence there is stenosis, the characteristic pulse and blood pressure of the former will be modified by the latter condition (see Fig. 41).

Prognosis.—The prognosis of aortic incompetence is usually serious. Sudden death is more frequent than in any other form of chronic valvular disease, and may occur even when there are few or no indications of cardiac failure.

In attempting to form a prognosis, the ætiology, the degree of the lesion, whether it is stationary or progressive, the condition of the myocardium, the aorta and the coronary arteries, and whether the patient is subject to syncopal attacks and attacks of angina pectoris should be considered. When the lesion is the result of a previous attack of acute endocarditis, the prognosis is much more favourable than when due to other causes; indeed, if there be no indications of cardiac failure, and if the character of the pulse, the pulse-pressure, and the size of the heart, exhibit little or no alteration, the patient may live to an advanced age. When it is due to primary chronic degenerative endocarditis, the prognosis is less favourable, as the lesion is more likely to be progressive, and to be associated with chronic myocardial disease and atheroma of the coronary arteries. If syphilis is responsible for the lesion, the outlook is much worse. When aortic incompetence is the result of rupture of a cusp, the prognosis is still more grave, and a fatal termination may rapidly supervene. As regards the degree of the lesion, the degree of modification of the pulse and of the blood pressure, and the size of the heart are of special significance. Attacks of angina pectoris are usually of grave omen.

Treatment. See p. 944.

Mitral Stenosis

Ætiology.—Mitral stenosis commences much more commonly in early life, and is much more frequent in females than in males. In the great majority of cases it is the result of an antecedent attack of acute endocarditis of rheumatic origin. Some are of opinion that it is always so. I do not share this view. It sometimes originates in adults as a result of primary chronic de-

generative endocarditis, not infrequently in association with chronic renal disease. In others the ætiology is obscure.

Pathology.—In mitral stenosis the commonest type of lesion is for the cusps to be united by their margins; but it may be situated elsewhere, as, for example, at the level of the auriculo-ventricular ring. When the lesion consists of a union of the margins of the cusps, two well-marked types of stenosis may result—(1) The 'funnel-shaped mitral,' which is more common in childhood; and (2) the 'button-hole mitral,' which is by far the more common in adults and persons of advanced years.

In the former, the cusps are simply adherent and form a funnel-shaped membrane which projects downwards into the left ventricle, the wide mouth of the funnel being situated at the ring, and the smaller end being drawn down towards the apex of the heart, by shortening of the chordæ tendineæ and papillary muscles. In the case of button-hole stenosis, the cusps are also shortened and form a diaphragm, perforated by a narrow slit-like aperture, which almost closes the orifice. A combined form, that is, a funnel having a narrow slit at its lower end instead of a circular aperture, has also been described.

Symptoms.—Not infrequently for many years there may be only shortness of breath on severe exertion. In other cases, subjective symptoms, most commonly dyspnœa and next fatigue, occur on less exertion. The most frequent symptoms are respiratory. In addition to shortness of breath on effort, cough is relatively frequent; the patient is liable to such affections as bronchitis and broncho-pneumonia; and hæmoptysis is not uncommon. There may be physical signs of chronic venous congestion or œdema of the bases or over a wider area of the lungs. Right-sided failure is apt to supervene. There may be a persistent dusky flush over the cheeks; later, lividity of the lips, cheeks, tips of the ears, and the finger nails; and still later, clubbing of the fingers. Cerebral symptoms are not uncommon. Paroxysmal dyspnœa and acute pulmonary œdema are rarely met with in marked stenosis with sudden tachycardia. Angina pectoris is rare. Embolism is of much more frequent occurrence in mitral stenosis than in any other variety of valvular disease. Pressure on the left recurrent laryngeal nerve, resulting in paralysis of the vocal cord, is rarely met with.

The supervention of auricular fibrillation, with its usual consequences (see pp. 897, 899), is relatively frequent. Acute or subacute endocarditis is liable to occur. The fatal termination is usually the result of gradually increasing right-sided cardiac failure. Sudden death is rare.

In uncomplicated mitral stenosis the following may be present. In a fair proportion of cases the pulse is small, the upstroke being short and soon attaining its maximum, the pulse-wave is long, and dicrotism is absent. If there is auricular fibrillation, there is complete irregularity of rhythm. Sometimes the systolic blood pressure is rather subnormal, and the diastolic may be rather raised, so that the pulse is full between the beats. The apex-beat may be in the normal position, or rather displaced to the left. It may be normal in character, or sudden and short, the latter being somewhat characteristic.

There may be pulsation in the pulmonary area, synchronous with the apex-beat, due to enlargement of the pulmonary artery and the conus arteriosus. There may be evidence of enlargement of the left auricle and

of the right ventricle (see pp. 955 and 956). The first sound at the apex is short and accentuated. The second sound in the pulmonary area is not infrequently accentuated and may be reduplicated.

Examination for the characteristic murmur and thrill should be conducted with the patient in the upright position, and lying on his back and on the left side, both before and after exertion, or the inhalation of amyl nitrite. The murmur has its point of maximum intensity at the apex or rather nearer the parasternal line. Its area is often very limited—which should be noted, as this sometimes results in the lesion not being recognised—but it may be fairly wide and occasionally even as high as the pulmonary artery. It is usually of a low pitch and rumbling character, but occasionally is of higher pitch and blowing. The murmur is at any time from early in diastole, *i.e.* separate from but quickly following the second sound, to right up to the next first sound. The portion (or portions) of this period occupied by the murmur (or murmurs) depends upon the velocity of the blood through the mitral orifice. This in turn depends upon the cardiac rate and the degree of the stenosis. The more rapid the cardiac rate and consequent shortening of the diastolic period, the greater the rate of flow required for a given quantity of blood to pass through the mitral orifice; and, in like manner, the smaller the orifice. In normal rhythm, if the cardiac rate is slow, the murmur is short. It is generally presystolic, in which case it increases in loudness, *i.e.* is crescendo, right up to the first sound; but it may be early diastolic, in which event it is diminuendo. In moderate tachycardia, there is usually an early or early and mid-diastolic, and a presystolic murmur, with an interval between. If the rate is very rapid, the whole of the diastole is occupied, with presystolic accentuation. In auricular fibrillation, if the cardiac rate is slow, the murmur is short and occurs early in diastole. In moderate tachycardia, in the longer cycles it occupies part of diastole and in the shorter ones the whole of it, with presystolic accentuation. If the rate is very rapid, it fills the whole of diastole, with presystolic accentuation. The portion of the diastolic period occupied by the murmur (or murmurs), will, in like manner, depend upon the degree of the stenosis, whether slight, moderate, or severe. A thrill is often present. Its point of maximum intensity is the same as that of the murmur, but its area tends to be more limited. The portion (or portions) of the diastolic period is also the same. The thrill increases in intensity up to the first sound, and there may be a sensation communicated to the hand resembling that produced by the purring of a cat. Sometimes there is a diastolic bruit, with its point of maximum intensity in the pulmonary area, due to relative incompetence of the pulmonary valve (see p. 942); it is called a Graham Steele's murmur.

If, as is usually the case, mitral incompetence is also present, the physical signs of both lesions will be evident.

For the results of electro-cardiographic examination, see p. 1007.

When cardiac failure occurs, the physical signs of dilatation (see p. 956) and of relative tricuspid incompetence may be present.

Diagnosis.—A diagnosis may be made from the characteristic physical signs. The results of X-ray and electro-cardiographic examinations, especially the former, are also valuable. Respecting the physical signs, the murmur and the thrill, particularly the former, are naturally the most important. The latter should be distinguished from a mere vibration of the chest-wall, which

may be occasioned by a forcibly acting heart when the ribs are rigid. In this case, by separating the fingers and placing them in the intercostal spaces the osseous vibrations are not felt. A short and accentuated first sound at the apex and an accentuation of the pulmonary second sound are more frequently met with in excitation of the cardiac action than in mitral stenosis. Even in the absence of a murmur and thrill, a combination of a history of acute or subacute rheumatism, subjective symptoms on physical exertion, and, excluding excitation of the cardiac action, an apex-beat, first sound and pulmonary second sound of the character described should arouse suspicion.

In cases in which there is a diastolic bruit with its point of maximum intensity at or near the apex-beat, the differential diagnosis between mitral stenosis and aortic incompetence may arise. In the latter the murmur commences with the second sound or immediately after it; it generally continues during the greater part or the whole of diastole; is diminuendo; there is never presystolic accentuation; the murmur is usually blowing and of a higher pitch instead of rumbling and low pitch; it is less localised; and is not louder on lying down. The first sound is not short and accentuated. In addition, the character of the pulse and blood pressure, whether there is exaggerated pulsation of the arteries and capillary pulsation, and whether there is evidence of hypertrophy of the left or right ventricle should be taken into consideration. It should be remembered that both lesions may be present at the same time. In this event, the characteristic pulse of aortic incompetence will be modified by the mitral stenosis.

A murmur during diastole at the apex may be due to what is sometimes called *relative* or functional mitral stenosis the result of considerable dilatation of the left ventricle, such as may occur in aortic incompetence, rheumatic myocarditis and hypertension; in the case of aortic incompetence it is known as a Flint's murmur. The murmur has the same features as in organic mitral stenosis, but usually it is not so loud and vibratory, or so constant, and a thrill is less common. In aortic incompetence, a previous history of acute or subacute rheumatism is in favour of organic mitral stenosis.

Prognosis.—Mitral stenosis ranks after aortic incompetence in gravity among the chronic valvular lesions, and the prognosis is much less favourable than in the case of mitral incompetence.

There is apparently a tendency for mitral stenosis to be progressive, pulmonary complications are frequent, and embolism is relatively frequent. When the lesion occurs in the early years of life, physical and mental development are apt to be retarded, and the patient is liable to fresh attacks of rheumatic valvulitis. The prognosis depends upon, among other things, the degree of stenosis, which when considerable is almost invariably accompanied by incompetence. The supervention of a diastolic murmur marks a downward grade. Sudden death is of rare occurrence, a fatal termination being usually the result of gradual cardiac failure, which in most cases is associated with the supervention of auricular fibrillation.

Treatment.—See p. 944.

Mitral Incompetence

Mitral regurgitation may be organic, or *relative* or functional.

Ætiology.—When organic, by far the most common cause is a previous

attack of acute endocarditis, but sometimes it is due to primary chronic endocarditis. Trauma and, in the opinion of some, syphilis are rare causes. In the case of the former, there is usually a rupture of a chorda tendinea or of a cusp. *Relative* incompetence is a somewhat common cause of mitral regurgitation. It may be due to acute febrile affections, acute myocarditis, chronic myocardial disease, aortic valvular disease, hypertension, chronic Bright's disease, anæmias, and primary cardiac strain.

Symptoms.—In organic mitral incompetence, occasionally there is an absence of subjective symptoms throughout the whole course. When symptoms are present, the clinical picture resembles that of mitral stenosis, but usually the degree of failure is less, and hæmoptysis, embolism, and perhaps auricular fibrillation are less common.

In uncomplicated cases, the pulse may exhibit some diminution in volume and the blood pressure may be rather subnormal. If there is auricular fibrillation, there is complete irregularity of rhythm. There is usually evidence of hypertrophy of the left ventricle, and it may be of enlargement of the right ventricle and the left auricle (see pp. 955, 956). Occasionally there is a systolic thrill at the apex, generally not rough. There is a systolic murmur, with its point of maximum intensity at the apex-beat. Almost always it accompanies the first sound and may also follow it, while rarely only the latter. It is usually blowing, occasionally musical, and less frequently harsh. Occasionally its loudness varies from cycle to cycle. The louder the murmur the larger the area of propagation. If loud, it may be audible over a wide area of the left chest, including posteriorly. The direction of selective propagation is towards the axilla and the angle of the scapula. It is generally heard as far as the former. The second sound in the pulmonary area may be accentuated and occasionally reduplicated.

When cardiac failure supervenes, the apex-beat may become more diffuse and less forcible, the transverse area of cardiac impairment may increase, both to the left and right, and the physical signs of tricuspid incompetence may be present.

Diagnosis.—It should be clearly understood that a systolic adventitious sound audible over the apex of the heart is not necessarily indicative of mitral incompetence, for such may be due to other causes, which should be excluded. These include cardio-respiratory or cardio-pulmonary murmurs, those due to excitation of the cardiac action, such as in thyrotoxicosis, the propagation of a systolic murmur from the base or elsewhere, and exocardial sounds due to pericardial friction, or to a local pleurisy at or near the apex causing friction.

The following are in favour of mitral incompetence, though not necessarily indicative of it: (1) Enlargement of the heart, and it may be hypertrophy—unless it pre-existed. (2) The relative constancy of the murmur, if of a harsh character, if audible over a large area, the direction of its selective propagation, and an absence of variation with the phases of respiration. (3) The existence of a thrill. (4) Accentuation of the second sound in the pulmonary area. (5) A history of rheumatism.

Cardio-respiratory murmurs vary with the different phases of respiration—such as increasing during inspiration and diminishing during expiration, or disappearing on holding the breath after full inspiration or expiration—and are usually short.

In *relative* mitral incompetence, there is an absence of evidence of left ventricular hypertrophy—unless this pre-existed; the size of the heart is generally less—in the absence of other factors; the loudness of the murmur is more affected by the adoption of the recumbent posture and by exercise; and there is often no accentuation of the pulmonary second sound. The opposite is in favour of organic mitral incompetence, as is also a history of rheumatism and the presence of mitral stenosis.

Prognosis.—The prognosis of mitral incompetence is more favourable than that of aortic stenosis or incompetence, or mitral stenosis. If the lesion be slight and the conditions of life favourable, the individual may even live to the normal span of life without experiencing much, if any, inconvenience. When, on the other hand, the lesion is severe, as indicated by marked cardiac enlargement, and more especially when symptoms of cardiac failure are present, the patient may live only for a few years. It should be remembered, however, that even when considerable or marked cardiac failure exists, if rest and other suitable therapeutic measures be adopted, the patient may improve for a considerable time. In attempting a prognosis, we should note, among other things, the pulse-rate, the degree of displacement of the right margin of cardiac impairment, and the existence or otherwise of any indications of venous stasis.

With regard to the prognosis of mitral regurgitation, due to *relative* incompetence, this depends upon the cause.

Treatment.—See p. 944.

Pulmonary Stenosis

Pulmonary stenosis may be due to a lesion of the cusps, or of the conus arteriosus.

Ætiology.—The disease is almost invariably congenital; indeed, it is perhaps the most common congenital cardiac affection. When it occurs as an acquired condition, it may be due to acute simple or septic endocarditis, while in some cases the ætiology is obscure.

Symptoms.—The symptoms of the congenital form of the disease will be discussed under Congenital Heart Disease. In the acquired form, in the opinion of some, the degree of dyspnœa is usually not severe, and there is little tendency to cyanosis, clubbing of the fingers, and systemic venous stasis; but perhaps this depends upon the degree of obstruction, and in any case it does not apply in the later stages.

There are physical signs of hypertrophy of the right ventricle (see pp. 955, 956), usually considerable, and it may be even of marked degree, and later it may be of dilatation. There is a systolic murmur, usually harsh, and it may be loud, with its point of maximum intensity in the second intercostal space just to the left of the sternum, which may be audible over a considerable area and may be conducted upwards and outwards towards the left shoulder and it may be to the back, in which event, in the opinion of some, it is some distance to the left of the spine, about the centre of the scapula. It is not audible over the vessels of the neck. There is generally a systolic thrill, as a rule rough. The pulmonary second sound is usually diminished or practically absent.

Diagnosis.—A systolic murmur in the second or third intercostal space,

or both, just to the left of the sternum is perhaps the most common of all murmurs and certainly so in the recumbent posture, and in a considerable majority of cases is of no significance.

Such murmurs may be found in anæmia (most frequently in this area), may be cardio-respiratory or cardio-pulmonary in origin (often and perhaps generally here), or may be due to excitation of the cardiac action, pathological dilatation of the pulmonary artery (see below), pulmonary stenosis, aortic stenosis, a circumscribed aneurysm of the aorta, and the propagation of a murmur from the third and fourth left intercostal spaces just to the left of the sternum in patency of the interventricular septum or from the apex in mitral incompetence, while in some cases the cause is not understood.

In the differential diagnosis, the following should be considered: The condition of the patient at birth. A history of acute endocarditis subsequently. The question of cyanosis. Whether there is enlargement of the heart, and if so right- or left-sided. Is the murmur only heard or louder on lying down; does it vary with the phases of respiration (see p. 939); is it harsh and loud; and is it audible over the vessels of the neck. Whether there is a thrill, and if present is it rough. Is the pulmonary second sound diminished or practically absent. Does an electro-cardiogram indicate right- or left-sided preponderance.

In pathological dilatation of the pulmonary artery there is evidence of the causal condition, the pulmonary second sound is accentuated, and occasionally a diastolic murmur is present. In aortic stenosis the character of the murmur and of the thrill and, in the absence of dilatation of the vessel, of the second sound resemble those in pulmonary stenosis. But the latter lesion is almost invariably congenital; cyanosis is one of the two chief symptoms; the character of the pulse differs; there is evidence of hypertrophy of the right and not left ventricle; the murmur is not audible over the vessels of the neck; and the electro-cardiogram is dissimilar.

Prognosis and Treatment.—See Congenital Heart Disease.

Pulmonary Incompetence

Pulmonary incompetence is the rarest of all valvular diseases.

Ætiology.—The morbid affection may be the result of antecedent acute endocarditis. It is, however, generally due to dilatation of the pulmonary artery, *i.e. relative* incompetence. This may occur in conditions which cause increased pressure in the pulmonary circulation, such as chronic mitral disease, especially stenosis, pulmonary fibrosis, and emphysema. The lesion is rarely of congenital origin.

Symptoms.—These depend upon the causal and any associated conditions, and are difficult to assess. They are principally those of right-sided failure (see p. 857). Hæmoptysis and epistaxis are occasionally met with.

There is evidence of hypertrophy of the right ventricle (see pp. 955, 956). There is a diastolic murmur, presenting the same character as that of aortic incompetence, with its point of maximum intensity in the pulmonary area, sometimes audible over a considerable area, with a direction of propagation downwards towards the lower end of the sternum, and occasionally a

thrill. When relative incompetence is due to mitral stenosis the murmur is known as the Graham Steele murmur.

In *relative* incompetence, the pulmonary second sound is usually accentuated and this may sometimes be recognised, and there is evidence of the causal condition.

The physical signs of tricuspid incompetence may supervene.

Diagnosis.—The diagnosis of pulmonary incompetence is frequently a matter of considerable difficulty. The lesion with which it is most likely to be confounded is aortic incompetence, because the point of maximum intensity of the murmur of the latter is often along the left border of the sternum from the level of the second to the fourth intercostal spaces. The differential diagnosis between these two conditions has been discussed on pp. 934, 935. The physical signs of pulmonary incompetence and patent ductus arteriosus resemble each other; in the case of the latter the murmur occupies both systole and diastole.

In *relative* incompetence there is evidence of the causal condition.

Prognosis.—When due to organic disease and when unaccompanied by any other valvular lesion, the prognosis in pulmonary incompetence may not be unfavourable; instances, indeed, have been recorded in which life has been prolonged almost to the normal span. In *relative* incompetence, on the other hand, the prognosis is usually very serious. Death in either case may result from right-sided cardiac failure, bronchitis or broncho-pneumonia, or pulmonary tuberculosis.

Tricuspid Stenosis

Ætiology.—This is similar to that of mitral stenosis. The affection commences much more commonly in early life, and is much more frequent in females than in males. In the great majority of cases it is the result of an antecedent attack of acute endocarditis of rheumatic origin. There is usually also mitral stenosis, and not infrequently, in addition, aortic valvular disease. The lesion is rarely of congenital origin.

Symptoms.—Cyanosis and shortness of breath on exertion are the chief symptoms. There may be coldness of the extremities. Systemic chronic venous congestion is prone to occur.

The apex-beat may be displaced to the left, and there is evidence of enlargement of the right auricle (see p. 956). There is a diastolic murmur, presenting the same features as that of mitral stenosis (see p. 937), with its point of maximum intensity in the tricuspid area, usually limited in extent but occasionally propagated to the right. A thrill, also diastolic in time and presenting the same character as in mitral stenosis, and having its point of maximum intensity in the tricuspid area, is frequently present. The first sound in the tricuspid area may be short and accentuated. There is often distension and pulsation of the jugular veins. When pulsation of the liver is present, it is of the auricular type. There are usually physical signs of some other form of chronic valvular disease (see Ætiology).

Auricular fibrillation may supervene, in which event pulsation of the liver is of the ventricular type.

Diagnosis.—As tricuspid stenosis is usually associated with mitral stenosis, in a considerable proportion of cases the lesion is overlooked.

The differential diagnosis from mitral stenosis is often a matter of great difficulty. The following is in favour of tricuspid stenosis: the early appearance of marked cyanosis and extensive dropsy; evidence of enlargement of the right auricle; a murmur with its point of maximum intensity strictly in the tricuspid area; and Mackenzie was of opinion that when pulsation of the liver is of the auricular type tricuspid stenosis in all probability exists.

It should be remembered that both tricuspid stenosis and mitral stenosis may rarely be present. In this event, two murmurs with separate points of maximum intensity, or a murmur with its point of maximum intensity midway between the tricuspid and mitral areas may be detected.

Prognosis.—The prognosis in this affection is by no means easy. The question largely depends upon whether mitral stenosis also exists, and if so, in what degree. When both lesions are present, the prognosis is usually very unfavourable.

Treatment.—See p. 944.

Tricuspid Incompetence

Ætiology.—It should be noted that the reflux of a certain amount of blood through the tricuspid orifice may occur under physiological conditions. In severe muscular exertion, for example, in which the intracardiac pressure on the right side of the heart is excessive, a natural function of the tricuspid valve is to provide for a certain amount of regurgitation, and thus afford relief to the temporary embarrassment due to distension of the right ventricle.

Pathological tricuspid incompetence is rarely congenital, and when it is, the condition is usually associated with pulmonary stenosis. Apart from those of congenital origin, there are two classes of cases: (1) Those in which the incompetence of the valve is primary; that is, due to a lesion of the cusps themselves—a rare condition; and (2) cases of *relative* incompetence, in which the cusps are normal. The latter constitute the great majority of cases.

With regard to the first group, the lesion may be the result of a previous attack of acute endocarditis, in which case there is generally tricuspid stenosis, and it may also be mitral or aortic valvular disease.

Relative incompetence is always consequent on conditions which cause increased pressure in the pulmonary circulation—such as chronic mitral disease, especially stenosis, pulmonary fibrosis and emphysema—pulmonary stenosis and incompetence, acute febrile affections, acute myocarditis, chronic myocardial disease, and anæmia.

Symptoms.—These depend upon the causal and any associated conditions, and the degree of the regurgitation. If the first two are favourable and the third is slight, the condition may be latent. Otherwise, shortness of breath on exertion and cyanosis are the principal symptoms, and other indications of right-sided failure are apt to supervene.

In organic tricuspid incompetence, there may be physical signs of enlargement of the right ventricle, and it may be of the right auricle (see pp. 955, 956). There is usually a systolic murmur, presenting the same character as that of mitral incompetence, with its point of maximum intensity in the tricuspid area. Its area is generally small, but sometimes the murmur

is conducted to the right and now and then is audible at the angle of the right scapula. Occasionally there is a systolic thrill, usually not rough. In the absence of a mitral or pulmonary lesion, the pulmonary second sound is diminished. There may be visible distension and it may be also pulsation of the jugular veins. If the vein is emptied from below by means of the finger and its upper extremity kept closed by pressure, it rapidly fills from below. The pulsation is usually of the ventricular, but occasionally of the auricular, type. The liver may be enlarged and may also be pulsating, the pulsation being systolic in time—unless tricuspid stenosis co-exists. There are generally physical signs of some other variety of chronic valvular disease (see Ætiology).

In *relative* incompetence, the physical signs of the causal and any associated conditions are present. A murmur is less frequent.

Diagnosis.—Tricuspid incompetence is very frequently overlooked because in the vast majority of cases there are signs of a causal or associated affection. On the other hand, it should be noted that, as in the case of mitral incompetence (see p. 939), a systolic adventitious sound in the tricuspid area may be due to other causes than incompetence. A correct diagnosis may be made by a consideration of the clinical features described above.

The differential diagnosis from mitral incompetence should be thought of.

Prognosis.—The prognosis of tricuspid incompetence depends upon the cause and associated condition. When the affection is due to organic disease, the outlook is serious.

With regard to *relative* tricuspid incompetence, when this is the result of left-sided valvular disease it is usually serious; it may be the precursor of a fatal termination in the near future. When, on the other hand, it is due to chronic pulmonary affections, acute febrile affections or anæmia, the prognosis may be good.

Treatment.—See below.

Treatment in Chronic Valvular Disease

The ætiology should be reviewed. In this connection, the treatment of syphilitic aortitis is described on pp. 979-981.

Explicit and detailed instructions with regard to his manner of life should invariably be given to the patient. The importance of always living within the limits of the heart's strength should be emphasised (see pp. 862, 863). As already mentioned, I am of opinion that in aortic incompetence the more strenuous forms of physical exertion should be avoided.

In children and young adults, preventive should be adopted against recurrent attacks of acute endocarditis; in all cases of chronic valvular disease the question of focal sepsis should receive attention, with the object of diminishing the risk of septic endocarditis; and, particularly in mitral stenosis, special care should be taken to avoid respiratory affections.

The various measures which may be applicable to any form of heart disease, described on pp. 863–875, should be considered in detail.

Surgical treatment in the form of valvulotomy, both by the auricular and ventricular routes, has been performed in a number of cases of mitral stenosis.

This procedure should be regarded as in an experimental stage. The mortality is high. Again, the change from mitral stenosis to incompetence is of doubtful value.

FREDERICK W. PRICE.

DISEASES OF THE MYOCARDIUM

Affections of the myocardium are of profound importance. It has been pointed out that valvular defects, diseased conditions of the blood vessels and disturbances of the cardiac mechanism should also be regarded from the point of view of their relation to the myocardium, and not so much as specific affections in themselves. It has also been noticed that, along with valvular lesions, coincident changes in the cardiac musculature, the aorta, or coronary arteries are, as a rule, present. We are, however, now concerned with affections of the myocardium occurring independently of valvular disease.

MYOCARDITIS

The varieties which may be met with are: (1) Acute (*a*) simple and (*b*) suppurative; (2) chronic; and (3) tuberculous myocarditis.

Suppurative myocarditis is of uncommon occurrence. It may be due to direct extension in infective endocarditis or to pyæmia. In this condition large abscesses in the myocardium are rare; they may perforate into the ventricle or pericardium. Minute abscesses, on the other hand, generally at the base of the left ventricle, are not rare. Chronic myocarditis will be discussed under Chronic Myocardial Disease.

Tuberculous myocarditis is almost always the result of extension from a tuberculous pericarditis. It usually takes the form of miliary tubercles.

ACUTE SIMPLE MYOCARDITIS

Strictly speaking, by this term is meant acute inflammation of the heart-muscle, but it is generally employed to include also morbid changes of a degenerative nature and I shall use the term in this sense.

Ætiology.—Acute simple myocarditis is most common in childhood and adolescence. Acute and subacute rheumatism, in one of its forms (see p. 913), accounts for the majority of cases. It may also be caused by diphtheria, influenza, acute pneumonia, small-pox, typhoid fever, and some other acute infective diseases. Some degree of myocarditis is present in at least most cases of endocarditis and pericarditis.

Pathology.—In some cases, especially in diphtheria, there is granular, hyaline and fatty degeneration followed by necrosis of the muscle-fibres, due to the direct action of the toxin, with cellular infiltration around. In others, particularly in rheumatism, the interstitial connective tissue exhibits cellular infiltration, but there is also degeneration of the muscle-fibres. Some

writers recognise two forms of myocarditis—the parenchymatous and the interstitial; in most cases, however, both the parenchyma and interstitial tissue are affected. In rheumatic myocarditis what are called *Aschoff's nodes*, described on p. 289, are often to be found, and, in the opinion of many, are pathognomonic of the rheumatic infection. Later, they become converted into fibrous tissue.

Dilatation of one or more chambers of the heart supervenes.

Acute simple myocarditis may be followed by—(1) Complete resolution in which no permanent changes supervene; or (2) the formation of fibrous tissue, which tends to contract as life advances, and which may occur in limited areas or may involve the whole myocardium. The latter condition is known as chronic myocarditis or fibrosis of the myocardium (see p. 949).

Symptoms.—In the first place, the reader is referred to the remarks on p. 913.

The clinical picture of acute myocarditis exhibits great variation as regards severity in different cases. On the one hand it may be indefinite and in rare instances the condition may even remain latent throughout its whole course, while on the other it may amount to a very serious or even grave illness.

The onset may be insidious, or there may be a definite change in the clinical picture of the causative disease. If pyrexia be already present, there may be a further rise of temperature, or if there has been no pre-existing pyrexia it may develop; it may be signalised by a rigor. The patient may complain of shortness of breath, palpitation, præcordial discomfort or pain. Not infrequently vomiting occurs, and indeed may be the first symptom. Cardiac failure, usually both-sided, may occasionally be of very severe degree. In some acute infective diseases, particularly diphtheria (see pp. 100, 102), there may also be acute peripheral circulatory failure.

The pulse is generally increased in frequency, but even bradycardia may very occasionally be present. It is feeble and soft. The blood pressure is usually diminished. In some cases there are extrasystoles (Fig. 42), or partial heart-block (Fig. 43), or auricular fibrillation, or complete heart-block, the second being most common and the fourth exceptional. There is usually dilatation of the heart, generally both-sided (see p. 857). In severe cardiac and peripheral circulatory failure the dilatation may be considerable and rapid, even early in the disease. If there is considerable dilatation of the left ventricle, there may be a soft diastolic murmur in the mitral area—the so-called relative or functional mitral stenosis (see p. 938). The second sound in the pulmonary area is sometimes accentuated and occasionally reduplicated.

A moderate leucocytosis and also a slight or moderate secondary anæmia may be present.

In some acute infective diseases, *e.g.* diphtheria and acute pneumonia, especially the first, there may be both cardiac and peripheral circulatory failure.

Diagnosis.—The diagnosis of acute simple myocarditis is often exceedingly difficult. The recognition of a mild form occurring during or after the febrile stage of any acute infective disease may be arrived at from a

consideration of the symptoms already enumerated. The presence of severe myocarditis may be presumed when there are indications of severe cardiac failure and it may also be severe peripheral circulatory failure coming on rapidly during the course of an acute infective disease, and out of proportion to the severity of the latter, an increase of cardiac impairment being perhaps especially significant. The occurrence of auriculo-ventricular block during

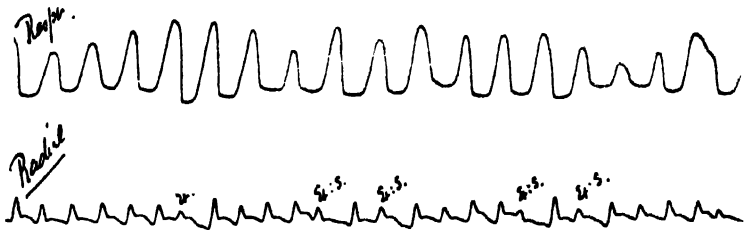


Fig. 42.—Tracing of the radial pulse, from a child suffering from croupous pneumonia, showing extra-systoles. Note the slight pulsus alternans following the extra-systoles

the course of an acute infective disease is indicative of myocardial involvement, and auricular fibrillation and extra-systoles are suspicious.

It may be necessary in any given case to differentiate acute myocarditis from acute endocarditis, and this is often a matter of extreme difficulty, for it should be remembered that both conditions may co-exist, and a mitral systolic murmur may be due to either (see also pp. 922, 923).

Prognosis.—This exhibits great variation. In the milder forms, recovery



Fig. 43.—Simultaneous tracings of the jugular and radial pulses, from a case of acute myocarditis occurring during diphtheria, showing partial heart-block. Every third stimulus from the auricle fails to reach the ventricle.

is the rule if early and adequate measures be adopted. The prognosis of the very severe forms is very grave, the mortality being high; the course of the disease is rapid, a fatal termination occurring usually within a week, and in some cases even within 24 hours, although life may be prolonged for several weeks. Sudden death is particularly prone to occur in diphtherial myocarditis, and may take place even when the patient is considered convalescent. Among the symptoms of bad omen are marked pallor, restlessness, syncopal attacks, vomiting, a greatly accelerated pulse of low tension, bradycardia, and a modifi-

cation of the heart-sounds resembling the fœtal type. As already noted, acute myocarditis may be followed by resolution, or by fibrosis of the myocardium.

Treatment.—This is of great importance.

The treatment of the causative disease should be adopted.

If the condition is at all severe, the measures regarding rest described under acute simple endocarditis (see p. 917) are applicable, excepting that the period of convalescence is not so long. Otherwise the reader is referred to the various therapeutic measures, including for peripheral circulatory failure, described on p. 875.

For acute myocarditis in diphtheria, see also pp. 108, 109.

DISEASES OF THE CORONARY ARTERIES

Before dealing with the various forms of chronic myocardial disease, it may be advisable to make some observations regarding diseases of the coronary arteries, as they bear an important causal relation to some of them, coronary disease being usually accompanied by morbid changes in the cardiac musculature.

Syphilitic mesaortitis and atheroma of the ascending aorta may give rise to narrowing or complete occlusion of the orifice of one or both of the coronary arteries.

Atheroma and, in the opinion of some, rarely syphilitic arteritis may affect the coronary arteries themselves, and result in narrowing or complete occlusion.

If the orifice of one of the coronary arteries be completely and abruptly closed, due to one of the causes mentioned, sudden death occurs. In those cases in which occlusion is only partial, or is gradual, atrophy of the muscle-cells with secondary fibrosis, *i.e.* ischæmic fibrosis of the myocardium or, less frequently, fatty degeneration, or both, usually ensues.

If one of the larger coronary arteries be completely and abruptly closed as the result of one of the causes mentioned, either infarction or sudden death results; while if the occlusion is only partial or gradual, ischæmic fibrosis, or fatty degeneration, or both, generally follow. If one of the smaller coronary arteries be completely and abruptly closed, infarction occurs; while if the occlusion is only partial or gradual, ischæmic fibrosis or fatty degeneration commonly ensues.

Complete occlusion of a coronary artery the result of atheroma is in the great majority of cases sudden and due to thrombosis. It is to be noted, however, that thrombosis does not necessarily give rise to occlusion, for the clot may not completely fill the lumen of the vessel. Complete occlusion in atheroma is sometimes the result of progressive narrowing of the lumen of the vessel caused by the disease-process itself, in which event the occlusion may or may not be completed by thrombosis. Complete and sudden occlusion is also rarely caused by embolism.

From the foregoing it will be seen that coronary occlusion and thrombosis are not synonymous terms, and this should be noted.

The causes of atheroma are described on p. 1038.

In conclusion, it is to be observed that while pain of cardiac origin is especially apt to occur in coronary disease, the latter is frequently present without the former.

CHRONIC MYOCARDIAL DISEASE

Of the various forms of chronic myocardial disease with which we have to deal, the most common are chronic myocarditis, fibrosis of the myocardium, fatty degeneration, and fatty infiltration.

CHRONIC MYOCARDITIS: FIBROSIS OF THE MYOCARDIUM

By chronic myocarditis is meant an increase of the interstitial tissue of the muscular wall, the muscle-fibres being largely replaced by fibrous tissue, which consequently contracts, and those which remain generally exhibit a varying degree of degeneration. The term chronic myocarditis connotes a productive or formative inflammatory process. Fibrosis of the myocardium is, however, frequently the result of other causes, for example, secondary to atrophy of the muscle-cells which may occur in disease of the coronary arteries, *i.e.* ischæmic fibrosis (see p. 948), and in the past chronic myocarditis has often been erroneously used to include such. It is better not to employ this term, and to use only that of fibrosis of the myocardium.

Ætiology.—Fibrosis of the myocardium is more common in late middle or elderly life, and in males. The condition may be a sequel to acute myocarditis. It may be due to an extension from the valves in chronic endocarditis, which is of common occurrence. Local fibrosis may be secondary to acute endocarditis or pericarditis. Fibrosis may be caused by syphilis. In such cases it may be the result of a diffuse primary chronic inflammation; or of coronary disease (see p. 1032); or, rarely, of gummata. There is a considerable diversity of opinion as to the frequency of the first. Some (amongst whom was the late A. G. Warthin) believe it is very common. The general consensus of opinion, however, with which I fully agree, is that it is of infrequent occurrence, and that the fibrosis is usually of ischæmic origin. Atheroma of the coronary arteries is perhaps the most common cause of fibrosis, in which case there may be co-existing fatty degeneration. The condition is occasionally due to chronic venous congestion of the myocardium, the result of chronic valvular disease or of chronic pulmonary disease, or to an old infarct. Not rarely it is impossible to determine the cause. In this connection, I am of opinion that it is at least possible that the same causes which produce atheroma, mentioned on page 1038, may give rise to fibrosis of the myocardium, independent of coronary disease.

Pathology.—The morbid affection may be general or local in its distribution, the latter being usually due to coronary disease. When the affection follows acute myocarditis, a more or less diffuse fibrosis, usually most marked beneath the pericardium and endocardium, is found. In both forms the auricles are little, if at all, affected, and the left side of the heart is much more commonly affected than the right, especially in the neighbourhood of the apex and the lower part of the interventricular septum. When the condition is the result of chronic venous congestion, however, it is more in evidence on the right side of the heart. There is an increase in the thickness of the cardiac wall—the so-called false hypertrophy—and ultimately dilatation occurs. White masses of fibrous tissue, varying in size from that

of a pea to a five-shilling piece or even larger, and irregular in shape, are to be observed replacing portions of the cardiac wall or interventricular septum. When the condition has continued for some time and the increase of fibrous tissue is extreme, the affected muscle-fibres may be entirely replaced by dense scar-like tissue.

See also pathology of causative condition.

Symptoms.—The reader is referred to the chapter on Cardiac Failure.

The clinical picture varies considerably in different cases. In rare instances, the disease is latent until a fatal termination occurs. In most of these cases, however, there had been symptoms on physical exertion for which the patient neglected to seek medical advice, or had not noticed; and also there would have been abnormal findings on clinical or instrumental examination.

The most common symptoms are shortness of breath and fatigue; less frequently discomfort or pain and palpitation; and occasionally there is slight cyanosis of the face; in each case referred to exertion. When the morbid affection is due to coronary disease, pain is apt to be the dominant subjective symptom. As a rule, sooner or later, these symptoms become more easily induced, and others supervene, in each case generally gradually. Usually the failure is both right- and left-sided (see p. 857) with, it may be, one predominating. While the congestive type of failure is very much more common, symptoms of cerebral anæmia and angina pectoris are not infrequent, and Adams-Stokes syndrome is occasionally met with. Ultimately there may be indications of severe, or even extreme, failure.

The pulse may be increased in frequency, or occasionally there may even be bradycardia. Its character varies considerably: it is usually fuller than normal, with increased pressure, although the latter is not pronounced unless there is co-existing hypertension or chronic renal disease. The apex-beat is usually displaced downwards and to the left, its area and force are sometimes increased, the area, however, being proportionately greater and the force relatively less than in pure hypertrophy. The area of cardiac impairment is generally increased in all directions. The first sound at the apex is often prolonged and muffled, while at the base it is occasionally diminished and may be scarcely audible or even absent. There is often, if not usually, heart-block, generally one of the three degrees of the auriculo-ventricular variety, but it may be bundle-branch or arborization block; or auricular fibrillation may supervene. A mitral, and less frequently a tricuspid, systolic murmur may be present.

If there is hypertension, see pp. 1066 1068. Not infrequently there are indications of general atheroma.

Diagnosis.—It is probable that chronic myocardial disease is overlooked more frequently than any other cardiac morbid affection. The two chief reasons for this, in my opinion, are a failure to obtain an accurate history regarding subjective symptoms on physical exertion and to detect enlargement of the heart, the latter especially in cases in which the apex-beat is either faint or absent. As regards the first, careful inquiry should be made as to whether the patient experiences any cardiac symptoms on physical exertion which formerly he was able to do (see p. 852). Respecting the second, while I do not share the view that percussion, provided this is performed with competence, is of little or no value, naturally examination

by the X-rays is of first importance. A combination of the existence of subjective symptoms on physical exertion and, it may be, of objective signs of cardiac failure together with enlargement of the heart and, it may be, modification of the character of the pulse, of the cardiac sounds and rhythm, and of the blood pressure, in the absence of other causes, is of especial value. An X-ray examination may also reveal co-existing atheroma of the aorta. An examination by the electro-cardiograph may be of supreme value. If there is auriculo-ventricular block, bundle-branch block, or intraventricular block, if persistent, the presence of chronic myocardial disease may be assumed. An electro-cardiogram may also reveal associated coronary disease. The differential diagnosis between fibrosis of the myocardium and fatty degeneration is described on p. 952.

It is necessary to distinguish chronic myocardial disease in which relative mitral incompetence has supervened from organic mitral incompetence, which may be very difficult. In the former, there is no history of chronic valvular disease, the subjective symptoms are frequently out of proportion to the physical signs, and angina pectoris and syncopal attacks are of more frequent occurrence.

Prognosis.—This varies very considerably. Taken as a whole the outlook is serious, but this may be partly due to the fact that as a rule the malady is not recognised in its early stages. The affection tends to be progressive. The various points dealt with in the section on Prognosis should be considered. Those of special importance are the ætiology and any associated morbid condition, the size of the heart, whether the lesion is progressing, the cardiac rhythm, and the question of heart failure and that of angina pectoris.

The most frequent cause of death is congestive heart failure. Sudden death is not rare, and may be due to angina pectoris, rupture of the heart, or other causes.

Treatment.—The ætiology should be reviewed with the object of treating the underlying cause, and the same applies to any co-existing associated morbid condition.

The various therapeutic measures described on pp. 861–875 should be considered carefully and in detail.

FATTY DEGENERATION

In fatty degeneration the muscle-fibres are more or less replaced by fat.

Ætiology.—Heredity is a factor. The condition is more common in males and in later middle or elderly life. Among the causes are: severe altered states of the blood, such as pernicious anæmia and leukæmia; chemical metallic poisoning, *e.g.* by phosphorus, arsenic, antimony, alcohol and chloroform; coronary disease, in which case, however, there is usually associated fibrosis and in much more degree, chronic pulmonary disease and in long-standing chronic valvular disease, giving rise to obstruction of the pulmonary circulation; as a sequel to marked fatty infiltration; and occasionally in diabetes.

Pathology.—The affection may be general or local in its distribution the latter being the more common. In both cases, but especially in the local

form, the ventricles are affected to a greater degree than the auricles, and the left ventricle than the right, except in chronic venous congestion of the lungs, and the musculi papillares and the muscle beneath the endocardium are principally involved. The heart may or may not be enlarged; indeed, in pure degeneration it may be even smaller than normal. In this connection it may be stated that fatty degeneration may accompany or succeed dilatation or hypertrophy, while, on the other hand, dilatation may follow degeneration. The organ is softer in consistence and flabby, and is more easily torn. The colour may be uniformly pale yellowish, or buff, or light yellowish brown—the so-called "faded-leaf" colour. The condition may, however, occur in patches, resulting in a streaked or mottled appearance as a whole, which has been likened to that of the breast of a thrush—'thrush's breast,' or to that of the fur of a tabby cat—"tabby cat striation." On microscopic examination of a section which has been stained with osmic acid, the small fat globules are seen inside the muscle-fibres, their envelopes being blackened by the acid.

Symptoms and Diagnosis.—The clinical picture of fatty degeneration resembles that of fibrosis of the myocardium, and in the opinion of some, a differential diagnosis is not possible, but I do not share this view. The following points are of help: In fatty degeneration symptoms associated with cerebral anæmia, general lassitude, debility, impairment of digestive functions, and a subnormal temperature are of more common occurrence; pain excepting angina, the congestive type of failure, and the Adams-Stokes syndrome are less frequent; the countenance may be pale and waxy; and, as in the case of fatty infiltration, there is a tendency to cyanosis on exertion—the association of cyanosis with dyspnœa on exertion being one of the most distinctive features of both. Usually the size and force of the pulse are less; the blood pressure is lower; the force of the apex-beat and any enlargement of the heart are less; the first sound is of shorter duration and may be sharp and clear; the second sound in the aortic area is less loud; and general atheroma is not so frequent.

Prognosis.—This somewhat resembles that of fibrosis of the myocardium. Here also the duration of life varies very considerably but, taken as a whole, the outlook is serious. In the acute forms, *e.g.* when due to altered states of the blood, the immediate prognosis is grave but the ultimate outlook not infrequently favourable. In the chronic forms, on the other hand, the opposite is the case. With further knowledge, it is now clear that the risk of sudden death has been much exaggerated.

Treatment.—The treatment of fatty degeneration is the same as that of fibrosis of the myocardium.

FATTY INFILTRATION

Synonyms.—Fatty Heart; Cor Adiposum.

Fatty infiltration consists in an excess of fat in those situations in which it is naturally found, and also in its deposit between the fasciculi of the cardiac musculature.

Ætiology.—Heredity is certainly a factor, and the condition is more common in males, and during or after middle life, being rare in early life

and comparatively so before middle age. It is usually associated with general obesity, though not always in proportionate degree, a generous appetite, and lack of exercise and fresh air. It is more especially found in over-indulgence in carbohydrates, fats and alcohol, particularly malt liquors and sweet wines, and faulty metabolism is generally present. The malady is also apt to occur in those suffering from affections of the lungs which cause embarrassment of the pulmonary circulation, such as emphysema, cirrhosis and chronic fibroid tuberculosis.

Pathology.—The affection is generally most marked over the right ventricle. The deposit of fat commences in the subepicardial fat, and may even extend to the subendocardial tissue. It is chiefly distributed along the arterial branches, often causing atrophy of the muscle-fibres by compression, and in some instances the latter become the seat of true fatty degeneration due to interference with their nutrition. In fatty infiltration, more or less dilatation of the cardiac chambers is usually present, and is often accompanied by hypertrophy.

Symptoms.—The patient is usually stout and flabby. The subjective symptoms are those of an enfeebled circulation. Exertion is frequently accompanied by fatigue, a tendency to perspire, dyspnœa with, it may be, slight cyanosis, and occasionally a sense of oppression in the chest, and giddiness or faintness. There may be early fatigue, and giddiness or faintness or mental effort, impairment of memory and the patient may be soporose, although, on the other hand, he may complain of insomnia.

The character of the pulse varies: usually it is weak, there is hypotension and the vessel wall is not thickened; but on the other hand it may present the opposite features. The cardiac impulse is generally feeble unless hypertrophy is also present. The area of cardiac impairment is usually increased. The heart sounds, especially the first, may be weak, low in tone, and muffled; while occasionally a mitral, and less frequently a tricuspid, systolic is present.

Later, there may be indications of a more pronounced degree of cardiac insufficiency.

Diagnosis.—Fatty infiltration may be diagnosed from the features described, occurring in a person who is the victim of obesity.

Prognosis.—If appropriate therapeutic measures be carried out, the prognosis is usually favourable; otherwise the condition is apt to be progressive. If the condition persist for some time, true degeneration is apt to arise. Again, in very severe fatty infiltration, rupture of the heart wall has been known to occur.

Treatment.—If, as is usually the case, general obesity is present, it should be treated (see pp. 481, 482). Regulated exercise in the open air is valuable, and systematic and graduated exercises and massage (see pp. 864, 865) may be tried. Spa treatment is not infrequently helpful.

HYPERTROPHY AND DILATATION OF THE HEART

Enlargement of the heart may be due to hypertrophy; or to dilatation; or, as is usually the case, to both together—excentric hypertrophy.

In simple hypertrophy there is an increase in the thickness of the walls of one or more of the cavities of the heart. The hypertrophy may include

the musculi papillares, columnæ carneæ, and the musculi pectinati. In dilatation there is an increase in the capacity of one or more of the chambers of the heart.

Ætiology.—Simple hypertrophy is a physiological reaction to continued overwork. Among the causes are aortic stenosis, essential hypertension, chronic interstitial nephritis, secondary contracted kidney, and diffuse hyperplastic sclerosis. It may also be due to long continued severe physical effort, as in heavy manual labour, athletic training and military training, chronic adhesive pericarditis, especially if there are extra-pericardial adhesions, and possibly continued excitation of the cardiac action, as in chronic thyrotoxicosis. In the case of the first, the hypertrophy is left-sided; in the second and fourth, it is at least chiefly left-sided; and in the third, it is likely to be general.

The causes of hypertrophy of the right ventricle are conditions which give rise to increased pressure in the pulmonary circulation, such as chronic mitral disease, especially stenosis, pulmonary fibrosis and emphysema, and pulmonary stenosis and incompetence.

For the development of full hypertrophy, an adequate blood supply is necessary, and in this connection the integrity of the coronary arteries is of fundamental importance.

Looking at the subject from the clinical standpoint, there are two kinds of cardiac dilatation, namely physiological and pathological. The former may be met with as a transient condition in severe muscular exertion. It also occurs in the form of compensatory dilatation in some varieties of chronic valvular disease (see pp. 927–930): of the left ventricle in aortic incompetence and in mitral incompetence; of the left auricle in mitral stenosis; of the right ventricle in pulmonary incompetence and in tricuspid incompetence; and of the right auricle in tricuspid stenosis. In this group there is also hypertrophy of the respective chambers.

Pathological dilatation is associated with impairment of the function of tonus or tonicity and cardiac failure. The affected chamber does not empty itself, and as the dilatation progresses, the contraction of the chamber becomes less effective and the amount of blood proportionately increases.

The condition may occur in any of the following: secondary to simple cardiac hypertrophy, however caused (see above); secondary to compensatory dilatation (see above); chronic myocardial disease; coronary occlusion; acute infective diseases; toxæmias; severe or prolonged pyrexia from any cause; the various forms of anæmia; and primary cardiac strain. In the first two there is hypertrophy and dilatation together.

In acute and subacute rheumatism, diphtheria, and in influenza, dilatation may be acute. It should also be noted that a common clinical condition in which acute dilatation occurs is the supervention of a new rhythm, such as auricular fibrillation.

Dilatation of the auricles is especially apt to occur in auricular fibrillation.

The causes of dilatation of the right side of the heart are the same as those of pathological *relative* tricuspid incompetence (see p. 943). In addition, in cardiac failure, whatever the cause, the pressure in the right heart rises and the chambers dilate.

Some of the causes of hypertrophy, by acting quickly, before there is time for hypertrophy, may produce dilatation; this is especially the case where the muscular fibres are already impaired.

Pathology.—Hypertrophy of the heart may be general or local, the latter being more common. In the former all the chambers are affected, the ventricles being more affected than the auricles. When the condition is local more than one chamber is usually involved, in varying degree.

When the left ventricle is affected, the apex of the heart is accentuated, and the whole organ is elongated and rather conical in form. When the right ventricle is concerned, the apex is less pronounced, and the whole organ broader and somewhat quadrate in form. The eccentric form of hypertrophy may give rise to enormous enlargement, in which case the organ is often spoken of as a "beefy heart" or a "cor bovinum." This is particularly apt to occur in aortic valvular disease.

Cardiac dilatation rarely affects one chamber alone, all of them being usually involved in some degree, although unequally so. When the condition is more or less general the organ approaches the globular form, especially when the right side is affected.

With the increase in the capacity of the ventricles, the dimensions of the auriculo-ventricular orifices also increase, with consequent *relative* incompetence. In dilatation of the auricles there is usually enlargement of the venous channels.

Symptoms.—In hypertrophy and compensatory dilatation there may be subjective symptoms associated with the causal affection. In pathological dilatation, there are symptoms of cardiac failure, in varying degree (see pp. 852–856). These may come on rapidly in the acute forms, and more gradually in the more chronic cases. In many of the cases associated with the supervention of a new cardiac rhythm the dilatation may sometimes take place so rapidly that in the space of a few hours there may be severe failure. In cardiac hypertrophy or cardiac dilatation the following may be present:

In hypertrophy of the left ventricle, the pulse-rate is apt to be rather slower. There may be some bulging and widening of the intercostal spaces to the left of the sternum, especially where the hypertrophy occurs during the growing period of life. The apex-beat may be displaced downwards and outwards, its area and force increased, and its out-thrust slower and longer than normal. The increase in force together with slowing of the out-thrust—the so-called "heaving" apex-beat—is the most characteristic feature of the condition. The area of cardiac impairment may be increased both from above, downwards and transversely. The first sound may be long, low in pitch and muffled, and the aortic second sound may be accentuated.

In hypertrophy of the right ventricle there may be, more especially in children, a certain amount of bulging in the region of the ensiform cartilage, while not infrequently there is pulsation in the epigastrium, which is inverted. When the condition is marked, there may be a heaving impulse in the epigastrium, and over the lower sternum and costal cartilages, and in such cases even in a more marked degree than in the case of the left ventricle. The apex-beat is displaced chiefly to the left and only slightly downwards, and may be normal, diffuse and indefinite, or altogether invisible. When the right ventricle is much enlarged, that chamber may displace the left ventricle backwards, so that the clinical apex-beat is formed entirely by the right, instead of the left, ventricle; in these cases systolic recession over the lower part of the præcordium is sometimes observed. Systolic recession in the third, fourth

and fifth intercostal spaces between the margin of the sternum and the parasternal line on the left side, or in the fourth and fifth intercostal spaces on the right side, may be present. The area of cardiac impairment is usually increased, especially to the right. The left border may also be displaced outwards, but rarely extends beyond the nipple line. The first sound in the tricuspid area is not infrequently louder than normal, and the second sound in the pulmonary area is usually accentuated.

In enlargement of the left auricle, the area of impairment may be higher than normal; when the right auricle is affected, there may be an extension outwards of the area of impairment in the third and fourth right intercostal spaces.

For the results of X-ray examination, see pp. 928–930; and of electrocardiographic examination, pp. 1005–1007.

In cardiac dilatation, the pulse may be more frequent, of smaller amplitude, and weaker, and the blood pressure lower than normal. The apex-beat is displaced chiefly outwards. It may be diffuse and weaker or occasionally tapping in character. The area of cardiac impairment is increased transversely, being more so to the left when the left ventricle is chiefly involved, and vice versa. The first sound may be diminished, and may also be short, sharp and clear, and the long pause may be diminished. A mitral systolic bruit may be present on account of relative incompetency of this valve.

The signs of dilatation of the right ventricle are the same as those of hypertrophy, excepting that there is an absence of a heaving impulse; and a tricuspid systolic bruit may be present, due to relative incompetency of this valve.

The signs of dilatation enumerated above may be modified by those of the cause of the condition or of accompanying hypertrophy.

In the case of chronic valvular disease, any pre-existing murmur or murmurs may become weaker or even inaudible when dilatation occurs.

When cardiac hypertrophy and dilatation co-exist in the same individual, there is a blending of the signs of both.

Diagnosis.—A diagnosis of cardiac hypertrophy or dilatation may be made from the signs described. The most reliable method of determining enlargement of the heart, including of the various chambers, is X-ray examination.

A diagnosis of enlargement of any chamber should not be made merely from displacement of the apex-beat, or the presence of pulsation or impairment of percussion in an abnormal area, for these may be due to other causes, as, for example, morbid conditions of the lungs or pleuræ. Again, a mere increase in the force of the apex-beat is sometimes met with in nervous subjects. The most reliable physical sign of hypertrophy of either ventricle is an increase of force together with slowing of the out-thrust. The diagnosis of enlargement of the left auricle is very difficult; that of the right auricle is more easily detected.

The diagnosis of dilatation from hypertrophy is readily made by comparing the physical signs of both. It is sometimes difficult to recognise great cardiac dilatation, especially of the right ventricle, from pericardial effusion. The matter is dealt with on p. 960. Cardiac dilatation should also be distinguished from those cases of mitral stenosis in which there is an absence of the characteristic murmur at the time of the examination. It is,

further, sometimes necessary to exclude a right-sided pleural effusion displacing the heart to the left.

Prognosis.—That of hypertrophy depends upon the cause. Whatever the cause, however, if long continued it is apt to be followed by pathological dilatation. The outlook of pathological cardiac dilatation depends upon the cause, the size of the heart, the degree of cardiac failure, and its response to treatment.

Treatment.—The treatment of hypertrophy depends upon the causal condition. In pathological dilatation, the first consideration is the recognition and treatment of the cause. In addition, the treatment is that of cardiac failure, and the various therapeutical measures described on pp. 861–875 should be considered in detail.

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DISEASES OF THE PERICARDIUM

PERICARDITIS

The varieties of pericarditis which may be met with are the acute—which may be divided into the fibrinous or dry, and pericarditis with effusion, which may be sero-fibrinous, purulent, or hæmorrhagic; and chronic adhesive pericarditis or adherent pericardium.

ACUTE PERICARDITIS

Ætiology.—The affection occurs most commonly in young adults, but may be found at any age, according to the infection which causes it, and is more frequent in males. It is generally due to one of the acute infective diseases, especially acute and subacute rheumatism—the most common cause—pneumococcal infections, particularly empyema, and septicæmia and pyæmia, while pulmonary tuberculosis is not rare. It also occurs as a terminal event in various chronic diseases, *e.g.* chronic nephritis, in coronary occlusion with infarction, neoplasm, usually metastatic, and in perforating wounds of the chest.

Sero-fibrinous pericarditis usually begins as the fibrinous form, this being quickly followed by a serous exudate, but it may start insidiously, *e.g.* in tuberculosis.

Purulent pericarditis may result from a general systemic pyæmia occurring in staphylococcal, streptococcal, pneumococcal, and rarely gonococcal infection. It may also follow the direct spread of infection from an adjoining focus of suppuration, as in empyema, or, much less common, a pulmonary vomica. *Hæmorrhagic* pericarditis usually results from tuberculosis or neoplasm.

Pathology.—Acute fibrinous pericarditis may be local or general in distribution. If local, the base of the heart adjacent to the great vessels is principally affected. In the early stages the smooth and shiny pericardium loses its lustre because the exudation of lymph coagulates on the surface,

and this may wholly cover both the visceral and parietal pericardium. This layer of fibrinous exudate may assume great thickness, and the resulting ragged honeycombed appearance has earned for it the title of "bread-and-butter" pericarditis. In at least most cases there is some degree of myocarditis.

Resolution of the fibrinous exudate is usually not complete and organization takes place, the results of which vary from what are called "milk spots" to various degrees of permanent fibrous adhesions between the two layers of the pericardium and adhesions outside the pericardium (see page 961).

A few words about "milk spots" or "soldier's spots" may here be made. These are probably much more often due to pressure outside the pericardium causing friction between the two layers than the result of acute fibrinous pericarditis. They are localized patches on the epicardium which are slightly thickened, smooth, opaque, and of milky-white colour.

In sero-fibrinous pericarditis the serous exudate may vary up to a great amount which may even distend the pericardial sac and produce the pressure on the heart, the adjacent structures in the mediastinum, the lungs, the superior and inferior vena cavæ, and the hepatic veins.

Symptoms.—In *acute fibrinous pericarditis* the clinical picture varies considerably. Occasionally there is an absence of symptoms throughout the whole course. Usually there is a rise of temperature, and occasionally the onset of this complication is signalled by a rigor. There is generally shortness of breath. Discomfort or pain is perhaps usual. It may be in the præcordium or referred to the upper part of the front chest, the neck, the left shoulder, the left scapular region, or upper part of the abdomen. It may be constant and dull, or intermittent and sharp in character. If there is pleuro-pericarditis, particularly if the diaphragmatic pleura is involved, it may be severe and increased by deep breathing and cough. There may be leucocytosis.

The cardiac rate is generally increased. The characteristic physical sign is a friction sound, and occasionally there is a corresponding fremitus. The former usually accompanies ventricular systole and diastole, is of a to-and-fro character, with generally a short pause between the two portions. Sometimes it is only ventriculo-systolic, while at others, when the inflammation involves the auricle, it occurs during auricular systole, ventricular systole, and ventricular diastole, giving rise to triple sounds. In any case, the different portions of the friction sounds do not absolutely coincide either in rhythm or duration with any period of the cardiac cycle, being rather later than any of them and usually heard during portions of more than one period. The adventitious sound is usually first audible over the apex or the base of the heart or over the right ventricle, but later may become audible over the whole præcordium. The area of the maximum intensity is variable, and does not absolutely correspond with any of the valvular areas. As a rule, the sound is either not at all or only slightly conducted, and there is no definite selective direction of propagation. It is of a rubbing quality, and either coarse or grating or fine and creaking, and is superficial, giving the impression of being produced immediately beneath the stethoscope, while moderate additional pressure with the bell of the stethoscope usually causes an increase in its intensity. The locality, the distribution, the character, and the loudness of the friction may quickly change from time to time. It

may also not be so well heard when the patient is lying down as when he is sitting up. The heart sounds are generally audible.

There may be physical signs of dilatation of the heart (see page 756).

In *sero-fibrinous pericarditis* the clinical picture varies with the amount of fluid and the rate at which it accumulates. If the amount is small there may be no symptoms. If, on the other hand, it is considerable or large and especially if the accumulation is rapid, discomfort and pain are usually increased though they may be even less. There may be a sense of oppression in the chest. Generally the patient has an anxious expression, and is pale and it may be cyanosed. Restlessness and insomnia are frequent, and there may be mild delirium, or drowsiness or coma, while occasionally acute cerebral attacks are met with. There may be effects due to pressure on the heart, the great vessels, the trachea, bronchi, lungs, the phrenic nerve, and the œsophagus. There may be such symptoms as faintness, orthopnœa, paroxysmal dyspnœa, an irritating cough, distension of the jugular veins, those of right-sided heart failure, hiccough, and dysphagia.

Unless the amount of fluid is such as to separate completely the two layers of the pericardium, friction sound usually persists.

The cardiac rate is usually increased. If the amount of fluid is large, the systolic blood pressure falls and the pulse pressure is diminished, and the radial pulse may become very small or disappear during inspiration —the pulsus paradoxus. Not infrequently, particularly in children, there is prominence of the præcordium, and the intercostal spaces may be widened or even bulge, as well as the ribs, and there may also be prominence of the epigastrium, which may be due to downward displacement of the left lobe of the liver. Occasionally there is local œdema of the chest wall. There may be diminished expansion of the left chest, and also lessened movement of the diaphragm, especially on the left side. As the amount of fluid increases, the apex-beat becomes less and less definitely felt, until it may be imperceptible unless the heart is fixed to the chest wall by adhesions resulting from a previous pericarditis. The area of cardiac impairment increases in all directions and progressively, in some cases considerably and even very greatly. The shape of the area is affected by a change of position of the patient. In the recumbent position, the base of the cardiac dullness is broadened and the outline of the area of impairment as a whole is globular; and there may be impairment of resonance in the cardio-hepatic angle—Rotch's sign. In the upright position the base becomes narrower and the outline of the area resembles a pear hanging down from its stalk. The foregoing may also be determined by radioscopy. This method of examination may, in addition, show diminution or absence of cardiac pulsation. With an increasing amount of fluid, the cardiac sounds become progressively diminished and muffled. The pressure of the effusion on the left lung may result in dullness of percussion note, tubular breathing, and ægophony over the base—Bamberger's or Ewart's sign. In some cases the electro-cardiograms are similar to those of coronary occlusion.

In *purulent pericarditis* marked tachycardia, persistent and severe pyrexia, which may be of the septic type, often with rigors and sweating, increasing pallor and prostration, and increased leucocytosis may be present.

Diagnosis.—The diagnosis of the fibrinous variety is usually not difficult. It rests upon the detection of the characteristic friction sound.

It should be differentiated from a double endocardial murmur or, if the friction sound be single, from a single one by the absence of the features already described. Moreover, the position, intensity, and character of the friction may alter in a few hours. It should also be distinguished from pleuro-pericardial friction. In the case of the latter, the friction sound is affected by the different phases of respiration and is abolished by the cessation of breathing. Further, pleuritic friction generally disappears with the effusion of fluid, whereas in sero-fibrinous pericarditis, friction is usually not abolished unless the quantity of fluid is great.

Sero-fibrinous pericarditis can be diagnosed from the clinical picture described, and valuable help may be obtained by X-ray examination. Acute dilatation of the heart, hydropericardium, left localized pleural effusion, pulmonary consolidation, thoracic aneurysm, enlarged glands, abscess of the mediastinum, and, particularly in the case of children, an acute abdominal condition should be excluded.

The differential diagnosis from acute cardiac dilatation is sometimes difficult. In its consideration the following are of help: The matter of ætiology. In dilatation the apex-beat is generally diffuse. The first sound may not only be diminished but may also be short, sharp, and clear. Excepting in mitral stenosis, the area of cardiac impairment does not extend so high; it is increased laterally more than upwards; and its shape is not affected in the manner described by a change of position of the patient. On X-ray examination there is also no diminution or absence of the cardiac pulsation. The abdominal organs are not displaced downwards.

Prognosis.—The immediate outlook in the fibrinous variety depends upon the ætiology of any associated morbid affection; in itself it is not of serious significance. That of sero-fibrinous pericarditis also depends upon the severity of the clinical picture, and the nature and the amount of the serous exudate. It is serious if the effusion is purulent or hæmorrhagic.

The ultimate prognosis in both varieties is related to the extent, the character, and the locality of any resultant chronic adhesive pericarditis.

Treatment.—Naturally the cause and any associated morbid condition should receive attention.

The general treatment is the same as that of acute simple endocarditis (see pp. 917, 918).

In sero-fibrinous pericarditis, paracentesis pericardii should only be considered if there is reason to believe that the amount of fluid is such as to cause very serious embarrassment to the cardiac action, and is comparatively rarely necessary in rheumatic cases. The site chosen for this procedure varies, and more than one may be tried if required, as the fluid may be localized due to a previous attack of acute pericarditis. It may be performed just outside the apex-beat and just inside the area of cardiac impairment. Or high up in the angle between the ensiform cartilage and the left costal margin of the sternum, passing the needle upwards, backwards, and slightly inwards. Or in the fourth, or fifth, or, if the amount of fluid be large, the sixth, left intercostal space close to the sternum. Failing these, if the amount of fluid is large, in the left posterior thoracic wall, in the seventh or eighth intercostal space in the mid-scapular line with the left arm in a raised position.

The treatment of purulent pericarditis consists in incision and drainage

of the pericardial sac, unless the general condition of the patient is too grave to allow of it.

Chronic Adhesive Pericarditis or Adherent Pericardium

In this form of pericarditis there are permanent fibrous adhesions between the two layers of the pericardium.

Ætiology.—The condition may follow acute pericarditis, or may be due to a primary chronic inflammation of unknown ætiology.

Pathology.—Chronic adhesive pericarditis varies considerably in its distribution and severity. The morbid affection may be conveniently divided into four groups, namely: (1) Localized, in which event it is usually situated at the base of the heart close to the great vessels, or near the apex, and the adhesions are generally light. (2) The adhesions are extensive or even complete, but light. (3) They are extensive or even complete, and dense and exhibit much thickness, obliterating the sac and even firmly binding together the visceral and parietal layers—*chronic constrictive pericarditis*. Sometimes the adhesions calcify. (4) The morbid process may occasionally extend outside the pericardial sac to involve the mediastinum—*mediastino-pericarditis*; in which condition there may be adhesions between the pericardium and the mediastinal structures, the chest wall, the pleura, or the diaphragm. In the third and fourth groups the large vessels entering and leaving the heart may be constricted by the adhesions, and this may interfere with the influx and egress of blood. The venæ cavæ are most affected. Constriction of the hepatic veins may give rise to chronic venous congestion of the liver, and ultimately some degree of cirrhosis—*Pick's disease or syndrome, or mediastino-pericardiac pseudo-cirrhosis of the liver*.

In the first and second groups, the condition in some cases gives rise to slight or at the most moderate cardiac enlargement. In the third and fourth, the heart is enlarged and, especially in the latter, it may be considerably so.

There is often co-existent chronic valvular disease, and if so it usually gives rise to cardiac enlargement, and there may also be involvement of the myocardium.

Symptoms.—Taking all cases of chronic adhesive pericarditis, in a large proportion of cases there is an absence of symptoms throughout, and the condition may only be discovered at necropsy, or, if there is calcification, during radioscopy of the chest. The degree of symptoms depends upon how much the morbid affection interferes with the cardiac action and so involves extra work on the part of the heart.

In the first two groups described, some cases in the course of time exhibit slight or moderate cardiac insufficiency.

The third and fourth groups always entail extra work on the part of the heart, and shortness of breath and evidence of congestive failure usually supervene in the course of time. The following signs may be present: Pulsus paradoxus. Prominence or, less frequently, flattening of the præcordium. The cardiac pulsation may be increased in area, and may occasionally extend even from the second intercostal space to the apex-beat and from the right parasternal line to beyond the mid-clavicular line, and may be wave-like and undulatory in character. If there are adhesions between the pericardium and the chest wall there may be systolic retraction in the vicinity

of the apex-beat, of the intercostal spaces on either side of the sternum, of the lower end of the sternum and of the adjacent costal cartilages, and in the epigastrium; and if there are adhesions between the pericardium and diaphragm, there may be the same in the region of the eleventh and twelfth ribs posteriorly on the left side—Broadbent's sign. The apex-beat and the left border of the heart may be displaced outwards, and the force of the former may be increased. There may be little or no change in the position of the apex-beat and that of the heart with a change of position of the patient or on deep respiration. When there are adhesions between the heart and the diaphragm or sternum, there is limitation, or absence of movement during respiration. Diastolic collapse of the veins of the neck (Friedreich's sign) is seldom present. A loud and rough first sound in the mitral area may be met with, and may simulate a presystolic murmur.

Radioscopy will reveal some of the foregoing, and in addition there may be: diminished amplitude of the pulsation of the heart; bands of adhesions connecting the parietal pericardium to the mediastinal structures, the chest wall, the pleura, or the diaphragm; and calcification of the adhesions.

In constrictive pericarditis, hepatic enlargement, ascites, and visible distension of the jugular veins are out of proportion to œdema of the lower extremities. There may be swelling of the face. There is persistent increase in the venous pressure. The pulse is small and the blood pressure is diminished. Pleural effusion is sometimes met with. Unless extra-pericardial adhesions are also present, any enlargement of the heart does not exceed that of moderate degree.

Electro-cardiograms usually show low voltage of the *Q*, *R*, *S* deflections, or diminished amplitude or inversion of the *T* deflections, or both.

Diagnosis.—This may be a matter of very considerable difficulty. A positive diagnosis should not be made from the presence of one physical sign alone excepting perhaps in the case of systolic recession of the sternum itself. It is, however, different when at least several are present, especially if there is right-sided cardiac enlargement and failure in the absence of mitral and chronic pulmonary disease, and particularly if there is a history of acute pericarditis, or of acute or subacute rheumatic infection. Pulsus paradoxus occurs also in sero-fibrinous pericarditis and some other conditions. Slight systolic recession in the epigastrium is not infrequent in health. Systolic recession of the apex-beat, of the intercostal spaces on either side of the sternum, and of the epigastrium may also be due to an enlarged right ventricle; and that of the lateral and posterior walls of the left side of the chest has been observed in marked enlargement of the heart. Systolic recession of the sternum itself is perhaps pathognomonic. An absence of alteration of the position of the apex-beat and of the heart with change of position of the patient or on deep respiration may be found in pleural adhesions. Radioscopy is a valuable aid in diagnosis. Evidence of calcification is pathognomonic.

Constrictive pericarditis may be diagnosed from the clinical picture described. Recurring ascites in the absence of œdema elsewhere is exceedingly suggestive. The result of electro-cardiographic examination is generally of help. The condition should be diagnosed from true cirrhosis of the liver, chronic renal disease, and polyserositis. Such is not difficult.

Prognosis.—The outlook in the first two groups is good, the duration

of life not being affected and the patient's capacity little or not at all. The same largely applies in the third group in the absence of constrictive pericarditis. If such is present, the immediate outlook is not unfavourable but in the absence of successful surgical treatment a life of invalidism is almost always inevitable. The prognosis in mediastino-pericarditis will depend upon the extent of the morbid affection and the degree of any existing cardiac failure.

Treatment.—If such is indicated, the various measures described on pp. 861–973 should be consulted. Otherwise the treatment consists in the consideration of surgical measures in certain cases.

There are two procedures, namely, that recommended and practised by Bauer, and the other by Delorme. The first is employed when there are extensive and firm adhesions between the pericardium and the chest wall. It consists in the removal of several ribs and costal cartilages on the left side over the præcordium, and dividing the adhesions. This is a comparatively simple operation with a relatively low mortality, and is often very successful. The other procedure is used in chronic constrictive pericarditis with an absence of external adhesions. It consists of decortication, *i.e.* the removal from the surface of the heart of as much as possible of the adhesive tissue, and also dividing any adhesions which may constrict the blood vessels. This is a much more difficult and dangerous operation, but in some cases the results have been brilliant.

Surgical measures are only indicated in carefully selected cases and if performed by those with special skill and experience.

HYDROPERICARDIUM

A certain amount of fluid is usually found in the pericardium after death. In hydropericardium, or dropsy of the pericardial sac, the amount is in excess.

The condition is always secondary. It is usually due to cardiac or renal disease, in which event there is generally hydrothorax or ascites, or both. Rarely it is the result of obstruction of the veins by aneurysm, enlarged glands, or new-growths, or of cachectic conditions.

The clinical features are those of the primary affection and of serofibrinous pericarditis except that there is an absence of friction on auscultation.

The prognosis is that of the primary condition.

The treatment is that of the causal affection together with the restriction of the daily amount of fluid and the administration of diuretics. If urgent symptoms appear to demand it, parancentesis may be performed; this, however, is rarely necessary.

PYOPERICARDIUM. (Purulent Pericarditis, see pp. 957, 958)

HÆMOPERICARDIUM

By this is meant the presence of blood in the pericardial sac, occurring apart from pericarditis.

The condition may be due to rupture of the aorta, one of the coronary arteries, or the heart, perforation of the œsophagus, punctured wounds, or the result of purpura or scurvy.

There may be sudden death; or there may be sudden pallor, syncope, and collapse, and the patient may live for some hours or even months.

Except in some traumatic cases in which surgical interference is possible, the outlook is hopeless.

The treatment is limited to immediate surgical operation in certain cases.

PNEUMOPERICARDIUM

Definition.—By pneumopericardium is meant the presence of air in the pericardial sac. It is a very rare condition. Pericarditis is always present, with serous (pneumo-hydropericardium), purulent (pneumo-pyopericardium), or hæmorrhagic (pneumo-hæmopericardium) effusion.

Ætiology and Pathology.—The affection may be due to wounds through the chest wall, or the result of communication with an air-containing organ or cavity, such as occurs in abscess or gangrene of the lung, pneumothorax, malignant disease of the œsophagus, gastric ulcer, and hepatic

Effusion of fluid, very frequently purulent, usually develops in the course of time.

Symptoms.—The onset may be sudden or gradual. Breathlessness, præcordial discomfort or even pain, faintness or syncope, and cyanosis are the most constant symptoms. There may be a certain amount of bulging of the præcordium; the apex-beat is diminished in force or even absent; on percussion, a tympanitic note is to be observed; and the cardiac sounds are diminished. On X-ray examination the air within the pericardium is evident.

If fluid is present the tympanitic area diminishes, and its site varies according to the position of the patient. In the recumbent position it may be heard over most of the præcordium, while if the patient be sitting upright the lower part of the præcordium becomes impaired and the upper part hyper-resonant. This is confirmed by X-ray examination. On auscultation, metallic and splashing sounds, resembling those produced by a water-wheel or a churn, synchronous with the movements of the heart, are audible; these sometimes become more pronounced on shaking the patient, and occasionally may be heard at a considerable distance. Pericardial friction is sometimes also to be noted.

Diagnosis.—The diagnosis is not difficult when the features enumerated are present. Care, however, should be taken to exclude a large pulmonary vomica in the neighbourhood of the heart, a left-sided pneumothorax, and dilatation of the stomach.

Prognosis.—The majority of cases die within the course of a few days. Traumatic cases, however, have been known to recover; the wound may heal and the air be absorbed.

Treatment.—In traumatic cases, paracentesis of the pericardial sac, with free incision and drainage if the fluid be purulent, is advisable. In other cases, treatment is usually palliative.

TUBERCULOSIS OF THE PERICARDIUM

Tuberculosis of the pericardium is not so rare as is generally supposed. It is usually secondary to tuberculosis of the mediastinal glands, the pleura, or elsewhere, but it may be part of a generalized tuberculosis, and some cases have been recorded in which apparently it was primary.

The morbid affection may be of the fibrinous type, ending in adhesions, which may be very thick; or it may give rise to effusion, varying from a small to a very large amount, in which event the membrane is often thickened and sometimes the fluid is hæmorrhagic.

In the case of fluid the onset may be slow and insidious. There may be pressure symptoms. The conditions may be recognised by percussion and X-ray examination.

In tuberculosis of the pericardium there may be, in addition to the usual symptoms, loss of weight and strength, and pyrexia.

A diagnosis may be made from an absence of rheumatism or other cause, the features described, and there may be evidence of tuberculosis elsewhere.

The fluid sometimes resolves spontaneously. The treatment is that of pericarditis together with that of tuberculosis.

FREDERICK W. PRICE.

OTHER DISEASES OF THE HEART OR PERICARDIUM

ANEURYSM OF THE HEART

Aneurysm of the heart may occur in its valves, or walls, or in the coronary arteries.

Acute aneurysm of the valves may occur in septic endocarditis, the semilunar being more commonly affected than the auriculo-ventricular valves. The aneurysm bulges in the direction of the blood current; rupture may take place, giving rise to perforation and valvular incompetence.

Acute aneurysm of the walls of the heart may take place in acute mural septic endocarditis, usually in the interventricular septum, in the neighbourhood of the undefended space. A diagnosis is scarcely possible.

Chronic aneurysm of the walls of the heart is comparatively rare. In the vast majority of cases it is the result of coronary occlusion with infarction of the heart (see page 991), but occasionally is due to fibrosis of the myocardium independent of such, and rarely to traumatism, the result of a stab, or to gummata.

In the majority of cases the anterior apical portion of the left ventricle is affected, or, less frequently, the aneurysm is found in the posterior wall of the left ventricle near the base. The aneurysm consists of a sac or localised depression, communicating with one or more chambers of the heart, the size varying from that of a small marble to an orange, or even larger. Its wall is formed of fibrous tissue and muscle-cells, in varying proportion,

according to the length of time it has been in existence. Occasionally a certain amount of calcareous matter is present. The endocardium is thickened and is often lined by laminated clot, which may give rise to emboli. The pericardium over the affected area is usually adherent.

The symptoms of aneurysm are those of general cardiac failure. The area of cardiac impairment may be increased, and occasionally a tumour in the region of the apex may be detected.

A diagnosis may be made from the history, the clinical features, and the results of X-ray examination.

Sudden death is not of uncommon occurrence, although rupture is comparatively rare.

Aneurysm of a coronary artery is rare and is usually due to atheroma.

WOUNDS OF THE HEART

Wounds of the heart are not of very uncommon occurrence. They may be the result of stabbing, bullet wounds, a paracentesis needle, or the passage of foreign bodies from the œsophagus. Recovery occurs in a fair proportion of cases, especially when due to stabbing. Treatment of these cases is purely surgical.

RUPTURE OF THE HEART

Rupture of the heart is a rare event, and recent observations suggest that in the great majority of cases it is the result of coronary occlusion with infarction of the heart (see above), but occasionally is due to fibrosis of the myocardium independent of such, and rarely to fatty degeneration or to traumatism. In the majority of cases the anterior apical portion of the left ventricle is affected, or, less frequently, near the base of that chamber or in the interventricular septum.

Rupture of the heart occurs nearly always during physical exertion. It may result in sudden death ; or its occurrence may be indicated by sudden agonising pain, intense dyspnœa, pallor, syncope, and collapse. In the latter case, the patient may live for some hours or even days.

CONTUSION OF THE HEART

This may result from the driver of a motor-car being thrown violently against the steering-wheel, or a very severe blow to the chest wall.

The symptoms and electro-cardiographic findings may resemble those of a coronary occlusion.

NEW-GROWTHS OF THE HEART AND PERICARDIUM

Neoplasms arising from the heart or pericardium are rare and relatively unimportant. Secondary neoplasms resulting from metastases from malignant disease elsewhere in the body, or from direct extension of malignant

disease of the œsophagus and lungs, are much more common than primary neoplasms, of which sarcoma and myxoma form the most frequent types.

It is seldom possible to diagnose neoplasms of the heart and pericardium before death. Radioscopy has permitted a diagnosis in rare instances. The prognosis is hopeless, and treatment by surgery or radiotherapy in the few cases recognised during life has been of little avail.

CONGENITAL HEART DISEASE

Ætiology.—Congenital heart disease is comparatively rare; it is found in about 2 per cent. of all patients suffering from organic morbus cordis. In the great majority of cases the condition is the result of some abnormality of development, but very occasionally a fœtal endocarditis would appear to be responsible. Heredity is probably a factor. The incidence is said to be relatively more frequent in first-born children. Some of the individual lesions are equally distributed among males and females, but in Maude Abbott's classical series, certain conditions, such as primary dextro-cardia, cor biloculare, cor triloculare and co-arctation of the aorta were found to be much more common in the male; and simple patency of the ductus arteriosus was more frequent in the female. The right side of the heart is more often affected than the left, and the pulmonary orifice very much more frequently involved than the tricuspid.

Other congenital anomalies are often present in congenital morbus cordis.

Varieties.—There are many varieties of congenital heart disease. A combination of several lesions is usually present, a single lesion being uncommon.

In ectopia cordis the heart is situated outside the thoracic cavity; it may lie in the neck (ectopia cervicalis) or outside the chest wall (ectopia pectoralis), or in the abdominal cavity (ectopia abdominalis). In meso-cardia, the heart occupies the mesial position of the thoracic cavity, the apex being in the epigastrium.

In dextro-cardia, the heart lies on the right side of the thoracic cavity, with the aortic and mitral orifices on the right, and the pulmonary and tricuspid orifices on the left, side. This variety of congenital heart disease is usually associated with transposition of the viscera. Dextro-cardia without transposition of other viscera is very uncommon, and when it occurs it is generally accompanied by some other cardiac lesion.

Defects of the pericardium may be met with.

Defects in the Interauricular Septum.—The foramen ovale is a valve-like opening between the auricles that during fœtal life allows the passage of blood from the venous to the arterial circulation without going into the lungs. It usually closes soon after birth and is generally completely impervious within a few weeks of life. The membrane closing the foramen ovale may, however, be defective at one point, leaving a valve-like slit, or it may be perforated by small fenestrations. Such changes may be observed in about one-fourth of all post-mortem examinations, and are not to be regarded as of any clinical importance. A widely patent foramen ovale may occur without other congenital abnormalities, but is generally associated with such lesions as pulmonary stenosis, or transposition of the great arterial

to divert most of the blood in the fœtus from the pulmonary artery into the aorta. It usually closes soon after birth. A patent ductus arteriosus is, however, a relatively frequent congenital lesion. It may vary in degree from a very fine passage to a comparatively wide canal. It may occur without any other congenital cardiac defect, but is more commonly compensatory to some such lesion. Thus, it may be associated with a pulmonary stenosis, in which case it serves to convey the blood from the aorta to the branches of the pulmonary artery; or with the congenital type of co-arctation of the aorta, in which event it will enable the aorta to be filled with blood from the pulmonary artery.

Congenital anomalies of the auriculo-ventricular valves occur very infrequently. In this connection, a considerable proportion of cases of tricuspid stenosis or atresia are congenital in origin, while tricuspid incompetence is rarely so, though it may be associated with pulmonary atresia. Congenital lesions of the mitral valve are much more rare than those of the tricuspid orifice.

Anomalies of the coronary arteries and of the great veins, and arteriovenous aneurysm are very rarely found.

Symptoms.—The subjective symptoms of congenital heart disease vary in intensity according to the site and degree of the lesion. Septal defects generally have a less disturbing effect upon the circulation than stenosis or atresia.

In congenital heart disease the symptoms are usually apparent soon after birth, but on the other hand nothing abnormal may be obvious until later on in life, and in some cases of septal defects the affection may be discovered only on physical examination or at necropsy.

Shortness of breath and cyanosis are the most common symptoms. The former is more frequent and may vary from a simple increase in the respiratory rate to extreme dyspnœa when cardiac failure is present. The degree of respiratory discomfort will depend upon the amount of oxygen unsaturation. Dyspnœa may occur in paroxysms during the time when there is a temporary increase in the amount of blood shunted into the systemic circulation, which in turn may lead to the occurrence or an increase of cyanosis. When there is marked dyspnœa, cough is common and hæmoptysis is not infrequent.

Cyanosis is found, in a slight to marked degree, in about half the cases; the term "morbus cœruleus" has, indeed, been applied to congenital heart disease. The cyanosis is in part due to the passage of unaerated blood directly from the right heart to the arterial system and in part to deficient oxygenation of the blood in the lungs, the latter the result of disturbances in the pulmonary circulation. Cyanosis will be seen in the skin and mucous membranes when the volume of reduced hæmoglobin in the capillaries rises above 7 per cent. It is usually most marked in the lips, nose, the malar region and the fingers and toes, being especially noticeable in the nails. It may be confined to these localities, or may be more general. The degree of cyanosis varies up to a deep purple, and is increased on exertion. The lips and nostrils may exhibit thickening, and clubbing of the terminal phalanges of the fingers and toes is usually present, due to chronic venous congestion. In cases showing cyanosis, the blood is found to have increased viscosity, and its specific gravity may be as high as 1070. There is a considerable

increase in the number of erythrocytes, and the number may occasionally reach 9,000,000 per cubic millimetre, and rarely even more. The hæmoglobin is also increased, and may be up to 160 per cent. The leucocyte count is unchanged, unless there is a complicating infection.

The temperature of the skin tends to be subnormal. The subjects of congenital heart disease are very susceptible to any fall of temperature, and are particularly liable to attacks of bronchitis. There is generally retardation of growth, and in many cases wasting. The mental condition is, as a rule, backward, and the patient is frequently dull and lethargic. As the result of anoxæmia, there may be syncopal attacks, which may even give rise to prolonged unconsciousness, while epileptiform attacks may also occur. There is a tendency to hæmorrhages from the nose and gums, and less often from the lungs.

The pulse may be quickened in rate. There is usually evidence of cardiac enlargement, of varying degree, the right side of the heart being especially affected. Frequently a murmur, and sometimes a thrill, usually systolic in time, are to be noted. While the point of maximum intensity of the murmur is commonly over the pulmonary area, it may be difficult or impossible to define. Usually the murmur is rough and harsh, and may be very loud, though it may be faint. The pulmonary second sound may be normal, diminished or increased in loudness. Distension or pulsation of the jugular veins may be present. The veins of the retina are dilated and tortuous, and both arteries and veins are much darker than normal. When there is marked congestion, retinal hæmorrhages may occur.

Other bodily malformations are not infrequently to be noted.

Indications of increasing chronic venous congestion, such as œdema, which at a later stage becomes general, hæmorrhages, hepatic enlargement, albuminuria, hæmoptysis and transudation of fluid into the serous sacs may supervene.

The chief complications of congenital heart disease are subacute bacterial endocarditis or endarteritis, one of the acute infective diseases, especially pneumonia and pulmonary tuberculosis, syncope, coma, convulsions, and hemiplegia, the result either of thrombosis or hæmorrhage. Paradoxical embolism may occur in subjects with a patent septum.

We will now pass to the consideration of the symptomatology of the individual lesions.

In dextro-cardia there is usually an absence of any subjective symptoms, and the lesion is only discovered accidentally, unless some other congenital abnormality causes symptoms. The apex-beat is on the right side of the thorax, and the point of maximum intensity of the aortic second sound is on the left instead of the right side. X-ray examination will reveal the condition. The other viscera are usually transposed, and if such is not the case, there is generally some co-existing cardiac lesion.

In uncomplicated patency of the interauricular septum when the defect is small, not infrequently there is an absence of subjective symptoms, and consequently the condition may not be discovered during life. In the case of a wide patency, the heart is enlarged, especially the right auricle and the right ventricle, which apparently receive additional blood from the left auricle. Systolic murmurs are present in about a quarter of the cases, and are best heard over the base or the midsternal region; and rarely a thrill has

been noted. Radioscopy may show enlargement of the right auricle and right ventricle, a prominent pulmonary arc and distension of the pulmonary branches.

When patency of the interventricular septum exists alone, *i.e.* Rogers's disease, the subjective symptoms may be slight. Cyanosis will not be present unless there is a veno-arterial shunt permitting one-third of the venous blood to pass through the septal defect from the right to the left ventricle. If the defect is large, the right ventricle will be hypertrophied. The characteristic signs of a patent interventricular septum are the presence of a systolic murmur, sometimes accompanied by a thrill, heard best in the third and fourth left intercostal spaces just to the left of the sternum, but it may be audible over the whole of the præcordium and both sides of the chest posteriorly. It is not conducted to the vessels of the neck. The intensity of the murmur will vary inversely with the size of the defect in the septum, and patients with loud murmurs may have no symptoms. In those cases described by Roger, the murmur commenced early in systole and was prolonged into diastole, and the point of maximum intensity was in the middle line over the upper third of the præcordial region. In patency of the interventricular septum, the second sound at the base in some cases is obscure, and in others is quite distinct. Usually there are manifestations of other congenital cardiac lesions, and these then predominate.

In congenital pulmonary stenosis, cyanosis is a feature in the vast majority of cases, because some other lesion is usually present. It is then noted within a few weeks of birth, but in rare instances may only make its appearance some years afterwards. Clubbing of the fingers, polycythæmia and defective growth are common. There is a harsh and loud systolic murmur, with its point of maximum intensity in the second intercostal space just to the left of the sternum, which may be audible over a considerable area of the chest and may be conducted upwards and outwards towards the left shoulder, but not to the vessels of the neck. There is often a systolic thrill. The pulmonary second sound is usually diminished or practically absent. X-ray examination is of considerable value in diagnosis. In cases of Fallot's tetralogy the cardiac apex is lifted away from the diaphragm, and there is sometimes concavity in place of the shadow of the pulmonary artery, but often the pulmonary arc is prominent. The ascending aorta is seen to pass up on the right side of the spine. The physical signs of congenital stenosis at the aortic orifice are the same as those of the acquired form of the disease.

The evidence of co-arctation of the aorta may be so slight that the lesion may entirely escape notice during life. The condition should be suspected when there is an inequality of blood pressure and pulse volume in the arms and legs respectively; the brachial systolic blood pressure may be considerably raised, even up to 200 mm. or more, while the femoral blood pressure is low, 100 mm., and the femoral pulse is small. The pressure in both arms is generally equal, except in those infrequent cases in which the co-arctation occurs proximal to the origin of the left subclavian artery. There is evidence of a compensatory collateral circulation, and the internal mammary, intercostal, scapular and deep epigastric arteries may be dilated and tortuous. A long systolic murmur, rarely accompanied by a thrill, may be heard over the aortic area and præcordium, and the murmur may be transmitted along the course of the dilated anastomosing vessels. X-ray examination will

show enlargement of the left heart, while there is a decrease or an absence of the shadow of the aortic knob with dilatation of the ascending aorta and the first part of the aortic arch. Erosion of the ribs by the dilated intercostal arteries may be seen. Marked co-arctation of the aorta may lead to heart failure, while rupture of the aorta, apoplexy due to cerebral hæmorrhage, and an infective endarteritis invading the area of the co-arctation may occur.

Hypoplasia of the aorta may be accompanied by a tendency to pallor, with slow and incomplete growth and a generally backward development.

When a patent ductus arteriosus occurs alone, there may be an absence of subjective symptoms. In other cases, there may be shortness of breath and slight cyanosis. When the lesion is compensatory to some associated congenital abnormality, such, for example, as a pulmonary stenosis, shortness of breath and cyanosis may be marked, and the patient is often under-developed. Characteristic of a patent ductus arteriosus is the presence of a murmur with certain features. Its point of maximum intensity is in the second left intercostal space close to the sternum. It may be systolic in time but usually is continuous during systole and diastole, beginning shortly after the commencement of the first sound and extending into a considerable part of diastole and it may be persisting throughout the cardiac cycle, frequently with systolic accentuation. The murmur is loud and harsh. It has variously been described as resembling the sound of a humming-top, or a mill-wheel. It is well conducted towards the left clavicle, but is not propagated downwards to the right or into the carotid arteries. There is generally a thrill. The second sound in the pulmonary area may be accentuated. Enlargement of the right ventricle and the conus arteriosus will tend to occur, and X-ray examination will show an abnormal bulging of the left upper border of the cardio-vascular shadow. As was pointed out by Gerhardt, the area of cardiac impairment may extend unduly to the left of the sternal border. In exceptional cases the patent ductus arteriosus may be the seat of an aneurysmal dilatation.

For Clinical Electro-cardiography in Congenital Heart Disease, see p. 1007.

Diagnosis.—While it is usually not difficult to say that congenital heart disease exists, the diagnosis of the variety is often fraught with great difficulty because of the frequent combination of defects and the variability of the physical signs.

In considering the question of diagnosis, the history of the case, the subjective symptoms, the existence or otherwise of evidence of enlargement of the right side of the heart, and the time of occurrence, the point of maximum intensity and the direction of selective propagation of any existing murmur, are all points which should be taken into account. X-ray examination may furnish valuable information with regard to differential diagnosis.

With regard to the diagnostic value of the various symptoms, it may be remarked
attack
anæmic and rickety subjects,
the fingers may exist in the acquired form of heart disease, more especially in mitral stenosis, while it may be absent in the slighter forms of congenital disease. It is also necessary to point out that in some cases of congenital

heart disease the right side of the heart may be only slightly enlarged. The murmurs are usually systolic in time, and loud, and their point of maximum intensity and direction of selective propagation are not so typical as those of the acquired form of heart disease. In cases of a non-functional systolic murmur, having its point of maximum intensity over the pulmonary area, the possibility of congenital heart disease should be thought of. It may, however, be exceedingly difficult, and indeed impossible, to distinguish functional basic murmurs from those of congenital heart disease during infancy and childhood by means of auscultation alone, though such murmurs are usually not so harsh as those due to congenital defects, and are not accompanied by cardiac enlargement or cyanosis. It should be recognised that a continuous murmur occupying systole and diastole may also be due to a venous hum transmitted from the neck as well as to arterio-venous aneurysm.

If there be a history of a marked cyanosis soon after birth, and of the presence of clubbing of the fingers, evidence of enlargement of the right side of the heart, and a systolic thrill and murmur whose point of maximum intensity and direction of selective propagation are not so typical as those of the acquired form of heart disease present in early life, a positive diagnosis of the congenital form of heart disease is not difficult. The discovery of congenital anomalies elsewhere in the body favours the diagnosis of congenital heart disease.

With regard to the differential diagnosis of the variety of the lesion or lesions, the reader is referred to the section on Symptoms, pp. 970–973.

Prognosis.—The prognosis of congenital heart disease exhibits wide variation. If the defect be slight, as, for example, a patent foramen ovale or a small opening in the interventricular septum, a considerable proportion of cases may live to an advanced age without experiencing at any rate pronounced subjective symptoms. Even in these cases, however, there is a liability to bacterial infection, especially of a streptococcal nature. Such is by no means infrequent, particularly in the case of bicuspid aortic valves and a patent ductus arteriosus, and is of serious significance, being always fatal. If the defect is severe, the prognosis is more serious. In a large proportion of cases the duration of life is brief and, indeed, the individual may die a few hours after birth. According to Paul White, the prognosis depends upon two factors: (1) The degree of anoxæmia, which is indicated to a certain extent by the degree of cyanosis; and (2) the amount of direct strain on the heart. It should be remembered that anoxæmia and cyanosis are not strictly comparable, for if there is a polycythæmia there may be a sufficient quantity of oxygen in the blood for the tissues, and yet there may in addition be enough reduced hæmoglobin to cause the cyanosis. Lastly, the prognosis is much influenced by whether the patient is well protected against an unfavourable environment and intercurrent disease.

Ectopia cordis is rarely compatible with extra-uterine life. Meso-cardia, dextro-cardia and defects of the pericardium are compatible with long life. Life cannot exist with a bilocular heart. Trilocular heart is compatible with life for some years, and, indeed, instances have been recorded in which individuals have lived to adult age; usually, however, the period of life is short. Persons suffering from septal defects not infrequently live to an advanced age. When patency of the interventricular septum occurs alone

and the opening is not large, the individual may live to past middle life; when it occurs in association with other lesions, the prognosis depends upon the latter. The prognosis of an individual suffering from pulmonary stenosis depends upon, besides those points already mentioned, whether there is a patent interventricular septum to afford relief to the over-distended right heart. Death may occur, on the one hand, within a few hours after birth, while, on the other, in the case of lesions of slighter grade, life may be prolonged for 5, 10 or 20 years, and occasionally even to middle life; indeed, if a patent interventricular septum be present in these slighter lesions, cases have been recorded in which patients have lived to the age of 60. Taking cases of pulmonary stenosis as a whole, however, most of the patients die at an early period of life. Pulmonary atresia is a much more serious condition, and life is prolonged for only a brief period. Cases of stenosis at the aortic orifice very rarely survive birth, and in those in which stenosis exists above the entrance of the ductus arteriosus, life is prolonged at the outside for a few months only, but when just below the entrance of the duct it may be prolonged till middle age or over. Cases of transposition of the great vessels do not survive for more than a few hours unless there is a septal defect, in which case they may live for some years, and instances up to adult or even middle age have been recorded. Persistence of the ductus arteriosus is not infrequently compatible with adult life, and individuals have been known to have lived even to old age.

Treatment.—The general measures previously laid down are applicable also to this affection. It is particularly important that the patient should be kept warm, and it is imperative that careful and detailed measures should be adopted for the prevention of bronchitis; if bronchitis should occur, adequate treatment should be adopted without delay. Even in the least serious lesions, care should be taken to guard against infection. When the tonsils are diseased, tonsillectomy is advisable in childhood if the risk is not unreasonable, but not during infancy.

If cardiac failure supervenes, or if any complication occurs, they are to be treated on the lines laid down elsewhere.

SYPHILITIC AFFECTIONS OF THE AORTA, THE HEART, AND THE PERICARDIUM

This subject is one of much importance and also of considerable difficulty, more especially as regards the relative frequency and diagnosis of the condition, which are intimately bound up with ætiological and pathological considerations. I shall confine my remarks to the acquired form of the disease.

Relative Frequency and Pathology.—Formerly the importance of syphilis as a cause of heart disease was not sufficiently recognised. Later the pendulum swung too much the other way. Thus, assertions that syphilis is responsible for a quarter to one-third of the total number of cases of organic disease of the heart, for about three-quarters of all cases of aortic incompetence and almost invariably for those in which there is an absence of a definite history of acute or subacute rheumatism, and is by far the most frequent cause of chronic myocardial disease are quite unwarranted.

As to the first, statistics vary exceedingly, but it is probable that syphilis accounts for less than 10 per cent. of all cases of organic heart disease in this country, though its incidence is higher in some non-European populations; it is the cause of about one-third of all cases of aortic incompetence and accounts for a considerable majority of those occurring between the ages of 40 and 60, especially in males; and is an important ætiological factor of angina pectoris under the age of 40. There is good reason for the belief that syphilis as a cause of heart disease is diminishing. Excluding the possible effect of the present war, it is much more often responsible for such in males than in females.

Syphilitic arteritis commences in the secondary stage but may only become marked in the tertiary.

Acquired syphilis may affect the aorta, which may involve the orifices of the coronary arteries; in the opinion of some writers, very rarely the coronary arteries themselves; the cardiac valves; and the myocardium.

The pathology of syphilis of the aorta (syphilitic mesaortitis) and its results are described on page 1031, and elsewhere.

The following considerations are among those noted: The first part of the aorta is the most commonly affected. Syphilis invades the aorta from without. The disease-process is the result of inflammation of the vasa vasorum and their terminations in the coats of the aorta. The adventitia and, later, the media of the areas of the aorta supplied by the inflamed vasa vasorum are secondarily affected, and the inflammation is mainly confined to these coats. The inflammation in the media is followed by absorption and, it may be, necrosis of the elastic tissue and muscle-fibres, and at a later date by new formations of fibrous tissues. The intima over the areas of inflammation is usually thickened. This is merely secondary, and is protective or compensatory. In its earlier stages, it is to be distinguished from atheroma by the naked eye. It is to be added, however, that in the later stages, atheroma usually occurs in the thickened intima over the areas of inflammation; also that syphilitic mesaortitis and primary atheroma may co-exist, especially in later life.

The weakening of the middle coat of the aorta by syphilitic aortitis leads to dilatation of its lumen. This may be general (diffuse aneurysm), or localised (circumscribed or saccular aneurysm); the latter is usually accompanied by some degree of the former.

Syphilitic aortitis may give rise to narrowing or complete occlusion of the coronary arteries (see p. 948). As stated, in the opinion of some, syphilis may rarely affect the vessels themselves. The disease-process in the aorta may spread to the aortic cusps, giving rise to incompetence of the valve (see p. 932), and in the opinion of some it rarely extends to the base of the aortic cusp of the mitral valve. Syphilis may cause fibrosis of the myocardium, (see p. 949). Gummata are relatively rare. The commonest site is in the septum, especially high up, and in the case of the latter the conducting system may be implicated and auriculo-ventricular block may result, but they may also occur in the wall of the heart.

In congenital syphilis, spirochætes are frequently numerous throughout the myocardium, but the latter usually shows little change although in some there is a good deal of proliferation of the connective tissue. Gummata may also be met with.

Symptoms.—Most patients do not consult a doctor for cardiac symptoms before 15 to 25 (usually about 20) years after the primary infection, whereas in the great majority of cases the aorta has been affected long before this.

The symptoms of syphilitic aortitis depend upon the extent of the lesion, that is, whether there is involvement of the coronary arteries, general dilatation of the aorta, aortic incompetence, implication of the myocardium, or saccular aneurysm.

The most common early symptoms are dyspnœa on exertion; oppression, discomfort or pain in the front of the chest, usually in the upper sternal region; and paroxysmal dyspnœa. It is important to recognise the characteristic features of the pain. It is often localised but may radiate to the arms and neck. Its degree may vary from slight to severe. It may come on spontaneously, *i.e.* apart from physical exertion, especially on lying down, in which event it may be intermittent or constant, and is generally aggravated by exertion; or it may occur only on exertion, in which case it may continue after the cessation of effort. There may occasionally be hyperæsthesia over the painful area. Severe paroxysms of dyspnœa, including nocturnal, are not infrequent. There may be paroxysmal pain together with paroxysmal dyspnœa while at rest. Sometimes a moderate or faint systolic murmur and an accentuation of the second sound, the latter of which may be of low pitch, in the aortic area are present. Some observers are of opinion that rubbing sounds along the right border of the sternum may be noted, especially when the patient leans forward; personally I have never been able to detect such. The foregoing manifestations may disappear after a few months or weeks, either spontaneously or the result of treatment.

The subsequent course and presentation vary very considerably. The latter may include general dilatation of the aorta; aortic incompetence; angina pectoris; involvement of the myocardium; pulmonary and systemic venous congestion; and saccular aneurysm. In the first, there may be pulsation in the suprasternal notch; not infrequently a systolic murmur and a modification of the second sound in the aortic area as described; and rarely impairment of percussion note over the manubrium sterni and on either side of it. For the results of X-ray examination, see below. Aortic incompetence may develop insidiously or otherwise. Involvement of the myocardium may reveal itself on electro-cardiographic examination by the presence of auriculo-ventricular block, or rarely by bundle-branch block, intraventricular block, or paroxysmal or persistent auricular fibrillation. If congestive failure occurs, it is usually progressive and may be rapidly so. As regards saccular aneurysm, see elsewhere. Sudden death is by no means rare. Subacute bacterial endocarditis may supervene. Lastly, relative or even complete recovery—either the result of specific treatment or spontaneously—may occur at any period.

X-ray examination may reveal general dilatation (Fig. 44), or saccular aneurysm, or both, of the aorta. With regard to the former, as the first part of the aorta is most commonly affected, the commonest X-ray finding is increased convexity of the right border of the supra-cardiac vascular shadow just above the right auricle. There may, in addition, be enlargement of the shadow to the left in the region of the aortic knob. Occasionally the descending thoracic aorta is affected. There may be also increased density of the shadow. If a saccular aneurysm projects mainly backwards, the

shadow of the sac, when viewed from the front, may be within that of the aortic shadow itself. In such a case, rotation of the patient to the right or left will enable the observer to separate the shadow of the sac from that of the aorta. In saccular aneurysm, there is usually also some degree of general dilatation. In syphilitic aortitis, there may be also the characteristic changes in the aortic shadow of co-existing atheroma, especially in later life. If there is aortic incompetence, the enlargement of the left ventricle is shown by extension of the heart to the left and increased convexity of the left border, and the latter may exhibit exaggerated pulsation.

In the early stages the Wassermann or other serum reaction is almost invariably positive, but as the disease becomes more chronic it is increasingly negative, although the frequency with which a positive Wassermann persists even in the case of patients who, clinically, have done well is surprising.

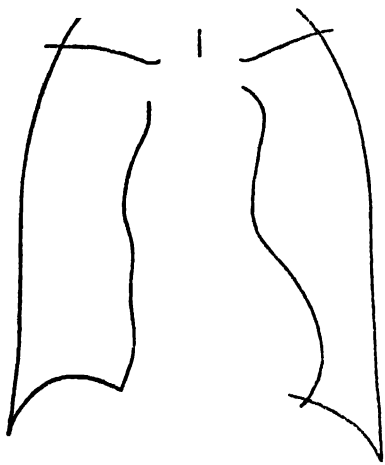


FIG. 44.—Orthodiagram from a case of aortic incompetence, of syphilitic origin. The left ventricle is moderately enlarged, and the aortic shadow is generally enlarged, especially on the right side.

Diagnosis.—The following should be considered: Whether a previous history of a rheumatic or syphilitic infection; the subsequent history; the age; the clinical picture; the results of X-ray and electro-cardiographic examinations, the first being much more important; the Wassermann or other serum reaction; and the presence or otherwise of syphilitic stigmata.

It is easy to overlook a rheumatic infection in childhood; and there may be a history of both rheumatic and syphilitic infection in the same patient. Rheumatic disease usually reveals itself in early life; syphilis generally in middle life; while a cardiac affection coming on in the elderly is commonly the result of primary degenerative processes. A cardiac malady between the ages of 40 and 60, in the absence of hypertension and hyperthyroidism, is very suggestive of syphilis. Syphilis is an important cause of angina before the age of 40.

The early manifestations of aortitis have been described. The pain

differs from that of angina pectoris in that its location is higher; it has far less tendency to radiate to a distance; it is more likely to come on spontaneously, and to be persistent; and if related to physical exertion, not to disappear on the cessation of such. Paroxysms of dyspnœa are very suggestive. A combination of aortic and mitral valvular disease, especially before 30 years of age, points to a rheumatic origin. Aortic incompetence alone, *i.e.* without stenosis and mitral disease, occurring between the ages of 40 and 60 is in a considerable majority of cases due to syphilis, especially in males. It is to be noted that sometimes a combination of valvular lesions the result of both rheumatic and syphilitic infection is occasionally met with.

X-ray examination is of supreme value in all stages of the disease, and the frequency with which the early stages are overlooked could, in large measure, be remedied if all those with a history of syphilis were from the outset periodically examined by this method for evidence of aortitis. The results of X-ray examination have been described. It is necessary to distinguish between general dilatation due to syphilis from that caused by atheroma, or hypertension, or both. This is dealt with on p. 996.

A serological test should be done in all doubtful cases. A negative is not so valuable as a positive reaction; a single negative does not exclude syphilis; and in some cases it may be advisable to employ a provocative dose of one of the organic arsenical preparations. We should, on the other hand, be careful not to place too much reliance on the result of the serum test; it should be considered in conjunction with other data. Lastly, a positive reaction does not indictae that the patient is necessarily syphilitic; and the same applies to the coexistence of other specific stigmata.

Prognosis.—This depends largely upon early diagnosis and the kind of treatment adopted. Taking cases as a whole, the prognosis is very unfavourable, in all probability owing to the fact that a correct diagnosis is not often made until the later stages of the disease. When untreated, the lesion is usually progressive, it may be rapidly so, and the mortality is high. If, on the other hand, a diagnosis is made early and treatment is prompt and suitable, there is a reasonable prospect of relative recovery, and not infrequently recovery is even complete. Naturally the prognosis is much more favourable in the absence of saccular aneurysm, angina pectoris, congestive failure, and aortic incompetence, especially the first three. The first is discussed elsewhere. Even in the absence of angina pectoris and aneurysm, in aortic incompetence the prognosis is generally very unfavourable, death often taking place within two or three years after the onset of symptoms. Congestive failure in syphilitic aortitis is particularly unfavourable, rarely responding to treatment, and it is improbable that such cases will live for more than six months. The results of electro-cardiographic examination are sometimes helpful. Lastly, in all types of cases, surprising improvement is occasionally met with when suitable specific treatment is adopted.

Treatment.—The question whether a preliminary rest is required, and, if so, how much should first be considered. I would add that even in the absence of obvious manifestations of cardiac failure a rest of four to six weeks is an advantage. The various measures which may be applicable to any from of cardiac disorder should be reviewed in detail. See pp. 861–875. Apart from these considerations, the indication is for anti-specific treatment, even in the absence of a positive serum reaction. This should be prompt,

suitable, and prolonged. I am a firm believer in the employment of the arsenical organic preparations, not excluding cases of angina pectoris and congestive failure, but only under certain conditions, as set forth below. Their indiscriminate use is attended with danger, even of grave degree; they may give rise to a focal reaction and consequent increased involvement of the orifices of the coronary arteries.

The scheme I recommend is the result of some conversations I have had with Col. L. W. Harrison, to whom I desire gratefully to acknowledge my indebtedness.

It is always advisable to begin treatment with bismuth or mercury, preferably the former. A very useful preparation for the first course is the iodo-bismuthate of quinine (see pp. 218, 219), which contains approximately 20 per cent. of the metal. A suitable course would be 20 intramuscular injections of the 10 per cent. emulsion, in doses of 3 or 4 c.c. twice weekly, the course lasting approximately 10 weeks. Alternatively, the iodo-bismuthate may be administered for 10 injections and the course be completed with 5 injections of a compound with a higher content of bismuth metal, such as the oxychloride (see pp. 218–221), which contains 80 per cent., at weekly intervals. In this case the weekly injection from the fifth week would be such as contained 0·16 to 0·24 g. bismuth metal. Another alternative is to give from the start a course of 20 injections of an oil-soluble preparation (see pp. 217–221) in doses of 2 c.c. twice weekly. For further details of bismuth preparations, their choice and the technique of their administration see pp. 217–221. Throughout it is important to keep a close look out for evidence of irritation of the kidneys. Any sign that the bismuth is producing this would be an indication to suspend the remedy and resume, with a smaller dose, only when the signs of irritation had disappeared.

Concurrently with the injections, potassium iodide should be given in doses of 15 grains thrice daily.

A month after the end of the first course a second one should be commenced, and continued until 10 injections of an insoluble compound of bismuth each containing 0·16 to 0·24 g. bismuth metal, have been given at weekly intervals. During this course, provided that there is no contra-indication in angina pectoris or congestive heart failure, a cautious start may be made with one of the arsphenamine preparations, either sulpharsphenamine (kharsulphan, metarsenobillon, myosalvarsan, sulfarsenol, or sulphostab) intramuscularly, or neoarsphenamine (neoarsphenamine-Evans, neokharsivan, neosalvarsan, novarsan, novarsenobillon, or novostab) intravenously twice weekly, in such doses as the following: $2\times0{\cdot}10$ g., $4\times0{\cdot}15$ g., $4\times0{\cdot}30$ g., and $10\times0{\cdot}45$ g. For technique of injection of the arsphenamine preparations see pp. 210–214.

It is important in administering arsphenamine preparations to these cases to avoid general reactions. These are more common after intravenous than intramuscular injection and after rapid than slow injection. Any general reaction is an indication to reduce the next dose to the minimum with which the course was started, and, if it is repeated, the administration of the arsphenamine preparation should be suspended.

If the arsphenamine preparation has been well tolerated, in the third course, commenced 6 weeks after the end of the second, it may be given once weekly concurrently with a weekly dose of an insoluble bismuth pre-

paration, the total injections of each type of remedy being 10. Following the third course, mercury and iodide may be administered by the mouth for about three months, and afterwards the specific treatment be continued as recommended for cases of latent syphilis on p. 223.

ANGINA PECTORIS

General Considerations.—The subject of angina pectoris is of much practical importance, more especially as regards diagnosis and the management of a case. Thus, in my experience, the malady is frequently overlooked and, moreover, many patients die many years earlier than need be.

At the outset it is of cardinal importance to understand what is meant by the term. Angina pectoris is a symptom-complex, which may be associated with a diversity of cardio-vascular organic disease, and may even be independent of such, *e.g.* severe anæmia. It is characterized by paroxysmal attacks of pain, in the great majority of cases in the front of the chest, most commonly in the retrosternal region, with a tendency to radiate in certain directions; frequently accompanied by a sensation of oppression or constriction; or, occasionally either of these sensations without pain; and the exciting cause of the first attacks is in the great majority of cases physical exertion.

Ætiology, Morbid Anatomy, and Pathogenesis.—Heredity is, in my opinion, certainly a factor, one of the reasons for this being that cardio-vascular degenerative changes are more prone to occur in certain families. The malady is found more frequently in those who are passing from middle into elderly life; if syphilis is the cause, not infrequently earlier; while in aortic incompetence the result of antecedent acute or subacute endocarditis it may be met with in the third or even the second decade. It is much more common in those classes of society who are subject to excessive mental or emotional stress or strain, being relatively uncommon in those whose occupation is of a manual character; in which connection, I am of opinion that mental and emotional stress and strain are undoubted, if not potent, causes of atheroma of the coronary arteries. It is more likely to occur in individuals with an unduly sensitive nervous system. Other predisposing causes are those of atheroma (see p. 1038); hypertension; syphilis; acute and subacute rheumatism; and occasionally one of the other acute infective diseases, particularly influenza and enteric fever. In syphilis the disease-process involves the orifices of the coronary arteries, or gives rise to aortic incompetence.

The most common structural changes are disease of the coronary arteries, disease of the aorta, aortic incompetence, especially of syphilitic origin, and chronic myocardial disease, the last usually the result of coronary disease. By far the most common is atheroma of the coronary arteries. There may be old infarcts in the myocardium.

In coronary disease there may be, in addition, spasm of the vessels. It is believed that the attacks are sometimes induced by spasm of the vessels even in the absence of organic disease. Angina occasionally occurs in aortic regurgitation, generally due to syphilis. It is rarely met with in paroxysmal tachycardia (or paroxysmal auricular flutter with a very rapid ventricular

rate or paroxysmal auricular fibrillation with a very rapid ventricular rate), thyrotoxicosis, and in severe anæmia, independent of organic cardio-vascular disease.

Among the exciting causes of the attacks are physical exertion, emotional excitement of any kind, mental effort, cold, such as exposure to a cold wind or atmosphere, and cold sheets, the ingestion of food, and dyspepsia, particularly attended with distension of the stomach or colon. There may be a combination of two or more factors. Thus, an attack is more likely to occur during physical exertion after a meal. An extreme example is hurrying uphill on a cold day against a strong wind and engaging in an excited conversation soon after a full meal. Physical exertion is much the most frequent exciting cause, and in the first attacks is so in the great majority of cases. In the case of physical exertion the attacks almost always occur *during* it; in that of emotional excitement, usually so; and in that of mental effort, generally *afterwards*.

Angina pectoris sometimes follows coronary occlusion. Again, the same individual may at one time suffer from angina and at another from coronary occlusion.

It is to be observed that angina pectoris rarely affects those with congestive heart failure or auricular fibrillation. Moreover, if either of these supervenes in those suffering from angina pectoris, usually no further attacks occur.

The hypotheses which have been advanced as to the actual cause of the attack include the following:

The current view, which is probably correct, is that the attack is due to transient relative anoxæmia of part, or less frequently the whole, of the myocardium. The supply of oxygen is insufficient for the demands made upon the heart muscle. The greater the degree of anoxæmia the more easily is an attack induced. The anoxæmia is in the vast majority of cases due to inadequacy in the amount of arterial blood supplied to the myocardium. In the great majority of these this is the result of structural disease of the coronary arteries. It is believed that it may be caused by functional spasm of the vessels. In aortic incompetence, there is a diminished coronary circulation due to the low diastolic pressure. In paroxysmal tachycardia, the shortening of the diastolic period also gives rise to a diminished coronary circulation. Thyrotoxicosis makes an excessive demand on the circulation. In severe anæmia the smaller hæmoglobin content results in a deficiency in the carrying power of the blood, *i.e.* the anæmic type of anoxæmia. Lastly, an attack can occur when there is a diminished oxygen saturation, *i.e.* such as obtains at a high altitude or in a partially exhausted chamber. In support of the anoxæmic origin of angina pectoris, the following may be mentioned. The pain of angina resembles that of coronary occlusion; transient changes in the electro-cardiogram similar to those of coronary occlusion have been noted during the attacks in some cases; and experimentally induced anoxæmia in the subjects of angina has in some brought on attacks of pain and, in some, transient changes in the electro-cardiogram.

The late Sir Clifford Allbutt regarded the phenomena as generally, but not always, produced by tension of the first part of the aorta, which is the seat of some inflammatory or degenerative lesion. He described certain rarer cases in which the morbid stress falls on the pericardium. He was

of opinion that the relief of pain by nitroglycerine was due to dilatation of the peripheral arteries and a diminution of the blood pressure in the aorta; and that sudden death, when it occurs, is the result of "vagus inhibition," the shock of the pain causing asystole, associated with myocardial and coronary disease, which is so frequently found in the subjects of angina. Wenckebach believed in the aortic origin of the attack in the majority of cases. The late Sir James Mackenzie's views were the following: That angina pectoris is an expression of exhaustion of the heart muscle, together with a susceptible nervous system. The pain is a viscero-sensory reflex; the sense of constriction a viscero-motor reflex, giving rise to spasm of the intercostal muscles. That sudden death is due to the lesion causing the pain, and is frequently the result of ventricular fibrillation. Other hypotheses are that the attack may be due to neuralgia of the cardiac nerves; or to cramp, or spasm, of the heart; or to distension of an enfeebled left ventricle.

In conclusion, it should be noted that the precise actual cause of the attack is not at present fully understood. While the anoxæmic origin may be accepted in the majority of cases, this does not exclude the possibility of the pain of angina arising in the aorta, as suggested by the late Sir Clifford Allbutt, in certain cases.

THE VARIETIES OF ANGINA.—Various methods of classification are employed by different writers, among which are the following: (1) Angina minor and angina major; (2) primary and secondary angina; (3) true and false or pseudo-angina; (4) angina of effort (or exertion) and angina at rest—the latter being sometimes called angina of decubitus; and (5) angina of effort and angina of coronary occlusion with myocardial infarction.

The first, in my opinion, serves no useful purpose. For angina may range from pain which is slight to that which amounts to anguish; between these two extremes there is an almost infinite variety in the severity of the attacks; there is no approximate line of demarcation between the two forms; and the same individual may experience attacks of considerable or even great variation at different times. Respecting the fourth, it is to be observed that the subjects of angina at rest almost always also suffer from angina of effort.

The last classification of angina, *i.e.* angina of effort and that of coronary occlusion rests upon the fact that in both the locality and distribution, and the character of the pain are similar; in the opinion of most, but be it noted not of all, the cause of the pain is the same, *i.e.* anoxæmia of the myocardium; and transient modifications of the electro-cardiogram resembling those of coronary occlusion have been observed in some cases of angina during the attacks. I am of opinion that this classification is fundamentally erroneous, for the following reasons: (1) In angina pain constitutes almost the whole clinical picture, whereas in coronary occlusion it is only a part and, moreover, the component parts of the clinical picture are usually very unlike. A careful comparison of the clinical features outlined on pp. 984, 985 and pp. 991, 992 respectively will readily reveal the foregoing. (2) Pain (or a sensation of oppression or constriction) may be absent in coronary occlusion. (3) As has been pointed out, angina may be associated with a diversity of cardio-vascular organic disease, and may even be independent of such; whereas in occlusion there is a uniformity of the pathological condition. (4) In angina there is a relative and transient anoxæmia, whereas in occlusion the blood

supply is completely and permanently cut off, and that part of the wall of the heart is permanently destroyed. (5) The appropriate therapeutic measures are very different.

The best classification, in my opinion, is (1) angina associated with organic cardio-vascular disease, and (2) that which is independent of such. The latter may occur in paroxysmal tachycardia, thyrotoxicosis, severe anæmia and, it is believed, functional spasm of the coronary arteries.

Symptoms.—The exciting causes of the attacks have been described. It is to be noted that an attack may exceptionally occur during rest and even during sleep.

Paroxysmal pain is the cardinal feature. Its onset is usually sudden, it increases rapidly in severity, and subsides more or less gradually. Its degree may vary from slight discomfort to that of intense anguish. In the great majority of cases, the pain is situated in some part of the front of the chest. It occurs most commonly in the retrosternal region; next, across the front of the chest; sometimes on either side of the front of the chest, more often the left; not infrequently in the epigastrium or lower in the abdomen—the so-called angina abdominis; rarely in the back of the chest; and more rarely in any of the areas to which pain arising in a more common site may spread (see later). The pain has a tendency to radiate in certain directions; frequently to the left shoulder and armpit; in many cases down the left arm, generally on the ulnar side, usually not beyond the elbow, but it may extend as far as the tips of the ring and little fingers; sometimes both arms; occasionally the right arm only; to near the angle of the scapula, on one or both sides, or to a wide area in the back of the chest; in an upward direction, to the infra-clavicular region, the neck, the jaw, especially the left, the occiput, or even the top of the head; or in a downward direction, to the abdomen, or even to the lower extremities. When the locality of the pain is in an area to which that arising in a more common site may spread, it may or may not radiate. As a general rule, the more severe the pain, the more frequently does it radiate and also the wider the radiation.

The pain is frequently accompanied by a sensation of oppression or constriction, and the latter may be so severe that the patient experiences a sensation as if the chest were held in a vice. Occasionally there is oppression or constriction without pain. Instead of pain, or a sensation of oppression or constriction, the patient may complain of a sensation of rawness or of burning in the front of the chest. There may be a sensation of weight or of tingling or numbness in the left arm. The breathing is generally restricted, and its rate is only infrequently increased. If the patient is in motion, usually he becomes immobile and remains so, and with a cessation of effort, the pain quickly subsides. Sometimes, however, he is able to continue his effort without pain. If the pain is at all severe, it is often accompanied by a sensation of anxiety out of proportion to its severity and, if still more severe, occasionally by a sense of impending dissolution—angor animi. It is believed by some that very rarely a sense of impending dissolution occurs alone, *i.e.* without pain—the *angina sine dolore* of Gairdner.

The expression of the face may be anxious. The skin may be pallid, and there may be a clammy sweat, but occasionally the opposite is the case. There may be flatulence, nausea, occasionally vomiting, and very rarely hiccough. The pulse-rate varies in different cases; in some it is increased,

while occasionally it is diminished. The blood pressure is generally increased to some extent during the attacks. The cardiac sounds may be weak. There may be irregularity of rhythm, usually due to extra-systoles.

The duration of the attack may vary from a few seconds to a few minutes or longer, the average being a few minutes, and even severe attacks rarely last much longer.

The term status anginosus is applied to prolonged attacks of pain, periodically increasing and diminishing, or a series of attacks, which are practically always due to coronary occlusion.

The severity of the attacks may vary from pain or a sensation of oppression or constriction or rawness or burning, each only of slight degree and lasting for a few seconds, to pain which amounts to anguish. The locality and distribution of the pain and how it is induced are of much greater significance than its variety.

As the attack subsides, the patient may belch up a large quantity of air, and it is often followed by the passage of abundant pale urine. After the attack there may be exhaustion, aching in the area of the pain, a sensation of weight, or of tingling or numbness in the left arm, and hyperæsthesia or hyperalgesia over the painful area, even for some time. On the other hand, it is surprising how soon the patient may be free from symptoms, even after a severe attack.

In the early stages the attacks may be related only to the more severe forms of physical exertion, and the same applies to other exciting causes; the symptoms may be only mild; the pain may not radiate; the attacks may be very brief; and the symptoms may disappear as soon as the exciting cause ceases. As the malady progresses, the attacks tend to become more and more easily induced, so that they may occur when the patient is walking at the ordinary rate or even slowly on the level, or even during the act of eating; the symptoms tend to become more severe; more frequently does the pain radiate and also over a wider area; the duration of the attacks is increased; and the symptoms last longer after the exciting cause ceases. Ultimately the attacks may appear to be independent of any obvious exciting cause. In this connexion, however, it is necessary to point out that in at least a considerable proportion of these cases such is really not the case, for, on careful inquiry, it will be found that they occur when the patient is tired, it may be some time after an exciting cause. On the other hand, the first attacks may be severe; the severity of the attacks may alternate; and the attacks may become less severe and even cease, either as the result of treatment, or spontaneously.

Death may occur during or after an attack, the result of ventricular fibrillation, or, less frequently, of coronary occlusion.

Diagnosis.—This may be very difficult when the symptoms are slight and there is an absence of evidence of cardio-vascular disease, particularly in the case of the former. Nevertheless, if all the avenues of investigation be fully taken advantage of, a correct opinion is possible in the great majority of cases. The following points, among others, require consideration: the age; the sex; the history of the patient's complaint; and the results of examination, this including by the X-rays and the electro-cardiograph.

The history of the patient's complaint is of pre-eminent importance, and is of infinitely more value than what is found on clinical and instru-

mental examination—indeed, there may be a complete absence of abnormal findings in the subjects of undoubted angina pectoris. It follows, therefore, that a searching and detailed inquiry of the patient's complaint, from its inception, should be made. The characteristic features of the pain and concomitant symptoms, together with the existence and nature of the exciting cause, have been described so fully that all that is needed is to refer the reader to such for his careful consideration. The following may be added: A noteworthy feature is that, in the same individual, excepting when the malady is increasing, if physical exertion is the exciting cause there is a remarkable constancy in the degree of such which induces an attack, so that the patient comes to know from experience what kind or rate or amount of effort which will probably, if not almost always, bring on an attack; and this also applies in considerable, though less, degree as regards the other exciting causes. Another is the relative absence of variation in the locality and radiation, the character, and the severity of the pain. These are of considerable diagnostic value. The infrequency of the increase in the respiratory rate is of some diagnostic significance; and if such is pronounced, it may be assumed that there is definite involvement of the myocardium. If the patient is seen during an attack his attitude and expression are of help. Lastly, in the vast majority of cases, at least in the earlier stages, the symptoms are immediately relieved by nitrites.

The results of clinical and instrumental examinations, those indicative of atheroma of the coronary arteries, atheroma of the aorta, and fibrosis of the myocardium, are the most important. For clinical electro-cardiography, see p. 1022.

Angina pectoris should be distinguished from indigestion; coronary occlusion; pain in the præcordium of extrinsic origin; the pain of cardiac failure; biliary, intestinal and renal colic, especially the first; acute pleurisy and acute pericarditis; pleurodynia and intercostal neuritis; arthritis of the dorsal spine or of the left shoulder joint; and intrathoracic aneurysm and new growth.

Angina pectoris, especially the less severe attacks, is very frequently mistaken for indigestion. There are three main reasons for this: (1) Patients suffering from angina are more likely to get an attack during physical exertion after a meal, and therefore not infrequently regard the attack as of gastric origin. (2) In angina pectoris, the locality of the pain is often in the lower part of the front chest, or epigastrium, or both. (3) As the attack subsides, the patient may belch up a large quantity of wind, with subsequent relief. In the differential diagnosis, *whenever an individual in middle or later life, especially a male, complains of pain in the epigastrium or lower part of the front of the chest after meals, inquiry should invariably be made whether such occurs only, or especially, on exertion after meals: and, moreover, whether he is subject to pain on exertion irrespective of meals.* In indigestion usually the pain does not reach so high, and there is an absence of radiation in certain directions. The response to nitrites and suitable remedies for indigestion respectively is of diagnostic value. The distinguishing features between angina and coronary occlusion are described on p. 992. Pain of extrinsic origin and that indicative of cardiac failure are described on p. 877, and should present no difficulty. Among other things, in angina pectoris the pain in the great majority of cases is situated either in the retrosternal region or across

the front chest; when physical exertion is the cause, the attacks almost always occur *during* it; and they are of shorter duration.

The diagnosis between severe angina pectoris and biliary colic in which the pain is situated in the epigastrium or lower retrosternal region may be difficult, especially as the pain of the latter may radiate upwards anteriorly, possibly as high as the neck; and, moreover, it should be remembered that the two maladies may co-exist. A careful consideration of the respective features will, however, almost always result in a correct diagnosis. Thus, in biliary colic there is an absence of an exciting cause; the onset and termination are still more sudden; the pain radiates also in other directions characteristic of that malady; it never involves the arms; there is great restlessness, and there is usually nausea and vomiting.

Prognosis.—This is less difficult than formerly, for it is now more possible to determine the nature and severity of any associated cardio-vascular morbid condition. Nevertheless, it is still very difficult, for the malady is exceedingly varied and one of its characteristic features is the uncertainty of its outlook. Death may occur even during one of the first few attacks; it may take place during what appears to be a mild attack; and the attacks may cease for years, and even after the severest attacks there may be no recurrence. Taking cases as a whole, the average duration of life after the first attack is certainly less than ten years. A few, however, live to old age.

In any given case, the following points require consideration: the ætiology; the nature and severity of any associated cardio-vascular organic disease; how easily the attacks are induced—for example, in the case of physical exertion whether on the one hand only on hurrying up an incline or on the other even when walking slowly on the level; the severity of the attacks, how long they persist after the cessation of the exciting cause, and their frequency; are they becoming more easily induced, or more severe, or more frequent; the nature of the exciting cause; do the attacks occur while at rest; whether in future it will be possible for the patient to modify his manner of life so as to avoid what he has found by experience to be the exciting causes of such; and the response to treatment.

As regards the first, among the most favourable cases are those which occur in paroxysmal tachycardia, thyrotoxicosis, severe anæmia, and focal sepsis, such as in cholecystitis. Hypertension as a cause is not unfavourable, unless of very severe grade, or there is much arterial degeneration or the kidneys are involved. When chronic valvular or chronic myocardial disease is the result of antecedent acute inflammation, the outlook is much more favourable than when due to primary degenerative processes. When syphilis is the cause, the prognosis depends upon the response to treatment but is usually unfavourable. The nature and severity of any associated cardio-vascular organic disease is perhaps the most important consideration of all. This is dealt with under their respective headings. It is to be remembered that atheroma tends to be progressive. How easily the attacks are induced is probably of more significance than their severity. When emotion is the exciting cause, the outlook is better than in the case of physical exertion since it affords an opportunity for successful treatment. The latter also applies in the case of a sensitive nervous system, and this is one of the reasons why the malady is more favourable in females than in males. If attacks occur while the patient is at rest, the prognosis is usually very grave.

Treatment.—This resolves itself into two parts: A. Treatment of an attack; B. The prevention of the recurrence of the attacks.

A. Treatment of an Attack.—The patient should be warned to remain still and, as far as possible, place himself in the position he finds by experience affords him most relief, until at least several minutes have elapsed after the cessation of the attack. In the majority of cases the most efficacious and suitable remedies are the nitrites. Those most frequently used are amyl nitrite (2–5 minims or more), glyceryl trinitrate (nitroglycerine) ($\frac{1}{200}$th–$\frac{1}{60}$th gr. or more), sodium nitrite ($\frac{1}{2}$–2 grs. or more), and erythrityl tetranitrate ($\frac{1}{2}$–1 gr. or more). The last two are much more useful for prophylactic purposes. The rapidity of action of the respective drugs is in the order in which they are placed, and the duration of such inversely so. While amyl nitrite is the most rapid in its action, glyceryl trinitrate is often, if not usually, to be preferred, among other reasons being that it is less likely to cause any disagreeable effects, and is more convenient. Amyl nitrite is inhaled from a glass capsule covered with silk, which is broken. Glyceryl trinitrate is best administered in the form of tablets, which should be chewed, or placed beneath the tongue and allowed to dissolve, instead of being swallowed. Care should be taken that the preparations are fresh and can be easily used by the patient, *i.e.* that the box containing the amyl nitrite can be opened and the capsules broken easily, and that the tablets of glyceryl trinitrate are not hard. The dose of amyl nitrite or glyceryl trinitrate should be sufficient to ensure complete relief without inducing any disagreeable symptoms; and it may be necessary to repeat the dose. The effects of these remedies are sometimes enhanced by a dose of a diffusible stimulant or, if there is gastro-intestinal flatulence, of a carminative mixture. The patient should invariably carry about with him the foregoing, with instructions under what circumstances and how they should be used. If amyl nitrite and glyceryl trinitrate fail, morphine hypodermically, in sufficient dose, is indicated. Failing these, the inhalation of ether or chloroform, cautiously administered, may be tried. If the remedies enumerated are not at hand, a large dose of a diffusible stimulant (brandy, whisky, ether, or ammonia), or the application of heat over the area of the pain may be helpful. When there is collapse, suitable measures should be adopted

I would emphasise that after a severe attack of angina, the patient should have a period of rest (see also later). I have known of a number of deaths because this has been omitted.

B. The Prevention of Recurrence of the Attacks.—In the first place, the ætiology and any associated cardio-vascular affection, such as hypertension, syphilitic aortitis, focal sepsis, and severe anæmia should be reviewed. In the next place, in a certain proportion of cases the question of a preliminary rest should be considered. Such is indicated if there is tiredness or exhaustion of the heart or nervous system; or if the attacks of pain are severe and frequent, or occur when the patient is even walking slowly on the level and, still more so, while at rest; or if, in other cases, suitable treatment has proved unsuccessful. The amount of rest varies considerably. In some cases partial rest for a period suffices. In severe cases, at least some weeks and it may be months of complete rest, both physical and mental, naturally followed by a period of partial rest, is required. Thirdly, in no cardio-vascular affection other than hypertension is the patient's

manner of life of such cardinal importance. A detailed investigation of the patient's general mode of life, his occupation, habits, hours in bed, the amount and character of his sleep, how long he takes off for his meals, his mental and emotional character, and the exciting causes of the attacks, should be made.

Having done this, I would ask my readers carefully to consider the various therapeutic measures described on pages 861–875.

There is no cardiac malady in which it is more necessary for a patient to live within the limits of his strength, according to the rules laid down there. He should carefully avoid anything he has found by experience likely to induce an attack. It is advisable that he should not engage in physical exertion soon after a meal, or against a strong or cold wind. Warm underclothes, and a locality which is non-hilly and of a mild climate, are to be enjoined; while cold rooms, cold sheets at night, and hot and cold baths are contra-indicated. Flatulent distension of the stomach or colon should be attended to. Any existing obesity should, without fail, be treated.

With the object of diminishing the incidence of the attacks, sedatives are often helpful, especially if the patient suffers from an unduly excitable nervous system. See p. 863. The xanthine group of drugs are perhaps occasionally of use.

It has been suggested that treatment by insulin and dextrose may be of value in angina pectoris. There is atheroma of the coronary arteries in the great majority of cases, which must lead to impairment of myocardial nutrition. If, as seems likely, metabolic derangement in the myocardium contributes to the production of anginal pain, the application of glucose-insulin therapy should be of benefit. Five units of insulin subcutaneously, followed in fifteen minutes by 50 grammes of dextrose by the mouth, is given once daily. This may be continued for one or some weeks. Although beneficial results have been reported by a number of workers, as yet there are insufficient data to determine the value of this method of treatment and also the special indications for its use. X-ray therapy and diathermy have also been employed, and they deserve further investigation.

Glyceryl trinitrate ($\frac{1}{200}$th–$\frac{1}{100}$th gr.) may be tried as a prophylactic measure a few minutes before engaging in reasonably necessary physical exertion. When the patient is subject to nocturnal attacks, sodium nitrite or erythrityl tetranitrate at bedtime may be of help, failing which a sedative or hypnotic, including a trial of bromide, chloral and opium, is indicated.

Surgical Treatment.—During the last two decades or so, surgical treatment has been resorted to for the relief of pain; and, quite recently, with the object of establishing a collateral circulation of the myocardium and so attacking the underlying cause. The first comprises varieties of cervical and dorsal sympathectomy, paravertebral injection of alcohol, dorsal laminectomy, and removal of the thyroid gland.

Jonnesco, in 1916, introduced a variety of cervical sympathectomy, and others were tried. Later, varieties of dorsal sympathectomy were substituted. As in the case of cervical sympathectomy, dorsal sympathectomy is an open operation and general anæsthesia is usually required, but if conducted with skill the mortality is relatively low. In the great majority of cases the opera-

tion is successful in the relief of pain, but there are often some disagreeable after-effects. Paravertebral injection of alcohol is a comparatively minor procedure, does not require a general anæsthetic, and is safe. There are difficulties connected with technique but these are gradually being overcome. While not so certain in its results as dorsal sympathectomy, it is very frequently successful. Much depends upon the competence of the operator. The procedure may be repeated. A disadvantage is that a persisting severe intercostal neuralgia sometimes follows. Some cases of dorsal laminectomy, followed by relief of pain at the level of the operation but not below, have been recorded. Total removal of the thyroid gland was introduced by Blumgart and others. By diminishing the metabolic rate, the work of the heart is reduced. There is, however, some reason to believe that the relief of pain is not entirely due to this but is partly the result of damage or section of various sensory pathways, and those who hold this view prefer partial thyroidectomy, as in the case of thyrotoxicosis. Removal of the thyroid gland, total or partial, is a long operation and is more severe than is sympathectomy but in skilful hands the mortality is comparatively low and the results are good in a large proportion of cases. It is contra-indicated if there is a history of recent coronary occlusion. A period of rest in bed before and a longer one after the operation are necessary. If myxœdema follows the operation minimum doses of thyroid should be administered. Revascularisation operations in the form of pericardial implantation of subpectoral muscle and cardio-omentopexy have been performed by a number of surgeons, very notably by Beck and O'Shaughnessy. These procedures are in the experimental stage, but some brilliant results have been recorded and they certainly deserve further investigation, including experimental, and trial. There must be undoubted evidence of a deficient coronary circulation due to organic disease.

As to the question whether surgical treatment should be employed and if so which method should be chosen, the following considerations apply: An adequate knowledge of the history of the case. A thorough examination, including by radioscopy and the electro-cardiograph. An accurate diagnosis. The patient should be under observation for some time. A very careful selection of cases. At least as regards grafting operations, removal of the thyroid, and sympathectomy, very special skill and experience on the part of the surgeon is indispensable. Operative measures should be considered when pain is severe and is very easily induced, such as on walking slowly on the level, and still more so if it occurs even during rest; the malady is increasing in severity; various other methods of treatment, including at least several months complete rest, have been tried and failed; and particularly if the condition of the heart itself is relatively little affected. If the disadvantage of troublesome intercostal neuralgia sometimes following the procedure could be overcome, paravertebral injection of alcohol might well be tried more frequently. The grafting operations appear to be the most likely of all to have permanent results. Formerly it was considered that when there is organic disease of the heart, the coronary arteries, or the aorta, the pain is a protective measure and its removal may be fraught with danger. Less is now thought of this. Even so, it is highly important that the patient should live within his cardiac strength. Lastly, it is probable that the attitude as a whole in this country towards the surgical treatment of angina is too conservative.

CORONARY OCCLUSION WITH INFARCTION OF THE HEART

Synonym.—Coronary Thrombosis.

Ætiology and Pathology.—Coronary occlusion with infarction of the heart occurs most frequently in those who are passing from middle to elderly life, and is much more common in males than in females. Not infrequently there is a history of hypertension. It has been pointed out that complete occlusion of a coronary artery is almost always due to atheroma, usually occurring suddenly as the result of thrombosis but sometimes gradually due to a progressive narrowing of the lumen of the vessel caused by the disease-process itself; and is also rarely the result of embolism, in which event the occlusion is sudden. See p. 948. The general consensus of opinion is that in about half the cases there is a previous history of angina pectoris. In my opinion, if a full and accurate history were obtained in all cases, the percentage would be materially higher.

The descending branch of the left coronary artery near its orifice is most commonly affected, with infarction of the wall of the left ventricle near the apex, especially the anterior portion, and the adjacent part of the inter-ventricular septum; and the next most frequent is either the right coronary artery or the circumflex branch of the left, with infarction of the posterior wall of the left ventricle near the base. A mural thrombus on the inner surface of the infarct is of frequent occurrence. This may give rise to embolism in the brain, kidneys, spleen, intestines, limbs or elsewhere. If the infarct extends to the pericardium, fibrinous pericarditis results. Connective tissue proliferation takes place around the necrosed tissue. Sometimes the infarction undergoes autolytic softening, a condition which is called myomalacia cordis. Rupture of the heart at the site of the infarct may take place at once, with resultant hæmo-pericardium; or an aneurysm may develop, which later on may rupture; or there may merely be a fibrous scar.

Symptoms.—The most common and prominent symptoms at the onset are pain, shock and circulatory collapse, dyspnœa, and perhaps nausea and vomiting, the first being the most frequent.

The pain is independent of any exciting cause excepting possibly fatigue, and may occur during sleep. Its onset is usually sudden. The locality and distribution are the same as in angina pectoris (see p. 984) except that probably the former is relatively more frequent in the epigastrium and there is less tendency to radiation. The pain is usually severe and may even amount to anguish, but it may be moderate or even slight. It generally persists, it may be for hours or even days—status anginosus. Angor animi is more frequent than in angina. Unlike angina, the patient is usually restless and may not be able to refrain from moving about, and the pain is not relieved by vaso-dilators or by rest. The pain is often accompanied by a sensation of oppression or constriction. Occasionally there is oppression or constriction without pain.

When there is shock and circulatory collapse, there is pallor, it may be tinged with cyanosis, the expression is anxious, the skin is cold and moist, and there may be profuse sweating. The mind is generally clear. The blood pressure almost invariably falls, usually immediately, and generally con-

siderably and it may be even markedly, and in some cases it continues to fall for some days. The diastolic is relatively less affected. The pulse is of smaller amplitude and weak and may be imperceptible. It is usually increased in frequency, it may be to 110–120 or more, but occasionally is not so and rarely there is bradycardia. The cardiac sounds, especially the first at the apex, and the force of the apex-beat are generally diminished.

Dyspnœa is present in the majority of cases, and is usually severe. When there is nausea and vomiting, it is usually at the onset but it may be later. The bowels may be moved, and very occasionally there is diarrhœa. Flatulence and distension of the abdomen are frequent. There may be acute left, or, less frequently, right ventricular failure.

Slight or moderate pyrexia is usual during the first few hours. There is often a moderate leucocytosis, the polynuclears being relatively increased in number. Localised pericardial friction in the area of the infarct is not infrequent, and is of great diagnostic importance. It generally occurs a few days after the onset, and may be transient but may persist for a few days. Embolism (see p. 991) may occur.

There is frequently some disorder of rhythm: extrasystoles, or, less frequently, paroxysmal or persistent auricular fibrillation or auricular flutter, paroxysmal tachycardia, or auriculo-ventricular block.

The foregoing is a description of the clinical features of a typical case. It is to be noted, however, that the clinical picture varies considerably in different cases. Thus: Pain (or a sensation of oppression or constriction) may be only slight and rarely completely absent. Shock and circulatory collapse, or acute left or right ventricular failure may be the most prominent and even the only symptoms. The clinical picture may resemble that of an acute abdominal condition, especially if embolism in the abdomen has occurred. Lastly, occasionally the symptoms develop insidiously.

For the results of electro-cardiographic examination, see pp. 1023–1027.

Diagnosis.—A correct diagnosis is almost always possible from the clinical features described, together with the results of electro-cardiographic examination; indeed, in the great majority of cases, it may be made from a careful consideration of the first alone. The diagnostic value of the electro-cardiograms is discussed on pp. 1023–1027.

Coronary occlusion should be differentiated from angina pectoris, acute left- or right-sided ventricular failure due to other causes, rupture of an aneurysm of the thoracic aorta, acute pericarditis, pulmonary embolism, lobar pneumonia, pneumothorax, and acute abdominal conditions, such as the perforation of a peptic or duodenal ulcer, biliary colic, and acute pancreatitis.

The distinguishing clinical features between coronary occlusion and angina pectoris are that in the former the pain is not related to any exciting cause, it generally persists and it may be for hours or even days, is usually accompanied by restlessness, and is not relieved by vasodilators or by rest; there is often shock and circulatory collapse; dyspnœa is generally present and is usually severe; there is frequently nausea and vomiting; there may be acute left- or right-sided failure; there is often some form of arrhythmia present; there is generally pyrexia and often leucocytosis; pericardial friction is not uncommon; and embolism may occur. Coronary occlusion and acute abdominal conditions are more likely to be confused when in the former the locality of the pain is in the lower part of the front

chest or in the epigastrium, and especially if there is nausea and vomiting; and when in the latter the pain involves the lower part of the front chest. Among the distinguishing features are the following: In acute abdominal conditions the pain is *chiefly* abdominal, does not spread so high in the chest, and never involves the arms; pallor is not tinged with cyanosis; there is not such an immediate considerable fall in the blood pressure; and severe dyspnœa, or acute left- or right-sided failure, does not occur. The age and sex, the previous history, *i.e.* whether pointing to a cardiac or an abdominal complaint, and the results of the examination of the heart and of the abdomen —in which connection it may be mentioned that if in coronary occlusion there should be muscular rigidity in the abdomen it is never pronounced. Lastly, in the differential diagnosis of coronary occlusion from any other malady, the results of electro-cardiographic examination are usually of great value.

Prognosis.—This exhibits a wide variation. It is less unfavourable than was considered some years ago, one of the reasons for this being that milder cases are now more frequently diagnosed. Taking cases as a whole, it would appear that somewhat more than half survive the attack. The first three weeks is particularly dangerous, and the prognosis must be very guarded.

In trying to form an opinion, the severity and duration of any existing pain, shock and circulatory collapse, dyspnœa, pyrexia, leucocytosis, the variety of any disorder of rhythm, whether there is acute left- or right-sided failure, the size of the heart, the degree and duration of any electro-cardiographic changes, and the question of complications should be taken into account. Treatment also is very important. As to the subsequent outlook, published statistics suggest that of those who survive about half live for two to three years, about a quarter for five years, relatively few for over ten years, and very rarely for more than fifteen years. In the vast majority of cases the reserve strength of the heart is diminished, in varying degree. A small proportion can lead a fairly active life. Angina pectoris occasionally supervenes. On the other hand, if the patient was previously subject to this malady, it may become less. Recurrence of occlusion is not infrequent. In conclusion, I wish to state that in my opinion, based on a considerable experience, if (1) as regards the attack there is a sufficiency of rest (see *infra* and p. 994), and (2) afterwards the patient is able and willing to live within the diminished strength of his heart, however limited a life may be involved (see pp. 862, 863), the prognosis in coronary occlusion would be very materially bettered than would otherwise be the case and the statistics suggest.

Treatment.—In 1933 I expressed the firm opinion that whenever a definite diagnosis of coronary occlusion has been made, at least three months complete rest, physical and mental, followed by a similar period of partial rest, is strongly indicated; and that in severe cases the duration should be longer. Further experience has confirmed this view. It is of the utmost importance to afford a full opportunity for the best possible healing of the infarct.

In the early stages the more absolute the rest and tranquillity of mind the better. For this purpose, adequate nursing, night and day, is essential. Great care should be taken regarding movement of the bowels; death may take place during the act of defæcation. They need not be moved for the

first 48 hours, and for some time afterwards every other day is usually sufficient. They should be opened by means of enemata. Warmth to the body is indicated. For the control of pain, morphine hypodermically, in sufficient dose and frequency, and for as long as is found to be necessary. Nitrites are contra-indicated. Later, milder sedatives may be very helpful to ensure a sufficient amount of sleep and for restlessness. Especially during the first one or two weeks or even longer, the diet should be fluid or semi-solid, easily digestible, limited in amount, and given in small quantities at a time and at frequent intervals. It is increasingly believed that a low calorie diet, with the object of diminishing the metabolic rate, is of notable assistance. If congestive cardiac failure occurs, digitalis should be administered but large doses should be avoided and caution exercised. The treatment of auricular fibrillation and of auricular flutter is dealt with elsewhere. If digitalis is employed, the precautions just mentioned should apply. Quinidine as described on p. 894 has proved successful and very valuable in some cases of paroxysmal tachycardia, especially of ventricular origin.

The greatest care should be exercised during convalescence. During the last few weeks that the patient is in bed, his back may be gradually raised by means of pillows. Afterwards, he is moved to a couch, at first only every other day, for at least four weeks. After the first two weeks of this time, massage, at first very gentle and for short periods only, and gradually increased, *may be tried*. Later, slight walking exercises may be permitted. If during any stage there are abnormal subjective symptoms, or lowering of blood pressure, or maintained increased frequency of the pulse, it means that the amount of exertion is too much and should be correspondingly reduced.

The patient should be impressed with the importance of living not only within the limits of his diminished cardiac strength (see pp. 862, 863), but even keep something in reserve, during the rest of his life.

THE HEART IN HYPERTENSION

Within recent years a good deal of attention has been paid to the heart in hypertension. The subject is of great importance.

In the vast majority of cases the hypertension is of the nature of hyperpiesia. The latter is one of the most frequent causes of heart failure. Again, in hyperpiesia, it is probable that more than half the patients die from cardiac causes.

Ætiology and Pathology.—This is mainly dealt with on pages 1065 and 1066. There is cardiac hypertrophy, especially of the left ventricle, and diffuse hyperplastic sclerosis. There may be co-existent atheroma of the coronary arteries and of the aorta, due to age, or, in the opinion of some, the result of the hypertension; fibrosis of the myocardium; dilatation of the aorta; and primary chronic degenerative endocarditis of the aortic and less frequently of the mitral valves. The fibrosis of the myocardium may be of ischæmic origin; or due to the same cause as that of the hypertension; or to the increased resistance to the work of the heart having an effect upon its nutrition and removal of waste products; or to a combination of some of these.

In the course of time dilatation follows hypertrophy, and at necropsy it is usual to find both present.

Symptoms.—The symptoms of hyperpiesia are described on page 1066. The most common cardiac symptoms are shortness of breath, palpitation, and precordial discomfort or pain, on exertion. Later, cardiac failure, usually left-sided, but it may be involving both sides, may supervene (see p. 857). Acute left-sided failure may occur (see p. 853). Angina pectoris is not very infrequent. There is occasionally coronary occlusion.

There are physical signs of hypertrophy of the heart, especially of the left ventricle (see p. 955), and in the course of time of dilatation (see p. 956). There may be a systolic murmur in the aortic area, the result of dilatation or of atheroma. In the case of the first, the second sound is accentuated and may be ringing. There is sometimes mitral incompetence and rarely aortic incompetence, in both usually relative, but it may be the result of primary chronic degenerative endocarditis. X-ray examination reveals hypertrophy of the left ventricle, and there may be, in addition, general dilatation of the aorta (see Fig. 45). The latter is shown by general widening of the supra-cardiac

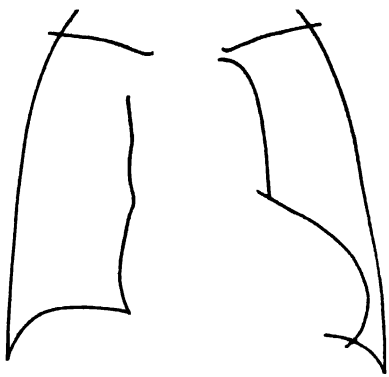


Fig. 45.—Orthodiagram from a case of hypertension, showing great enlargement of the left ventricle, and general widening of the aortic shadow.

vascular shadow. There may be also increased density of the shadow. The rhythm of the heart is usually regular, but extrasystoles are not infrequent, while occasionally there is paroxysmal tachycardia, or auricular fibrillation, or auricular flutter—in that order of frequency. There may be one of the varieties of auriculo-ventricular block, bundle-branch block, or arborization block. The electrocardiogram almost always indicates preponderance of the left ventricle. It is frequently inverted.

During the last few days or weeks the blood pressure may fall, especially the systolic, with a resultant diminution in the pulse-pressure.

Diagnosis.—The diagnosis is easy in the absence of any material fall of the raised blood pressure. When the blood pressure has diminished with the onset of heart failure, or on account of the associated coronary disease, it may present difficulty. In these cases a relatively high diastolic pressure is significant. Gross hypertrophy of the heart in the absence of chronic valvular disease is generally due to hypertension. The results of X-ray examination of the heart and aorta provide valuable evidence. In this con-

nection it is necessary to distinguish between general dilatation of the aorta due to hypertension from that caused by syphilitic mesaortitis. The changes of the aortic shadow in the latter condition are described on page 977. Moreover, in atheroma, on account of lengthening with tortuosity of the aorta, localised bulging of any part of the shadow is far less common. Gallop rhythm and pulsus alternans are valuable signs. Ophthalmological examination may show characteristic changes.

Prognosis.—This depends upon the blood pressure readings, especially the diastolic, the size of the heart, the condition of the myocardium, of the aorta, the coronary arteries, and of the kidneys, and the degree of any existing cardiac failure. If the state of the myocardium, the aorta, the coronary arteries and the kidneys is good, it is surprising how long the heart is able to support a raised blood pressure. Gallop rhythm and pulsus alternans are of serious significance; and cardiac asthma and acute pulmonary œdema are usually of grave import.

Treatment.—The treatment of hyperpiesia is dealt with on pages 1068–1070. When congestive cardiac failure occurs, complete rest in bed for a time, its duration depending upon the degree of the failure, and digitalis are indicated. Venesection may be helpful when there are indications of great distension of the right side of the heart. The various other therapeutic measures, including the question of diuretics, described on pages 861–875 should be carefully considered.

HYPERTHYROIDISM IN RELATION TO HEART DISEASE

The effects of hyperthyroidism, due either to Graves's Disease or to secondary thyrotoxicosis (toxic adenoma), on the heart and circulation have been discussed under their respective headings. It is, however, appropriate to make some observations on one of the varieties of "masked" hyperthyroidism (see p. 488), namely, that in which the cardio-vascular symptoms dominate the clinical picture or may even entirely mask any other manifestations.

Clinical Features.—The condition occurs most commonly in middle-aged or elderly subjects, and females are much more often affected than males. It is relatively more frequent in secondary thyrotoxicosis.

The onset of symptoms is usually gradual. The patient seeks medical advice for cardiac symptoms. Palpitation is the most frequent; it is without apparent cause. There is tachycardia, and an abnormal response of the cardiac rate to physical exertion and emotion. The tachycardia is little affected during sleep; and persists in spite of rest. The pulse is fuller and of increased force, and may resemble that of aortic incompetence. There is exaggerated pulsation of the arteries, which may be particularly noted in the carotid and trachial arteries. There may be capillary pulsation. The systolic blood pressure is generally moderately increased; the diastolic may be subnormal, normal, or slightly raised; the pulse pressure is increased. In some cases the systolic and diastolic pressures are proportionately raised. In the opinion of some this is not always due to a co-existing condition, but may be the result of the thyrotoxicosis. There may be extra-systoles; in which connection, the association of extra-systoles with tachycardia, in the absence

of other causes, is very suspicious of hyperthyroidism. There may be auricular fibrillation, at first usually paroxysmal, and later it may be persistent. Paroxysmal tachycardia and auricular flutter are of relatively rare occurrence. The apex-beat is more forcible than normal, but the out-thrust is quicker and shorter—unlike in hypertrophy, in which it is slower and longer than normal. It is often diffuse. There may be a sensation communicated to the hand resembling a systolic thrill. The first sound is increased in loudness, and not infrequently is short and sharp. There may be a systolic murmur in the pulmonary area, or at the apex, especially the former, in which event the murmur is usually harsh and may give the impression of being superficial, and cases have been recorded in which a slight thrill was present. X-ray examination of the heart is of considerable help in diagnosis. It almost always shows overaction of the organ, as revealed by increased pulsation. Even in the early stages, the left contour of the cardiac shadow is straight, due to increased prominence of the pulmonary arc. This may be diagnosed from mitral stenosis by examining the patient in the right oblique position, when absence of enlargement of the left auricle is to be noted. The size of the heart is less than would be supposed from clinical examination. In cases of considerable severity and duration, however, there is enlargement to both sides, often mainly to the left. When enlargement is very considerable, there may be relative mitral incompetence.

Breathlessness is less pronounced than palpitation, unless there is cardiac failure. Angina pectoris is occasionally met with, especially in the elderly, in which there is more likely to be coronary disease. Ultimately congestive cardiac failure occurs in the great majority of cases, in which event there is usually auricular fibrillation. The most common complications are auricular fibrillation and congestive failure.

There is nothing characteristic about the electro-cardiograms.

The skin may be warm and moist, and there may be flushing and excessive sweating. In some cases there is slight pigmentation of the skin. There may be slight enlargement or increased consistency of the thyroid gland. Occasionally there is a substernal or rarely an intrathoracic goitre. Exophthalmos is rare, but there may be a slightly staring expression. Fine tremors are present in most cases. Usually there is loss of weight, but generally not rapid and only occasionally severe.

The estimation of the basal metabolism is a valuable aid in diagnosis. It should be done under suitable conditions, and in doubtful cases on a number of occasions. The rate is almost invariably increased. In this type of case a great augmentation is ralatively rare, the increase usually being between plus 30 and 50. And even if the rate is within the normal limit of plus 15, if the administration of iodine is followed by a pronounced effect on the rate and the clinical picture is suspicious, in all probability there is hyperthyroidism. It should be noted that congestive failure may give rise to a slight or moderate increase in the basal metabolic rate.

Diagnosis.—Formerly a large proportion of these cases were missed and even now such is not infrequent. Whenever a patient, especially if middle-aged or elderly, complains of cardiac symptoms, in the absence of other causes, such as rheumatism, hypertension, and syphilis, the possibility of a thyroid origin should always be borne in mind. In this regard, a careful consideration of the various features just described is indicated. Evidence of overaction of

the heart, together with a straight left contour of the shadow is exceedingly suggestive.

In addition, the effect of digitalis, quinidine, and iodine therapy respectively should be taken into account. There may be little response to digitalis, even when auricular fibrillation (or auricular flutter) with a rapid ventricular rate is present. Although quinidine not infrequently restores the normal rhythm, if the thyrotoxic state persists, relapse almost invariably recurs. The question of iodine has been referred to.

In possible early cases, neurocirculatory asthenia should be excluded.

Prognosis.—The degree of damage to the heart in hyperthyroidism seems to depend on the age of the subject and its duration rather than on the type of goitre or the severity of the symptoms of hyperthyroidism. It is more serious with advancing age. The prognosis in this group of cases depends almost entirely on treatment. Provided partial thyroidectomy is performed before the cardiac condition is hopeless, improvement is almost invariable. Those with congestive failure respond very well. In cases of auricular fibrillation, the abnormal rhythm sometimes ceases spontaneously after operation, although such may be delayed to even three to six months. If this does not occur, the administration of quinidine is usually successful. Any co-existing hypertension usually persists after operation.

Treatment.—The primary indication is to remove the thyrotoxic condition. This has already been dealt with on pp. 488–491. As far as my experience goes taking a long view, in the vast majority of this group of cases partial thyroidectomy is the best form of treatment. And, given time for preliminary treatment, it should not be postponed. Severe congestive failure, even requiring mercurial diuretics, is not a contraindication. Needless to say, however, I am not referring to moribund cases.

The opinion I have expressed does not diminish the importance of medical treatment, both before and after operation. With regard to the former, the indication is to get the patient to the optimum. Measures include rest, diet, sedatives, iodine, and perhaps digitalis and the removal of foci of infection. These have been dealt with elsewhere. It is a good thing to commence the various forms of treatment at various times, so as to secure the maximum beneficial result simultaneously. If after operation auricular fibrillation or auricular flutter does not cease spontaneously, provided there are no contraindications, the administration of quinidine should be resorted to.

THE HEART IN HYPOTHYROIDISM

The heart is affected in some manner in the vast majority of cases of hypothyroidism, whether myxœdema, either natural or following thyroidectomy, or cretinism.

In such cases there is often some degree of cardiac failure. Slight degrees, such as some shortness of breath on exertion and slight œdema, are the rule; and severe failure is probably of rare occurrence unless there is co-existing chronic myocardial disease or hypertension. The heart is sometimes enlarged, both sides being implicated. The degree of the enlargement is usually not great, but it may be very great or even enormous. The cause of the enlargement is uncertain. In the opinion of some it is mainly due to dilatation and to

a less extent to a myxœdematous state of the heart muscle. The degree of cardiac failure is not always related to that of enlargement. The rate of the circulation is diminished. On screening, in addition to possible enlargement of the heart, there is diminished pulsation. Changes in the electro-cardiogram are the most constant features (see p. 1029).

There may be indications of co-existing chronic myocardial disease, atheroma or hypertension.

A diagnosis may be made from the general symptoms of hypothyroidism, together with the clinical features described and an electro-cardiogram; and the response to appropriate treatment.

Treatment consists of thyroid therapy, given cautiously. The beneficial effect is very quick, including the cardiac enlargement and the electro-cardiogram.

FREDERICK W. PRICE.

CLINICAL ELECTRO-CARDIOGRAPHY

By means of the electro-cardiograph it is possible to obtain graphic records of the movements of both auricles and ventricles, to study the time-relations of their contractions, and to measure the function of conductivity not only of the auriculo-ventricular junctional tissues but also that below the division of the auriculo-ventricular bundle into two branches. In addition. it tells us the point of origin of the impulse formation and also the path along which the wave of excitation travels.

All the various forms of irregular action of the heart can be identified with certainty. The electro-cardiograph affords the most precise means of investigating the function of the myocardium. Disease of the myocardium may, by interfering with the normal path of the wave of excitation, modify the form of the ventricular complex. The instrument is often of great value in the diagnosis of coronary disease and infarction of the heart; it contributes the most certain sign of transposition of the heart; it gives evidence of left- or right-sided preponderance when either exists; it is sometimes of value in the diagnosis of chronic valvular disease and congenital morbus cordis; and during the administration of quinidine in the treatment of persistent auricular fibrillation and persistent auricular flutter, the changes in the cardiac rhythm induced by the drug may be followed, and the dosage controlled accordingly.

It has been known for a considerable time that changes in electric potential take place in muscle when it contracts, and, further, that a record of these changes may be obtained by connecting the muscle with a sensitive galvanometer by means of electrodes.

A. D. Waller, in 1887, employed a capillary electrometer to register the changes in electric potential in the human heart during contraction. He demonstrated that these changes were distributed through the body, and he used the moist skin surfaces of the arms and legs as leads, connecting them with a galvanometer.

Einthoven employed the string galvanometer to register the changes

in electric potential in the human heart. He modified this instrument, the Einthoven string galvanometer being now generally employed in physiological and clinical investigations. In the Einthoven galvanometer there is an exceedingly fine silvered glass fibre, which is suspended in a box and placed vertically between the poles of a powerful electro-magnet. When a current passes through this fibre, minute movements of the fibre take place. The shadow of the oscillating fibre is magnified, and projected on to a photographic screen, and in this way a photograph of these movements is obtained. The sensitiveness of the fibre can be adjusted by altering the tension, the standard generally adopted being that of Einthoven, *i.e.* that when a difference of potential of one millivolt is passed through the fibre, this gives a deflection on the plate of 1 cm. in amplitude.

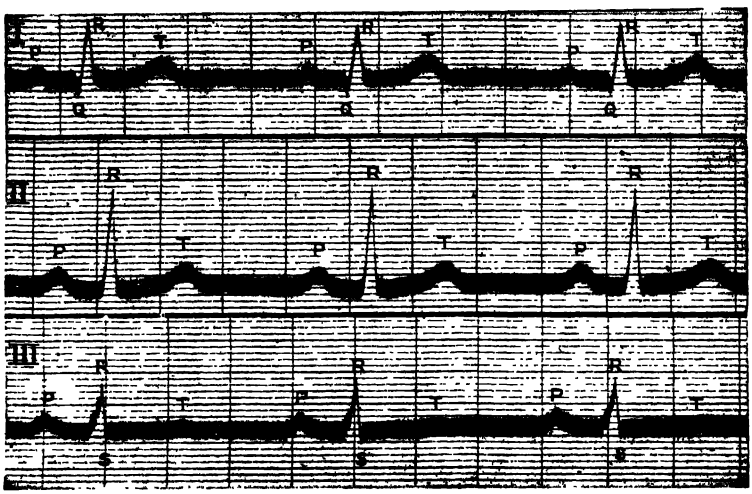


FIG. 46.—A normal electro-cardiogram of leads I, II, and III. The first deflection, *P*, is due to the contraction of the auricles: the others are the result of the contraction of the ventricles, and are termed *Q*, *R*, *S*, and *T*. In normal subjects the amplitude of all the deflections is usually greatest in lead II, especially the deflection *R*.

Recently some workers employ valve modification and a mirror galvanometer instead of the string galvanometer.

Both varieties of electro-cardiographs are now made in reliable portable form, which can be taken to the bedside of the patient.

Formerly the common practice was to accept three leads and the following nomenclature, *i.e.* lead I, or the transverse, a lead from the right and left hands; lead II, or the axial, from the right hand and left foot; and lead III, or the left lateral, from the left hand and left foot. Now a fourth or chest lead is also employed, in which one electrode is applied over the præcordium and another over some distant part of the body. This lead, on the joint recommendations of the Cardiac Society of Great Britain and Ireland and the American Heart Association, is arranged as follows: One electrode is placed over the extreme left border of the apex-beat, or, if this

cannot be determined by palpation, it may be applied in the fifth intercostal space immediately outside the left border of percussion dulness, or just outside the left mid-clavicular line. The other electrode is applied either to the left leg or to the right arm. The leads so arranged are referred to as leads IV *F* and IV *R* respectively. In using either of the foregoing connections, the correct polarity is obtained as follows: The lead switch is turned to lead I; the left arm terminal is connected to the præcordial electrode; and the right arm terminal is connected to the distant electrode—to the left leg for lead IV *F*, or to the right arm for lead IV *R*.

The record of the changes in electric potential which take place in the heart during contraction is called an electro-cardiogram.

If a normal electro-cardiogram of leads I, II, and III be studied, certain

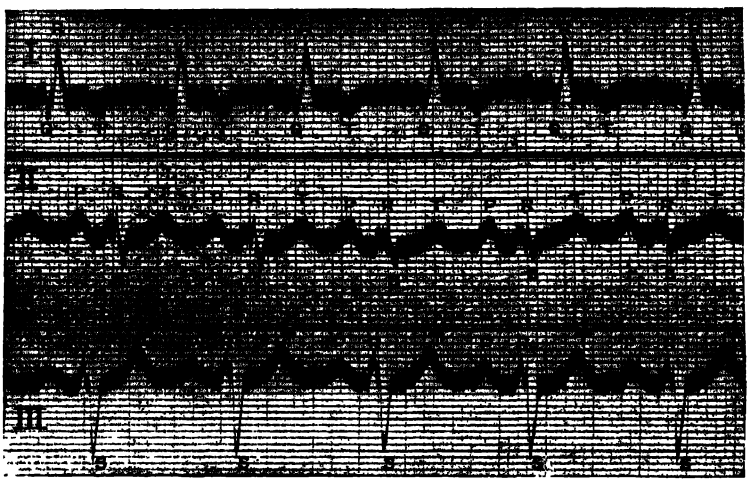


FIG. 47.—Electro-cardiogram, showing inversion of *T* in lead I. There is also left-sided preponderance.

upward and downward deflections or waves are seen in each cardiac cycle (Fig. 46). Following Einthoven, the deflections are called *P*, *Q*, *R*, *S*, and *T*, in some instances *T* being followed by *U*. *R* and *T* are the most constant deflections, the former especially so; *Q* and *S* are not infrequently absent, particularly the first; while the *U* deflection is of very uncommon occurrence.

P, *R*, *T*, and *U* are upward deflections, while *Q* and *S* are downward ones.

The *P* deflection is due to the contraction of the auricles. *Q*, *R*, *S*, and *T* are due to the contraction of the ventricles. *U*, if present, occurs early in diastole, and its significance is not fully understood.

That portion of the elcctro-cardiogram from the beginning of *P* to the commencement of *Q* is called the auricular complex. *P* represents the spread of the wave of excitation over the auricles. It is an upward, small, and usually rounded deflection, but it may be pointed. It is succeeded by an

isoelectric interval indicated by the string either remaining at the zero level, or descending or ascending slightly, in which event usually the former.

That portion of the electro-cardiogram from the beginning of *Q* to the end of *T* is designated the ventricular complex. *Q*, *R*, *S* constitute the initial group of deflections, while *T* is the terminal or final deflection. *Q* passes at once into *R*, and *S* follows immediately upon the latter. *Q* and *S* are downward steep deflections, and usually very small. *R* is an upward, conspicuous, sharp spike, and of greater amplitude than any of the other deflections. The *S–T* interval usually exhibits a pronounced zero-line, which however may descend or ascend slightly, but, on the other hand, there may even be no zero-line. *T* is an upward, prominent, broad and rounded deflection, but in lead III it not infrequently points downward (see p. 1004).

In normal subjects, the amplitude of all the deflections, especially *R*, is

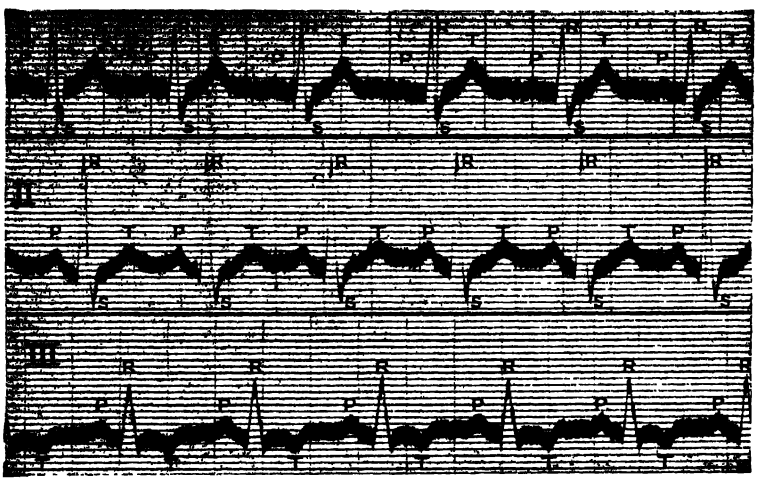


FIG. 48.—Electro-cardiogram showing inversion of *T* in lead III.

usually greatest in lead II, while those in lead III are not infrequently of small amplitude.

The time-distance between the beginning of *P* and the commencement of *Q*, or between *P* and *R*, as the case may be, is an index of the *As–Vs* interval, that is, the interval separating the commencement of auricular and ventricular contraction, and is a measure of the function of conductivity of the auriculo-ventricular node and bundle above its division into two branches; it is called the *P–Q* or *P–R* interval. The rule is to employ the latter, on account of the frequent absence of the *Q* deflection. The *P–R* interval is a more reliable indication of the rate of conduction of the wave of excitation than the *a–c* interval in a polygraphic tracing, because the presphygmic interval and the period between the opening of the aortic valves and the carotid pulse are not included. In normally acting hearts the interval varies between 0·12 and 0·18 second. If it exceeds the latter, and certainly if more than 0·20 sec. (Fig. 78), we may conclude that the

function of conductivity is definitely depressed. The *P-R* interval is diminished in auriculo-ventricular nodal rhythm and in functional bundle-branch block (see Fig. 82).

The period of time occupied by the ventricular complex is approximately that of the ventricular systole. That occupied by the *QRS* group of deflections is of much importance. It should not exceed one-tenth second. If it does it indicates a delay in the conduction of the wave of excitation through the ventricular muscle. This occurs in bundle-branch block, arborization block, ventricular extrasystoles, in the ventricular variety of paroxysmal tachycardia, and, it may be, in extreme preponderance of either ventricle.

The *Q–T* or *R–T* duration varies considerably. With a normal cardiac rate, it probably averages between 0·32 to 0·35 second. It is diminished by an increased cardiac rate, and *vice versa*. When the cardiac rate is unusually frequent the duration of the diastolic interval is so shortened that the deflection *T* approaches more and more to the following *P*, and *P* and *T* may even coincide and are superimposed (Fig. 49).

In auricular hypertrophy, such as in mitral stenosis and congenital

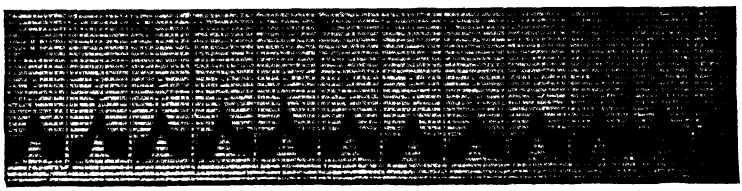


FIG. 49.—Electro-cardiogram in which *P* and *T* coincide and are superimposed.

pulmonary stenosis, especially the former, the *P* deflection, particularly in lead II, is of increased amplitude (Figs. 53 and 54), and not infrequently is also broad and has a flat top, and may be notched or bifurcate (Figs. 55 and 56). Some writers are of opinion that a mere increase in the amplitude of *P* is occasionally met with in normal hearts.

A large *Q* in lead III is often a feature of the *T*3 type of infarction, either recent or old. It should be noted, however, that it may also occur with a horizontal or transverse position of the heart due to a high diaphragm, as, for example, in ascites, pregnancy, or obesity. In the differential diagnosis, whether there is also a *Q* of somewhat smaller amplitude in lead II and a characteristic alteration in the *R–T* (*S–T*) interval and in the form of the *T* deflections are of cardinal importance. In addition, a large *Q* due to upper displacement of the diaphragm is diminished or abolished by holding the breath after a deep inspiration. A *Q* in lead I is strongly suggestive of an old infarct of the wall of the left ventricle near the apex and the adjacent part of the interventricular septum.

Notching or splintering or slurring of the *QRS* complex of slight degree may be found in normal conditions, and in preponderance of either ventricle. These in pronounced degree and also notching which is irregular signify that the wave of excitation is speading in the different parts of the ventricular musculature in an abnormal manner. They may be met with in bundle-

branch block, arborization block, ventricular extra-systoles, and in the ventricular variety of paroxysmal tachycardia.

Diminution in the amplitude of *T* occurs during forced expiration, and it may be with advancing age. The *T* deflections may be flattened or inverted in the three leads in hypothyroidism (see Fig. 95). Diminution of *T* in lead II is frequently met with in marked left- or right-sided preponderance. Inversion of *T* in lead III alone (Fig. 48) is not infrequently found in health, and therefore its significance in a single examination is uncertain and it is of essential importance to know whether the deflection was formerly upright. Among pathological conditions, it is found in marked right-sided preponderance. Inversion of *T* in lead III and lead II may occur during forced expiration. Apart from this, it is probably pathological.

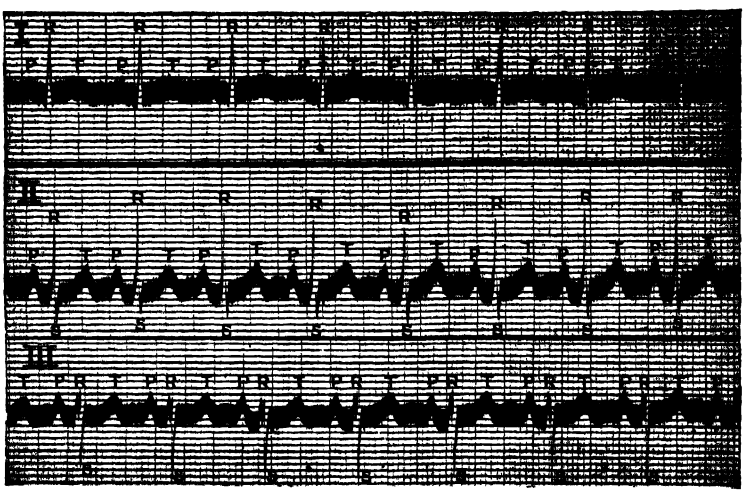


FIG. 50.—Electro-cardiogram showing predominant hypertrophy of the left ventricle.

Inversion of *T*1 and *T*2 may be regarded as pathological, suggesting coronary or myocardial disease. Inversion of *T*1 is also to be met with in gross left-sided preponderance.

The changes in the *T* deflections which occur in bundle-branch block, coronary occlusion, and with full doses of digitalis are described elsewhere.

The characteristics of a normal fourth lead are as follows (Fig. 51). The first deflection, *P*, is upright, and is rather smaller than in the other standard leads but less so in lead IV *F*. The initial group of ventricular deflections is of larger amplitude than in leads I, II, and III, and is diphasic, the first wave, *R*, being positive and the second, *S*, negative, and they are approximately of equal size. The *S–T* interval, as in the other three leads, is usually iso-electric but it may, on the other hand, show a slight inclination to rise above or to fall below the zero line. The *T* deflection is positive, and is of increased amplitude.

The form of electro-cardiographic curves depends upon the point of origin of the impulse formation, the paths along which the wave of excitation travels, and the manner of conduction of the latter; any departure from the normal in respect of one of these will result in an alteration in the form of the electro-cardiogram.

A typical *P* signifies that the impulse arises in the sino-auricular node and that the wave of excitation spreads over the whole of the auricles along the normal paths. When the auricle contracts in response to impulses not generated at the sino-auricular node, almost always the *P* deflection is of abnormal form. The degree of this depends upon the distance of the site of origin from the normal, for example, if near the node *P* may be almost normal. Often the deflection is inverted. The various forms of abnormal *P* deflections which may be found in auricular or auriculo-ventricular nodal extra-systoles, auricular or auriculo-ventricular nodal paroxysmal tachycardia, auriculo-ventricular nodal rhythm, and auricular flutter are described later. A diphasic or inverted *P* in lead III alone may occur in left-sided preponderance and in the absence of any pathological condition.

Similarly, a typical ventricular complex signifies that the contraction of

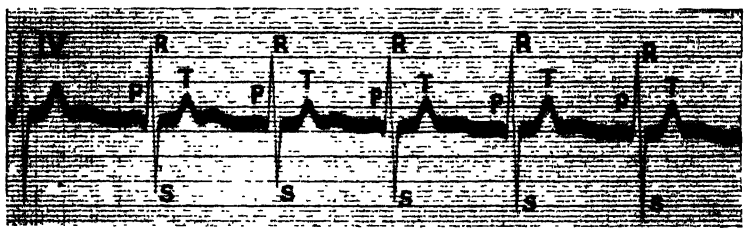


FIG. 51.—A normal electro-cardiogram of lead IV.

the ventricles is supra-ventricular in origin, *i.e.* they have contracted in response to an impulse which arises above the division of the auriculo-ventricular bundle, and that the wave of excitation proceeds along the normal paths. An atypical ventricular complex means that the contraction of the ventricles is ventricular in origin, *i.e.* the stimulus arises below the division of the auriculo-ventricular bundle. When the ventricular contraction is *aberrant* (see p. 847), the complex, while fundamentally typical, differs from the normal to some extent, this varying from a slight degree to even, rarely, that in which the complex resembles one of ventricular type.

CARDIAC HYPERTROPHY.—It has been previously pointed out that in cardiac hypertrophy, while both ventricles are more often affected than one alone, one ventricle is frequently involved to a greater degree than the other. This predominant hypertrophy or preponderance of either ventricle is revealed by the electro-cardiograph. If in cardiac hypertrophy an electro-cardiogram does not indicate either right- or left-sided preponderance, we may assume that the hypertrophy involves both ventricles approximately equally.

In left-sided preponderance, the amplitude of *R* is greater in lead I than in lead III, and the amplitude of *S* in lead III is greater than in lead I (Figs. 47 and 50). The deflections of greatest amplitude in leads I and III, there-

fore, point away from each other. In right-sided preponderance, the amplitude of *S* is greater in lead I than in lead III, and that of *R* in lead III is greater than in lead I (Fig. 52), and so the deflections of greatest amplitude point towards each other.

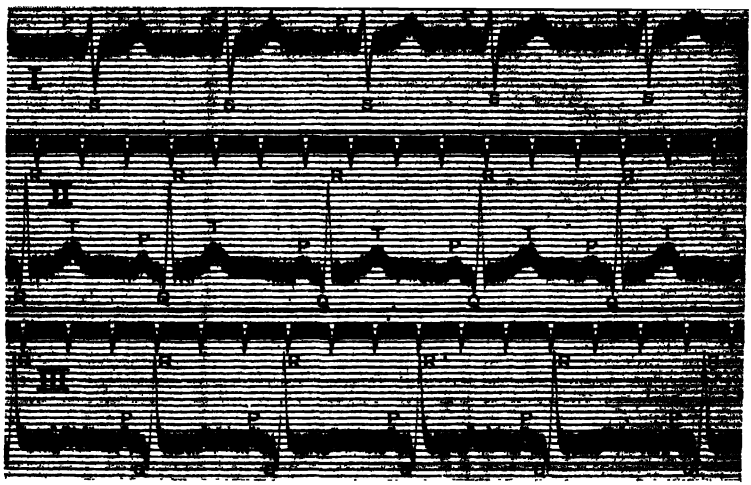
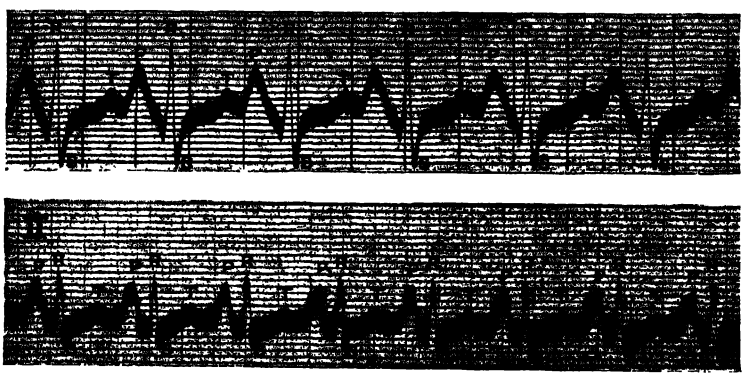


FIG. 52.—Electro-cardiogram showing predominant hypertrophy of the right ventricle.



FIGS. 53 and 54.—Electro-cardiograms from two different subjects showing increased amplitude of the deflection *P*.

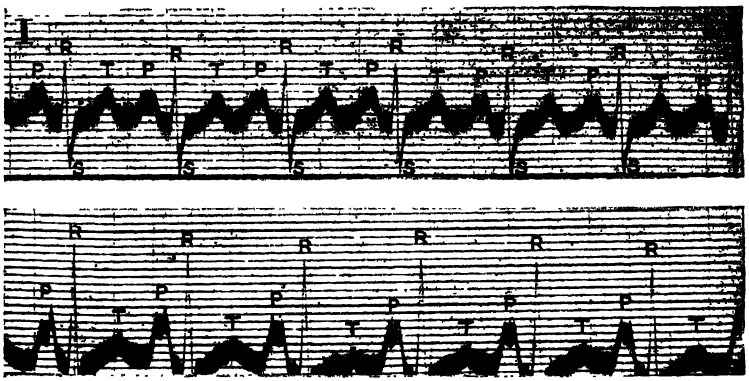
In marked preponderance of the left side, there is often inversion of *T* in lead I; and in that of the right side, inversion of *T* in lead III. Barnes and Whitton have suggested that these changes in the *T* deflection result from mechanical strain on one ventricle rather than actual disease of the myocardium other than hypertrophy. In extreme preponderance of either

ventricle, the period of time occupied by the *Q*, *R*, *S* group of deflections may be increased, exceeding one-tenth of a second.

In the diagnosis of preponderance of either ventricle it is necessary to exclude displacement of the heart, for the following reason. The electrical axis of the organ is influenced by the anatomical axis, so that displacement may give rise to electro-cardiographic curves of right- or left-sided preponderance. Thus, a horizontal or transverse position of the heart due to a high diaphragm tends to produce a curve of left ventricular preponderance; while a vertical position of the organ with a low diaphragm, as seen in asthenic subjects, tends to produce that of right ventricular preponderance.

It is also necessary to distinguish between predominant hypertrophy of the left or right ventricle and a lesion of the left or right main branch of the auriculo-ventricular bundle (new nomenclature) respectively. This is referred to on p. 1020.

CHRONIC VALVULAR DISEASE.—In aortic valvular disease there is usually



FIGS. 55 and 56.—Electro-cardiograms from two different cases of mitral stenosis. The deflection *P* is increased in amplitude, and is also broad, has a flat top, and is bifurcate.

left-sided preponderance. In mitral stenosis there is generally right-sided preponderance; and the *P* deflections may show the changes indicative of auricular hypertrophy described on p. 1003. The latter, when present, are of diagnostic value, especially when there is also right-sided preponderance. When auricular fibrillation supervenes, the curves will present features characteristic of that condition.

CONGENITAL HEART DISEASE.—The amplitude of the deflections is sometimes greater than in the acquired form of valvular disease. There is frequently right-sided preponderance, often of marked degree, especially in pulmonary stenosis.

In dextro-cardia all the deflections of a curve from lead I are inverted, while lead III is equivalent to the normal lead II, and lead II to the normal lead III (Fig. 57). This form of electro-cardiogram is pathognomonic of the condition. It is to be noted that if there is also a lesion giving rise to enlargement of the right ventricle, the electro-cardiogram will be that of left-sided preponderance with inversion of *P* in lead I. In uncomplicated wide patency of the interauricular septum there may be deviation of the electrical axis

to the right. In patency of the interventricular septum the electro-cardiogram is usually normal, except when the defect in the septum involves the

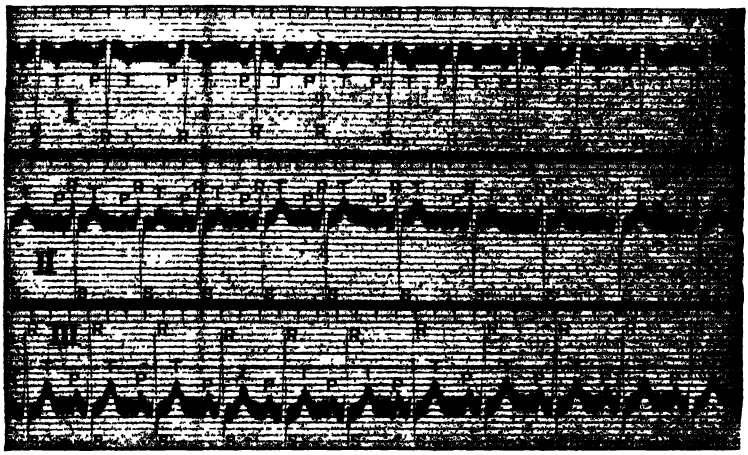
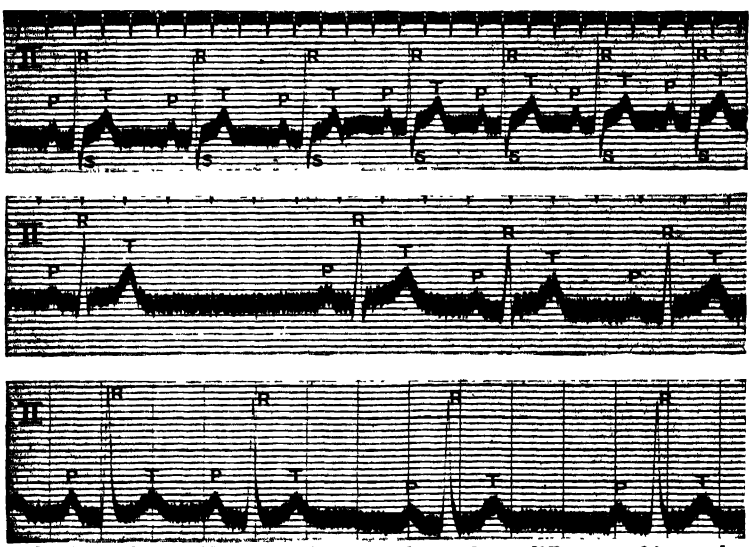


FIG. 57.—Electro-cardiogram from a case of transposition of the heart. All the deflections in lead II are inverted.



FIGS. 58, 59 and 60.—Electro-cardiograms from three different subjects showing sinus irregularity. The auricular and ventricular deflections are of normal form, but there is a variation in the length of the intervals between *T* and *P*.

auriculo-ventricular bundle and so gives rise to congenital heart-block. In congenital pulmonary stenosis the electro-cardiogram will reveal a marked right ventricular preponderance.

SINUS ARRHYTHMIA.—The electro-cardiogram of this rhythm may readily be identified (Figs. 58–60). There is merely a variation in the length of the diastolic periods, *i.e.* the intervals between *T* and *P* (see p. 885).

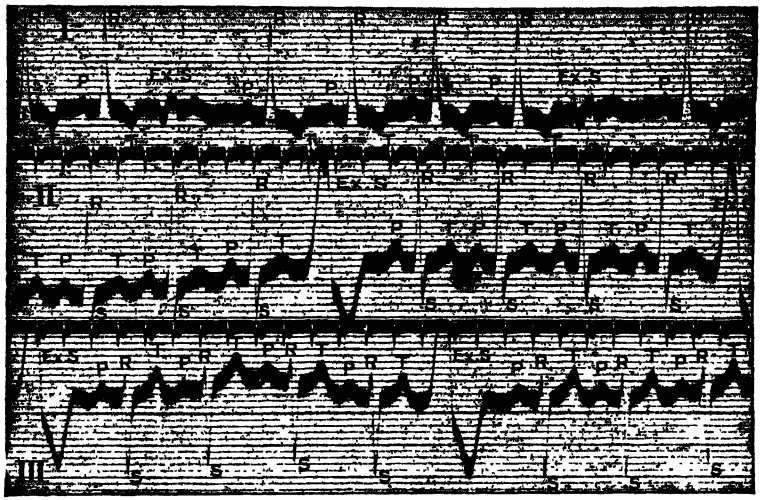


FIG. 61.—Electro-cardiogram showing ventricular extra-systoles, marked *Ex.S*. The corresponding *P* deflections are embedded in the diphasic variations. There is also inversion of *T* in lead I, and left-sided prepondesance.

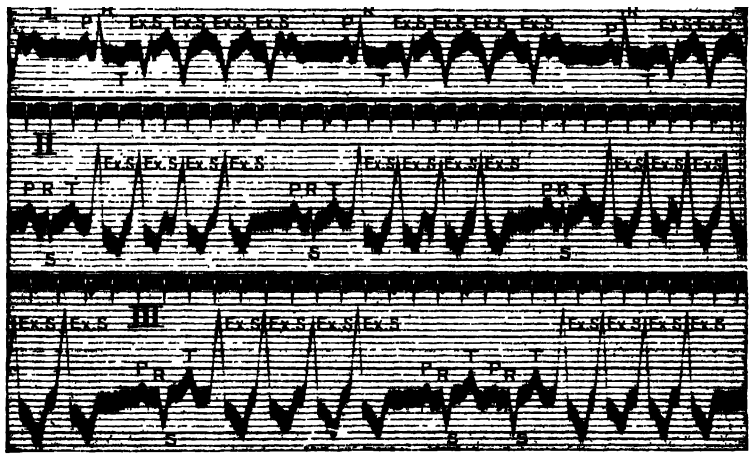


FIG. 62.—Electro-cardiogram showing rapid successions of ventricular extra-systoles. There is also inversion of *T* in lead I and left-sided preponderance.

EXTRA-SYSTOLES.—Extra-systoles may be readily recognised by means of the electro-cardiograph, and usually their site of origin.

In the ventricular variety (Figs. 61 and 62) the ventricular complex occurs

earlier than the anticipated time. As the ventricular contraction is ventricular in origin and therefore the wave of excitation travels along abnormal channels, the ventricular complex is wholly atypical: it is diphasic, and is of increased amplitude. It is of the same duration as that of the rhythmic contraction.

There are two main varieties of ventricular extra-systoles, and it is usually possible to differentiate them by means of the electro-cardiograph. In one, the ventricular complex consists of an upward, tall and pointed deflection, and then of a downward and broader deflection, in lead I; and of a downward, deep and pointed deflection, and then of an upward and broader deflection, in lead III. In the other variety, the ventricular complex consists of a downward, deep and pointed deflection, and then of an upward and broader deflection, in lead I; and of an upward, tall and pointed deflection, and then of a downward and broader deflection, in lead III. It was formerly thought, largely as the result of experiments in animals, that the first variety has its origin in the left ventricle or apical portion of the heart, and the second in the right ventricle or basal portion. Recent evidence has been adduced, based partly on direct observations on the exposed human heart, which strongly suggests that the opposite is the case. The direction of the deflections in lead II is usually the same as in lead III, but the reverse may be the case.

In the ventricular variety of extra-systoles, the auricle maintains its usual rhythm and contracts as the result of the normal stimulus from the sinus. It follows, therefore, that the corresponding *P* deflection appears at the anticipated time and is normal in form. But it is usually embedded in the ventricular complex, although it may be detected in this part of the electro-cardiographic curve in some cases, and occasionally is nearly separate.

If the ventricular extra-systole takes place after the normal auricular contraction, and the wave of contraction from the auricle has reached the ventricle and met that of the premature ventricular contraction in the ventricular wall, the ventricular complex of the premature contraction of the ventricle will present both typical and atypical features.

The site of origin of a ventricular extra-systole may occasionally be at one time in the basal or right portion of the ventricle, and at another in the apical or left portion, in the same subject.

A ventricular extra-systole is usually followed by a compensatory pause, which is complete. Sometimes, when the cardiac rate is slow, an interpolated extra-systole occurs.

In the auricular variety of extra-systole (Fig. 63) the *P* deflection takes place before the anticipated time. As the point of origin of the stimulus for contraction is at a site other than the sino-auricular node, almost always the *P* deflection is of abnormal form. The degree of difference depends upon the distance of the site of origin of the impulse from the sino-auricular node; and if near or at the node, *P* may be practically normal. Often the deflection is inverted (see lead II). The premature contraction of the auricle may take place so early as to coincide with the ventricular contraction of the preceding cycle, in which case *P* and the preceding *T* are superimposed. The *P*–*R* interval may be increased. The *P* deflection is usually followed by a premature ventricular complex. This is of typical form, since the ventricular contraction is of supra-ventricular origin and therefore the wave of excitation to the ventricle travels along the usual paths,

but it may be aberrant. Almost always aberrant ventricular beats are found only when there is diminished auriculo-ventricular conductivity. In some cases, the stimulus for contraction does not reach the ventricle at all, in which case the premature contraction of the auricle is not followed by a premature contraction of the ventricle—"blocked auricular extra-systole" (third extra-systole in lead I of Fig. 63).

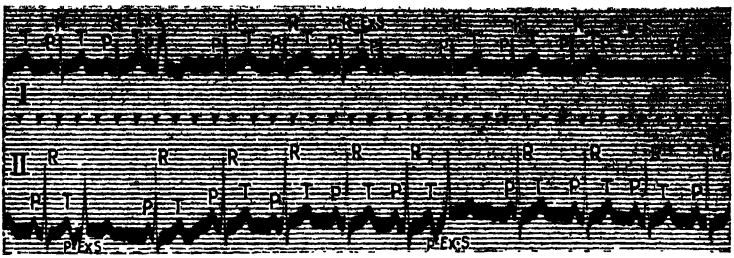


FIG. 63.—Electro-cardiogram showing auricular extra-systoles, marked *Ex.S.* The premature *P* deflections are of normal form in lead I, and of abnormal form—being inverted—in lead II. The premature ventricular complexes are of abnormal form. The third extra-systole in lead I is blocked.

In auricular extra-systole the compensatory pause is rarely complete.

In the auriculo-ventricular nodal variety of extra-systole (Fig. 64) there is prematurity of the *P* deflection and also of the ventricular complex. In cases in which the contraction of the auricle and ventricle is absolutely synchronous, the *P* deflection coincides with, and is embedded in, the *Q*, *R*, *S* complex (see lead II). When the contraction of the auricle begins before that of the ventricle, the *P* deflection precedes *R*, and the *P–R* interval is

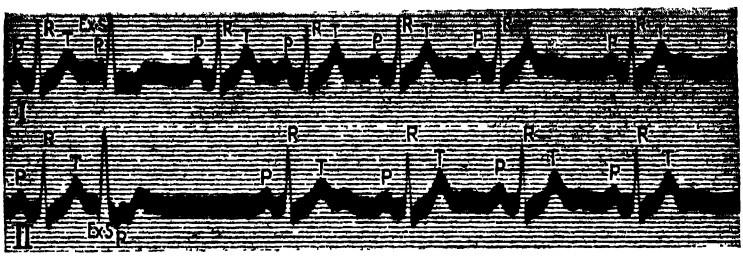


FIG. 64.—Electro-cardiogram showing auriculo-ventricular extra-systoles, marked *Ex.S.* In that of lead I the premature *P* deflection occurs before that of the ventricular complex, while that in lead II is embedded in the ventricular complex.

diminished (see lead I). When the auricular contraction commences after that of the ventricle, the *P* deflection follows the *R* deflection. When the *P* deflection is to be observed, as the auricular contraction is due to an impulse which arises at an abnormal point, it is almost always abnormal in form, often being inverted. As the ventricular contraction is supra-ventricular in origin, the ventricular complex is of typical form but may be aberrant.

In the auriculo-ventricular variety of extra-systole, the compensatory pause may, or may not, be complete.

Occasionally the beat immediately following an extra-systole arises from the same site as that of the premature contraction.

PAROXYSMAL TACHYCARDIA.—The first *P* deflection of the paroxysm is premature, and usually the paroxysm is followed by a long pause.

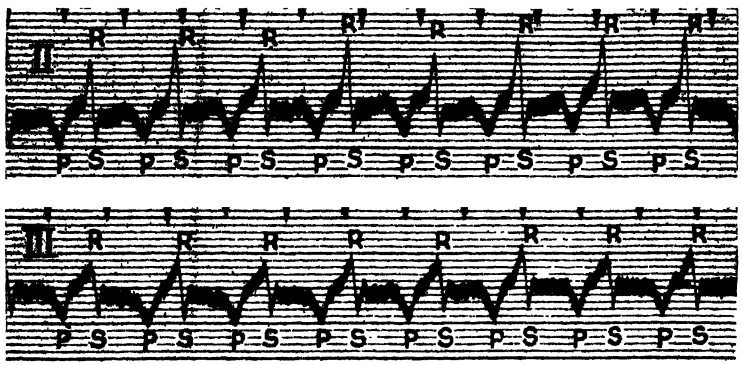


FIG. 65.—Electro-cardiogram showing the auricular variety of paroxysmal tachycardia.

There is no essential difference between the complexes of the individual beats during a paroxysm and those of single extra-systoles in the same individual.

In auricular paroxysmal tachycardia (Fig. 65) there is a rapid succession of *P* deflections occurring at regular intervals. As in the case of auricular extra-systoles, these are almost always of abnormal form, often being inverted. The contraction of the auricle may take place so early as to coincide with the ventricular contraction of the preceding cycle, in which

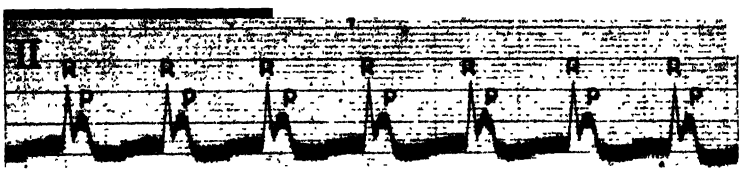


FIG. 66.—Electro-cardiogram showing the auriculo-ventricular nodal variety of paroxysmal tachycardia.

case *P* and the preceding *T* may be superimposed. The *P–R* interval may be increased. The *P* deflections are usually followed by ventricular complexes of the same form, or approximately so, as those preceding and following the paroxysm. There may be auriculo-ventricular block or bundle-branch block. In the latter case the ventricular complexes may resemble those of ventricular paroxysmal tachycardia. In this connection, in the differential diagnosis between the ventricular complexes of supra-ventricular and of ventricular origin, it is important to note whether any part of the *P* deflection

can be detected in the ventricular portion of the electro-cardiographic curve or not.

In auricular paroxysmal tachycardia, the rhythm is regular.

In auriculo-ventricular nodal paroxysmal tachycardia (Fig. 66) the electro-cardiogram is often difficult to determine. There is a rapid succession of auricular and also of ventricular complexes. In cases in which the contractions of the auricle and ventricle are absolutely synchronous, the *P* deflections coincide with and are embedded in the *Q*, *R*, *S* complexes. When the contractions of the auricle begin before those of the ventricle, the *P* deflections precede the *Rs*, and the *P–R* interval is diminished. When the auricular contractions commence after those of the ventricle, the *P* deflections follow the *Rs*. When the *P* deflections are to be observed, they are

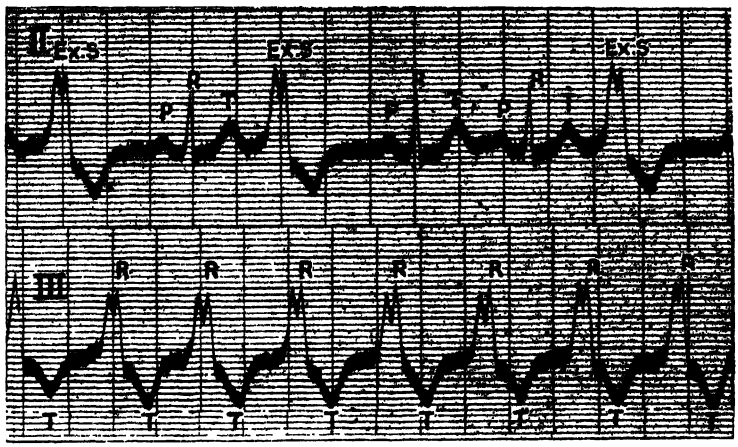


FIG. 67.—Electro-cardiogram of leads II and III. Lead II shows three isolated extra-systoles of ventricular origin. Lead III shows the ventricular variety of paroxysmal tachycardia, the complexes of which are of the same form as those of the isolated extra-systoles in lead II.

usually of atypical form, often being inverted. The ventricular complexes are of typical form but may be aberrant.

In auriculo-ventricular nodal paroxysmal tachycardia the rhythm may be regular or irregular.

In ventricular paroxysmal tachycardia (Figs. 67 and 68) there is a rapid succession of ventricular complexes. Usually each of these is of the same form as those of isolated extra-systoles arising in one ventricle (see p. 1010). In some cases, however, the point of origin of the beats is sometimes in one ventricle and at other times in the other, resulting in complexes of different form; and this may occur in the case of every other beat, so that complexes of different form alternate, which condition is sometimes called bi-directional ventricular tachycardia, and is of very serious significance. Sometimes the ventricular complexes are of indefinite form.

In the ventricular variety of paroxysmal tachycardia, the auricle generally maintains its usual rhythm, contracting as the result of an impulse arising

in the sino-auricular node. It follows, therefore, that the *P* deflections occur at the usual intervals and also are of normal form. They are generally embedded in the ventricular complexes, but in some cases they may be detected in this portion of the electro-cardiographic curve and occasionally they are nearly separate. In some cases, however, the ventricular rhythm gives rise to retrograde auricular beats, either with each ventricular contraction, or, less frequently, *i.e.* retrograde heart-block. Rarely there is auricular fibrillation, and more rarely auricular paroxysmal tachycardia, or auricular flutter.

In ventricular tachycardia, any existing irregularity of rhythm is usually so slight that it is detected only by means of graphic methods.

In the differential diagnosis of paroxysmal tachycardia by the electro-cardiograph, it is to be observed that, as the difference in the form of the complexes of the abnormal and the normal rhythms may be only slight it may be necessary to compare carefully the complexes of the paroxysm with those of the beats which either preceded or followed it—indeed, an analysis of either transition periods may be necessary.

AURICULO-VENTRICULAR NODAL RHYTHM.—In this condition, when the

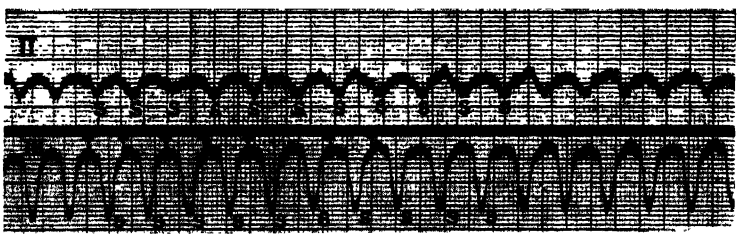


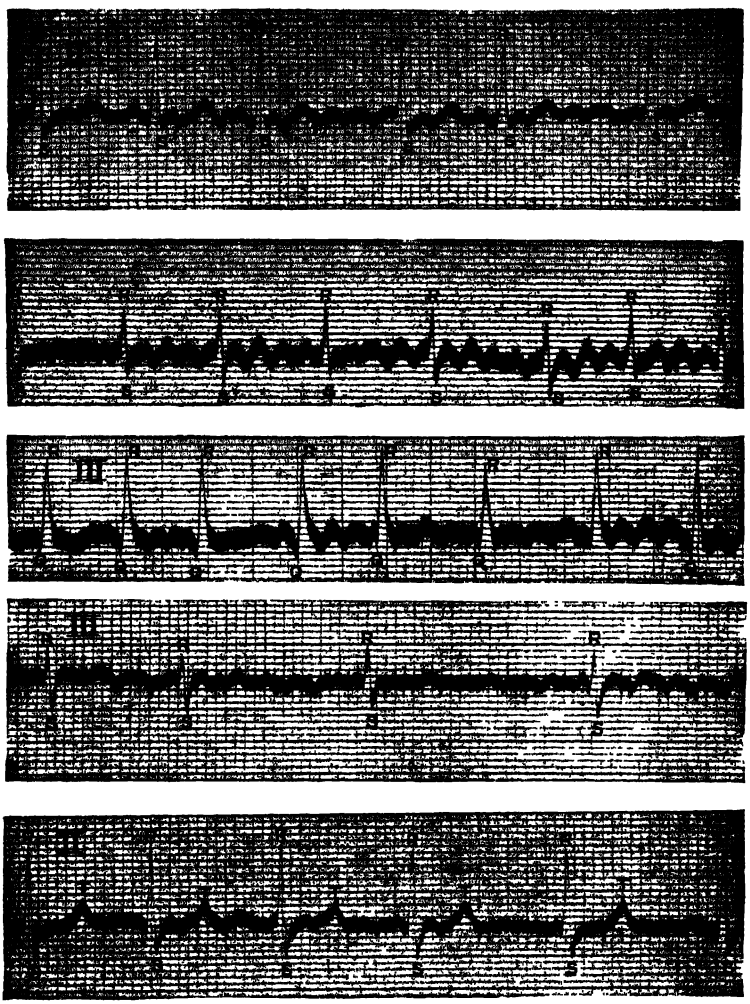
FIG. 68.—Electro-cardiogram of leads II and III showing the ventricular variety of paroxysmal tachycardia.

contractions of the auricle and ventricle are absolutely synchronous, the *P* deflections coincide with and are embedded in the *Q*, *R*, *S* complexes. When the contractions of the auricle begin before those of the ventricle, the *P* deflections precede the *Rs*, and the *P*–*R* interval is diminished. When the auricular contractions commence after those of the ventricle, the *P* deflections follow the *Rs*. When the *P* deflections are to be observed, they are usually of abnormal form, often being inverted. The ventricular complexes are of typical form but may be aberrant.

AURICULAR FIBRILLATION.—In auricular fibrillation the electro-cardiogram is characteristic (Figs. 69–73).

There is an absence of *P* deflections. There are, on the other hand, oscillations caused by the fibrillating auricle, called fibrillary waves, during ventricular diastole, at a rate ranging from 300 to 600, and usually about 450 times, per minute. They occur at irregular intervals, and their form and size vary, the latter being sometimes very minute and sometimes considerable. They are most evident in cases of slow cardiac action. They may coincide with the *T* deflections, in which case the outline of the latter is altered. Apart from the very rare cases in which complete auriculo-ventricular block is present, the ventricular rhythm is completely irregular, *i.e.* the *R* deflec-

tions occur at irregularly irregular intervals; their amplitude varies from cycle to cycle; and often there is no relationship between the length of a pause and the amplitude of the *R* deflection which follows it. When the



FIGS. 69–73.—Electro-cardiograms from cases of auricular fibrillation.

ventricular rate is slow or very rapid, this may be difficult to determine. As the ventricular beats are supra-ventricular in origin, the complexes are of typical form but they may be aberrant. There may be superadded ventricular extra-systoles, usually during the administration of one of the digitalis group of drugs (see p. 868).

In the differential diagnosis between the electro-cardiograms of auricular fibrillation and those of auricular flutter, in the former almost always the ventricular rhythm is completely irregular, while in the latter, it will be found that such is not the case, even when the rhythm is very irregular. Further, the deflections due to auricular systole in auricular flutter may be distinguished from the fibrillary waves in auricular fibrillation in that they are less frequent, rhythmic, of larger amplitude, and almost invariably of constant form and size.

Auricular Flutter.—In this condition it is of particular importance to analyse the three leads (Figs. 74–76). The *P* deflections may range from 180 to 360, the usual rate being about 300, per minute. In all the leads the deflections occur at regular intervals, and as soon as one terminates the next

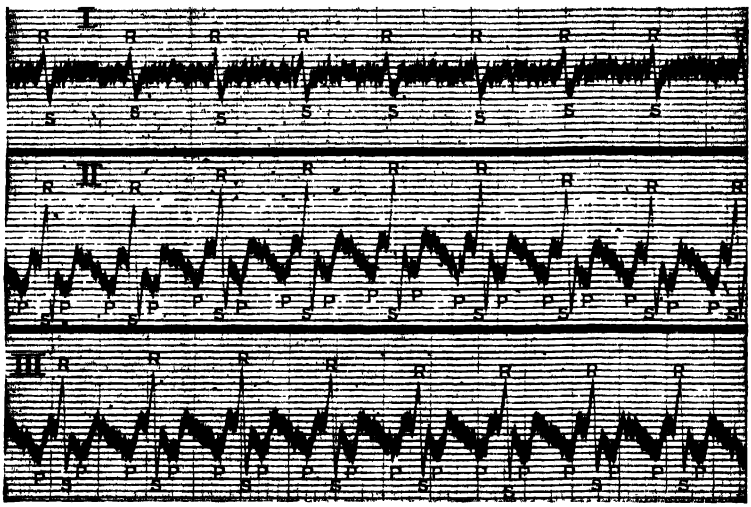


Fig. 74.—Electro-cardiogram from a case of auricular flutter, with 2 : 1 heart-block. The rate of the auricle is between 320 and 330 per minute.

one commences. In each lead of any given case they are almost invariably of constant form. In lead I the amplitude is comparatively small. As the impulse arises at an abnormal point, the deflections are atypical in form. The ascending limb is rather sharp, and the descending more gradual, and the summit may be dome-shaped. It is difficult to say at what part the deflection begins. As the ventricular complexes are supra-ventricular in origin, they are of typical form. They are superimposed upon the *P* deflections, modifying their outline. In some cases *T* may be detected. Excepting in the very rare cases of 1 : 1 rhythm, in which event there is an equal number of *P* deflections and ventricular complexes, there are two or more *P* deflections to each ventricular complex, according to the degree of auriculo-ventricular block (see p. 900). When the response of the ventricle to auricular contraction is at irregular intervals, the ventricular rhythm may be even very irregular.

It is necessary to differentiate the electro-cardiograms of auricular flutter from those of auricular fibrillation. This is dealt with on p. 1016.

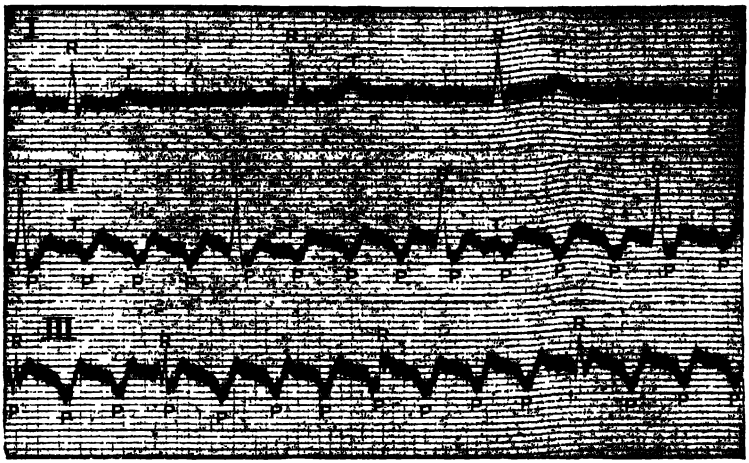


FIG. 75.—Electro-cardiogram from a case of auricular flutter, with 4 : 1 heart-block.

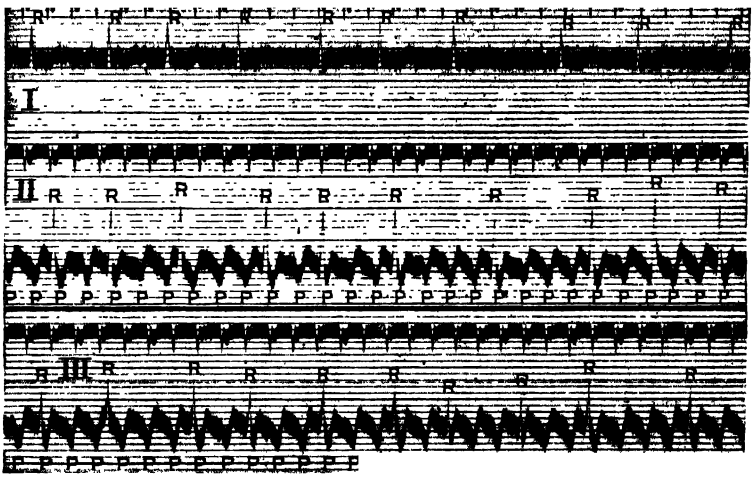


FIG. 76.—Electro-cardiogram from a case of auricular flutter. The auriculo-ventricular ratio is sometimes 2 : 1, at others 3 : 1, and at others again 4 : 1. The response of the ventricle to auricular contraction being at irregular intervals, there is irregularity of the ventricular rhythm.

VENTRICULAR FIBRILLATION.—The ventricular complexes are replaced by oscillations, occurring at very rapid and irregular intervals, and their form and size vary.

SINO-AURICULAR BLOCK.—In this condition there is an absence of both the auricular and ventricular complexes during an abnormally long pause. (See p. 904 and Fig. 77.)

AURICULO-VENTRICULAR BLOCK.—In the first grade (leads I and III of Fig. 78) there is merely an increase of the *P–R* interval, it exceeding 0·18



FIG. 77.—Electro-cardiogram showing an abnormally long pause due to sino-auricular block.

second. It may be increased to such a degree that *P* coincides with the preceding *T*.

In the second grade (lead II of Fig. 78) the *P* deflections are found at regular intervals and are of typical form. Sometimes the *P* deflections are not followed by ventricular complexes, the frequency of such depending

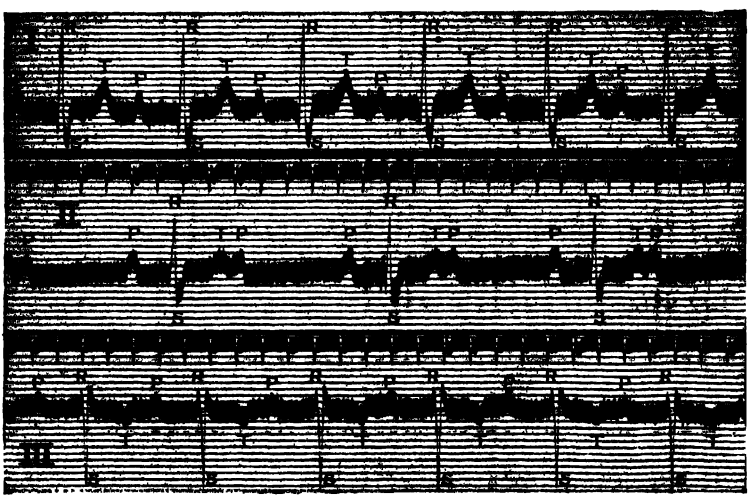


FIG. 78.—Electro-cardiogram showing partial heart-block. In each lead there is an increase of the *P–R* interval, and in lead II there is also continuous 2 : 1 rhythm, every other stimulus from the auricle failing to reach the ventricle. There is also inversion of *T* in lead III and left-sided preponderance.

upon the degree of block, as described on p. 905. Unlike complete heart-block, on each occasion the ventricular complex is preceded by a *P* deflection. In the case of dropped beats, almost always there is a progressive increase of the *As–Vs* interval preceding and a progressive shortening of the interval following each dropped beat, so that the prolonged pause during a dropped beat is not equal to two regular pulse-beats. As the ventricular beats

are of supra-ventricular origin, the ventricular complexes are of typical form.

In complete heart-block (Fig. 79) the *P* deflections are found at regular intervals, and are of typical form. They are more frequent than the ventricular complexes. In addition, the time-relation between the *P* deflec-

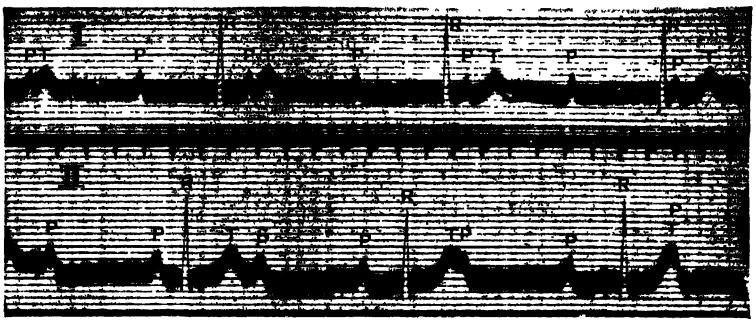


FIG. 79.—Electro-cardiogram of leads I and II showing complete heart-block, or dissociation of the auriculo-ventricular rhythm, the auricles and ventricles beating independently of each other.

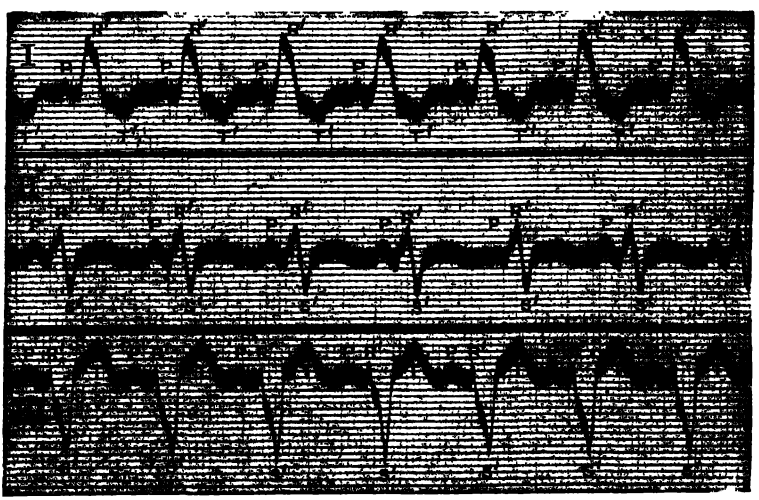


FIG. 80.—Electro-cardiogram showing a lesion of the left main branch of the auriculo-ventricular bundle (new nomenclature).

tions and the ventricular complexes is a constantly varying one, the former at one time preceding, at another following, and sometimes, again, coinciding with the latter. In the last case the *P* deflection is superimposed upon the ventricular complex. As the ventricular beats are of supra-ventricular origin, the ventricular complexes are of typical form. Sometimes there are superadded ventricular extra-systoles.

BUNDLE-BRANCH BLOCK.—A lesion of either of the two branches of the auriculo-ventricular bundle may be recognised by means of the electro-cardiograph (Figs. 80 and 81).

The ventricular complex is diphasic and of increased amplitude. The initial group of deflections (*Q*, *R*, *S*) is of increased duration, exceeding one-tenth second and comprising more than one-third of the whole complex, and usually exhibits pronounced or irregular notching. The terminal deflection (*T'*) points in the opposite direction to the initial group of deflections in leads I and III. In lead II, *Q*, *R*, *S* is usually of less amplitude and is often diphasic; *T'* may point in either direction. In the diphasic ventricular complexes of leads I and III there is usually no iso-electric period between *Q*, *R*, *S* and *T*. The *P*–*R* interval may be increased.

Two types of curves may be recognised: (1) The common type, in which

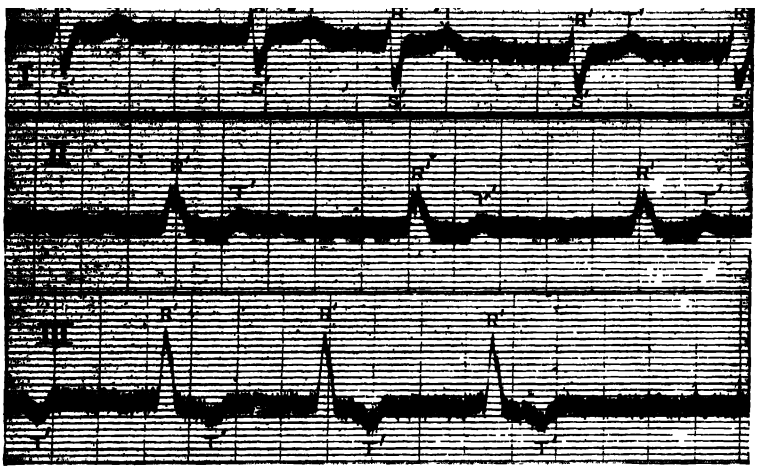


FIG. 81.—Electro-cardiogram showing a lesion of right main branch of the auriculo-ventricular bundle (new nomenclature). There is also auricular fibrillation.

there is a large *R'* in lead I and a large *S'* in lead III, *T'* pointing downwards in lead I and upwards in lead III. (2) The rare type, in which there is a large *S'* in lead I, and a large *R'* in lead III, *T'* pointing upwards in lead I and downwards in lead III. It was formerly supposed that the first type was indicative of right bundle-branch block, and that the second signified left bundle-branch block. It is now believed that the opposite is the case.

It is necessary to distinguish between a lesion of the left or right main branch (new nomenclature) and preponderance of the left or right ventricle respectively. The distinguishing features are that in bundle-branch block the initial group of deflections is of increased duration and usually exhibits pronounced or irregular notching, and *T* points in the opposite direction to the main initial deflection in leads I and III. As already noted, increased duration of the *Q*, *R*, *S* complex may be met with in extreme preponderance of either ventricle. But taking cases of preponderance as a whole, the

period of time is materially less. In addition, pronounced or irregular notching does not occur, and T is not of increased amplitude and, apart from exceptional cases, points in the same direction.

FUNCTIONAL BUNDLE-BRANCH BLOCK.—A condition, which is rare, in which there is increased duration of the Q, R, S group of deflections together

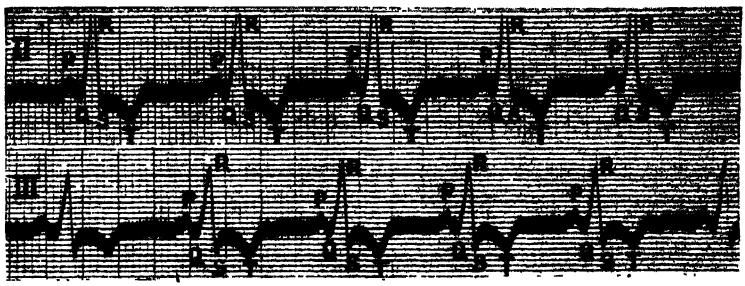


FIG. 82.—Electro-cardiogram showing functional bundle-branch block.

with a diminished P–R interval (Fig. 82) has been termed functional bundle-branch block.

ARBORIZATION OR INTRA-VENTRICULAR BLOCK.—The initial group of deflections is of increased duration and usually exhibits pronounced or irregular notching, and is of low voltage (Fig. 83). Some believe that occasionally the T deflection points in the opposite direction to the initial

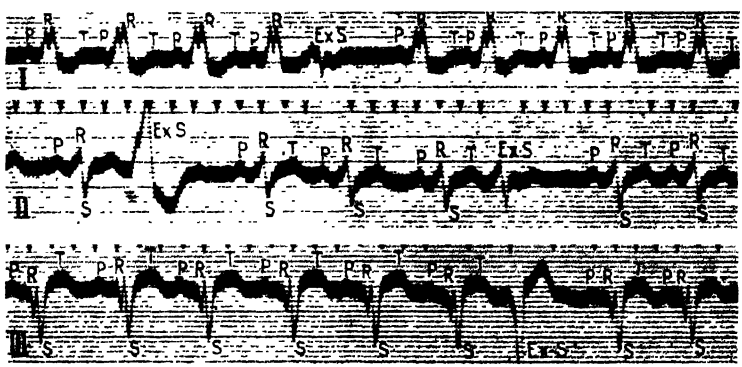


FIG. 83.—Electro-cardiogram showing arborization block. There is an extra-systole, marked Ex.S, in lead I, two extra-systoles in lead II, and one in lead III.

deflection in leads I and III. Even if such should be the case, its form is not so abnormal.

It should be pointed out that some writers are of opinion that the electro-cardiogram just described indicates a delay of the wave of excitation along the right or left main division of the auriculo-ventricular bundle, *i.e.* incomplete or partial bundle-branch block.

ALTERNATION OF THE HEART.—This may sometimes be recognised by means of the electro-cardiograph, by an alternation in the amplitude of the deflections due to the contraction of the ventricle (Fig. 84). Both the *R* and *T* waves may be affected, or one more than the other. It should be noted that alternation of the heart is sometimes shown in a sphygmogram without any corresponding evidence in an electro-cardiogram, while rarely the opposite holds good. It should be further noted that the alternation in a sphygmogram and electro-cardiogram does not always correspond ; *i.e.* the smaller ventricular deflections correspond with the larger pulse-wave.

ANGINA PECTORIS.—Left-sided preponderance is usual. In a proportion of cases the ventricular complexes are abnormal. Most varieties of these

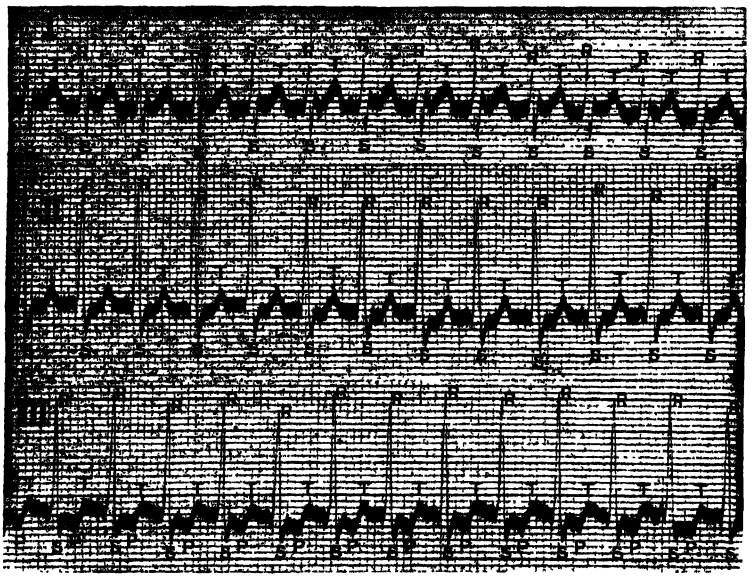


FIG. 84.—Electro-cardiogram from a case of paroxysmal tachycardia. There is alternation in the amplitude of the *R* deflections.

abnormalities may be met with, including flattening or inversion of *T* in lead I or II, or both ; increased duration, and notching of the *Q*, *R*, *S* group of deflections ; bundle-branch block ; and a large *Q* deflection in lead III (see p. 1025). There may be extra-systoles and some degree of heart-block Other abnormalities of rhythm are exceptional. The changes in the ventricular complexes may be of considerable value in doubtful cases. Negative findings, on the other hand, are of no importance.

Transient modifications of the electro-cardiograms similar to those of coronary occlusion with infarction have been observed in some cases of angina pectoris during the attacks. Such are of much diagnostic significance.

CORONARY OCCLUSION WITH INFARCTION OF THE HEART.—Electro-cardiograms of this disease are usually characteristic and of great diagnostic value. They are as follows :

Within a few hours there is usually a deviation of the *R–T* or the *S–T* segment. This portion of the curve commences from the *R* or *S* deflection either above or below the iso-electric level and proceeds in a more or less horizontal direction, resulting either in a plateau-shaped elevation or in a depression respectively. This alteration is generally most noticeable in

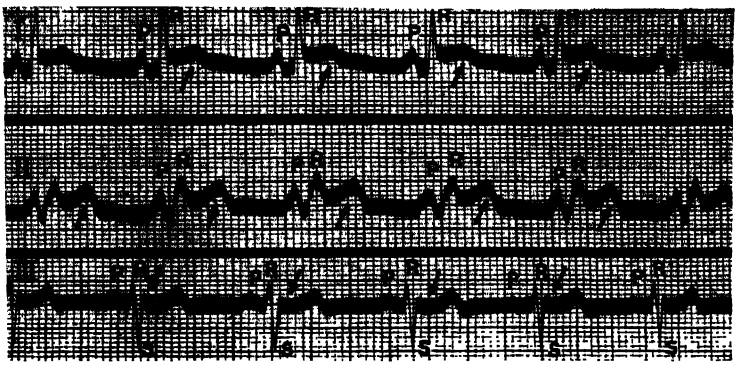


FIG. 85.—Electro-cardiogram from a case of the T^1 type of infarction of the heart taken early after the onset of symptoms. The *R–T* portion of the curve commences above the zero level in leads I and II, and slightly below the zero level in lead III, as indicated by arrows.

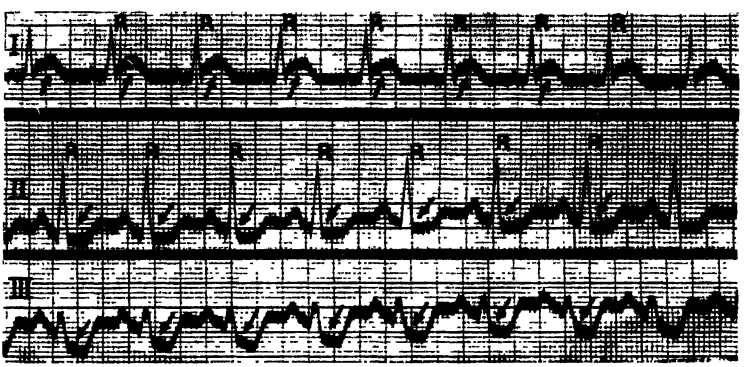


FIG. 86.—Electro-cardiogram from a case of the T^1 type of infarction of the heart taken early after the onset of symptoms. The *R–T* portion of the curve commences above the zero level in lead I, and below the zero level in lead III and rather so in lead II, as indicated by arrows.

leads I and III. In this event, the corresponding portions of the curves in these leads are divergent. Thus, if there is *R–T* elevation in lead I there is *R–T* depression in lead III (Figs. 85 and 86); and *vice versa* (Figs 87 and 88). Sometimes the deviation of the *R–T* segment is best observed in leads III and II, or in leads I and II; or the alteration may be present in one lead only. The foregoing features are perhaps pathognomonic of the condition.

After a few days or more, the *R–T* portion of the curve gradually returns to the iso-electric level, and the *T* deflections gradually reappear. The latter assume a direction opposite to that to which the *R–T* segments were

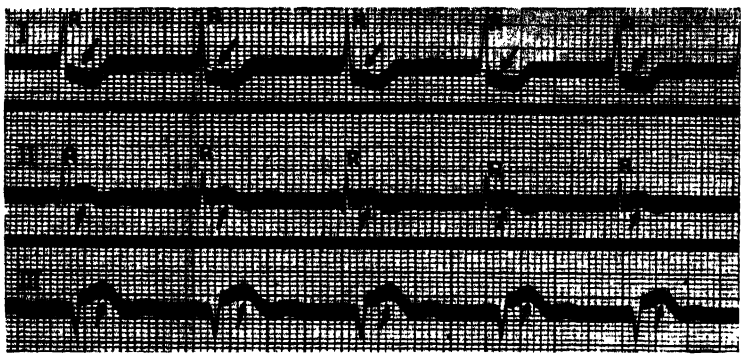


FIG. 87.—Electro-cardiogram from a case of the T^3 type of infarction of the heart taken early after the onset of symptoms. The *R–T* portion of the curve commences above the zero level in lead III and slightly so in lead II, and below the zero level in lead I, as indicated by arrows.

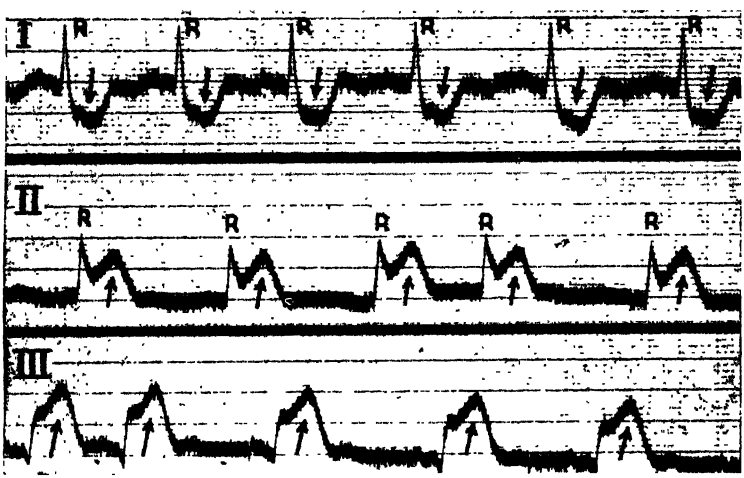


FIG. 88.—Electro-cardiogram from a case of the T^3 type of infarction of the heart taken a few hours after the onset of symptoms. The *R–T* portion of the curve commences below the zero level in lead I and above the zero level in leads II and III, as indicated by arrows.

previously deviated. Thus, inversion of the *T* deflections follows elevation of the *R–T* segments, and upright *T* waves follow depression of the *R–T* segments. (Figs. 89–91.) The *T* deflections are usually sharply defined, and their amplitude is often large. The *R–T* intervals preceding the

altered *T* waves frequently exhibit convexity or concavity. The foregoing features are not so characteristic as are those of the first stage, but, taken together with the clinical features, they afford strong corroborative evidence of the disease.

In both stages, sometimes there is diminished amplitude and increased duration of the initial group of ventricular deflections (*Q*, *R*, *S*), and the latter is generally associated with notching or splintering.

There are various types of curves, the two commonest being: (1) Lead I shows *R–T* elevation and, later, inversion of the *T* deflections; and in lead III, the *R–T* segments are depressed, with the subsequent development of upright *T* waves. (Figs. 85, 86 and 89). (2) Lead III shows *R–T* elevations and, later, inversion of the *T* deflections; and in lead I, the *R–T* segments are depressed, with the subsequent development of upright *T* waves (Figs. 87, 88, 90 and 91).

The first type, which is the more common, is associated with occlusion

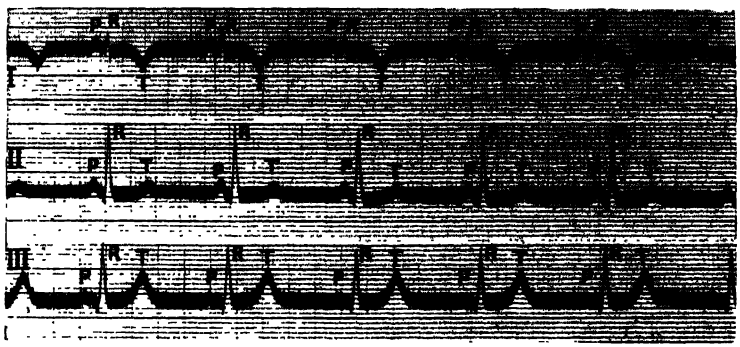


FIG. 89.—Electro-cardiogram from a case of the T^1 type of infarction of the heart. The *T* deflections in lead I are inverted, and are rather sharply defined and of increased amplitude. Those in lead III are upright, and are sharply defined and of increased amplitude.

of the descending branch of the left coronary artery and infarction of the wall of the left ventricle near the apex, especially the anterior part, and the adjacent part of the interventricular septum; and is termed the T^1 type. The second is associated with occlusion either of the right coronary artery or the circumflex branch of the left and infarction of the posterior wall of the left ventricle near the base; and is designated the T^3 type.

In both types of curves the *T* deflections in lead II are often slightly inverted or flattened.

Some changes in the *T* deflections towards the normal usually supervene within a few weeks or months, and ultimately the *T* deflections in all leads may become normal, but sometimes those in one lead remain inverted and sharply defined, and even these changes are very suspicious.

A large *Q* deflection in lead III (see Figs. 90 and 91) is often a noticeable feature of infarction of the posterior wall of the left ventricle, either recent or old. It is to be noted, however, that it may also occur in other conditions (see p. 1003).

Lead IV is particularly valuable in occlusion of the descending branch of the left coronary artery, *i.e.* the T^1 type. This lead alone may be affected, while in some cases the changes are more evident, or occur earlier and last longer than in the three other leads. They resemble those of lead I of this type. Thus, there is elevation of the *R–T* intervals, and subsequently in-

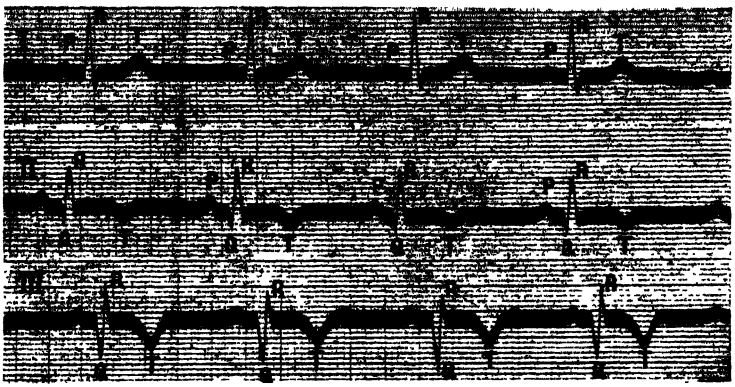


FIG. 90.—Electro-cardiogram from a case of the T^3 type of infarction of the heart. The *T* deflections in lead II are inverted. Those in lead III are inverted, and are sharply defined and of increased amplitude. There is a large *Q* in lead III.

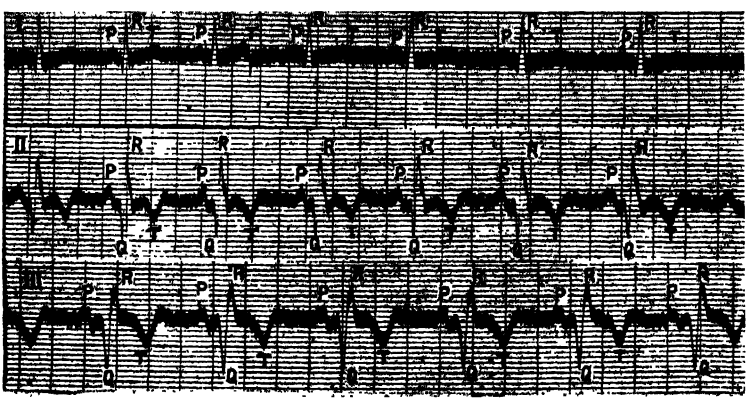


FIG. 91.—Electro-cardiogram from a case of the T^3 type of infarction of the heart. The *T* deflections in leads II and III are inverted, and are sharply defined and of increased amplitude. There is a large *Q* in leads III and II.

verted *T* waves. (Figs. 92 and 93.) Lead IV is of less value in infarction of the posterior wall of the left ventricle, *i.e.* the T^3 type. There may be no changes, or if present they are less marked. If there are changes, they generally resemble lead I of this type. Thus, there is depression of the *R–T* intervals and, later, upright *T* deflections. The latter are of increased amplitude, and may be huge. (Fig. 94.)

The foregoing changes in the electro-cardiograms of coronary occlusion with infarction of the heart are not constant. But they are frequent, and when they do occur are of great diagnostic value. It is necessary to point out that it is the successive changes in the curves which are especially



FIG. 92.—Electro-cardiogram of the fourth lead from a case of the T^1 type of infarction of the heart. There is R–T elevation, as indicated by arrows, and inversion of T. There is also a large Q.

important. For this reason, serial records taken over a period of time are of much greater value than a single one, for in cases in which the latter does not reveal the characteristic changes, later curves may do so. It is unusual to find an absence of these changes during the whole of the first two weeks



FIG. 93.—Electro-cardiogram of the fourth lead from a case of the T^1 type of infarction of the heart. There is slight R–T elevation, and the T deflections are inverted, sharply defined and of increased amplitude. There is also a large Q.

after the onset of symptoms, though transient changes may have disappeared in later electro-cardiograms.

In conclusion, it is to be noted that a similar deviation in the R–T (or S–T) interval has also been recorded in rheumatic carditis, pericardial

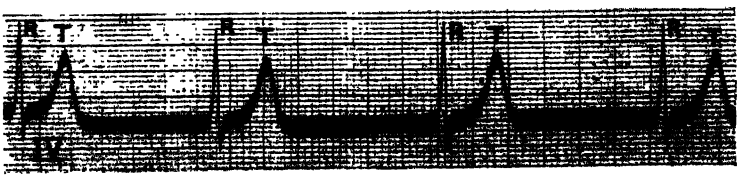


FIG. 94.—Electro-cardiogram of the fourth lead from a case of the T^3 type of infarction of the heart. The T deflection is positive, sharply defined and huge.

effusion, uræmia, and pneumonia. The clinical features of these conditions, however, do not resemble those of coronary occlusion.

It has been pointed out that transient changes in the electro-cardiograms similar to those of coronary occlusion have been observed during attacks of angina pectoris.

Low Voltage.—The term low voltage is used when no part of the *Q*, *R*, *S* complex exceeds five millimetres in the three leads. It is almost always of

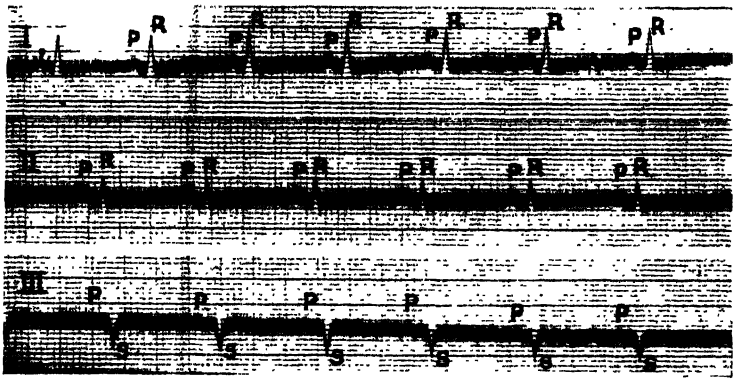


Fig. 95.—Electro-cardiogram from a case of hypothyroidism. The *T* deflections are absent in the three leads; and there is also diminished amplitude of the *Q*, *R*, *S* complex.

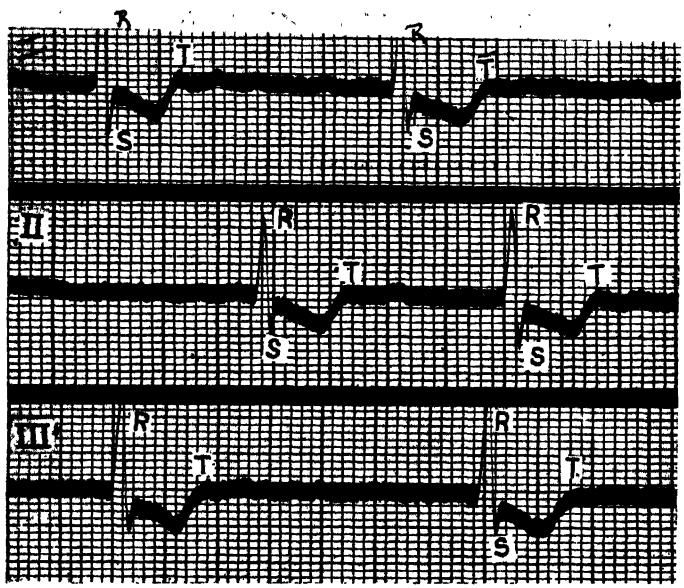


Fig. 96.—Electro-cardiogram from a case of auricular fibrillation fully under the influence of digitalis.

pathological significance, and may be met with in marked chronic myocardial disease, severe congestive failure from any cause, coronary occlusion, pericardial effusion, and hypothyroidism. In the last named there are also

changes in the other deflections (see below). As stated on p. 1021, low voltage is one of the various features found in arborization or intraventricular block.

HYPOTHYROIDISM.—The *T* deflections are flattened or inverted in the three leads; and frequently there is also diminished amplitude of the *Q*, *R*, S complex. See Fig. 95.

THE EFFECT OF DIGITALIS.—Electro-cardiograms of patients fully under the influence of digitalis may show depression of the *R–T* interval with flattening or inversion of the *T* deflections (see Fig. 96). This should be distinguished from the *R–T* deviation due to coronary occlusion. In the former the corresponding portions of the curves always point in the same direction; while in the latter usually they point away from each other in leads I and III.

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DISEASES OF THE BLOOD VESSELS

The term arterio sclerosis, which means no more than arterial hardening, has led to much confusion as it has been employed by various authors in different senses to describe different pathological conditions of the arteries. Thus, it has been used to comprise the following conditions:

(*a*) Diffuse hyperplastic sclerosis, characterised by intimal hyperplasia and hypertrophy of the media;

(*b*) Degeneration of the middle coat of the artery, known as Mönckeberg's medial sclerosis, in which lime salts are deposited more or less symmetrically in rings around the artery; and

(*c*) Arterial degeneration of the intima, known as atheroma, or, because of the tendency to calcification, as atherosclerosis.

Or it is confined to the first and second. Or it is restricted to the first. Or it is employed to include the three mentioned above and, in addition, arterial inflammation, which when chronic is most often the result of syphilis but may be caused by other infections. Or, finally, it is employed by a few writers to include even other pathological conditions, such as infiltration. It is, therefore, clear that the term arteriosclerosis should not be used except in a very general sense.

It is proposed to adopt the following classification of diseases of the arteries:

(i) Arterial inflammation
- (*a*) Acute arteritis
- (*b*) Chronic arteritis
- (*c*) Thrombo-angiitis obliterans
- (*d*) Polyarteritis nodosa or periarteritis nodosa

(ii) Diffuse hyperplastic sclerosis
(iii) Mönckeberg's medial sclerosis
(iv) Fatty Degeneration of the Media
(v) Atheroma (Atherosclerosis)
(vi) Other Degenerations allied to atheroma
(vii) Arterial infiltration.

And the following will be dealt with separately: (1) The syndrome of intermittent claudication, caused by several of the foregoing pathological conditions; (2) Aneurysms, whether (*a*) saccular, most frequently caused by syphilis; (*b*) aneurysmal dilatation, most often due to atherosclerosis; or (*c*) the less common forms of aneurysm.

ARTERIAL INFLAMMATION

The arteries may be infected from their intima, either by micro-organisms settling on the surface or by the arrest of an infective embolus within the lumen. They may also be infected by micro-organisms reaching the media or adventitia through the vasa vasorum or by direct inward spread of inflammation from the surrounding tissues.

Acute Arteritis

Acute arteritis was formerly described as a common event in many diseases, the staining of the intima being mistaken for inflammation. Acute inflammation of the arteries is, however, a rare disease, and is usually met with as a complication in the acute infections. The intima of the aorta may be infected in cases of septicæmia and pyæmia, and most commonly in cases of progressive septic endocarditis, when the organisms usually found are streptococci. Vegetations may be seen upon the intima and the inflammation rapidly involves the subjacent coats. Occasionally the aorta may be infected in a septicæmia or pyæmia, through embolism of the vasa vasorum, or the ascending aorta may be infected by spread through the vessel wall from a pericarditis. The wall of the aorta may rupture, or an aneurysm be formed, but this is rare. Acute multiple arteritis is most frequently seen as a sequel of typhoid fever, but cases have been observed after small-pox, scarlet fever, influenza, and pneumonia. In many cases the organisms of the disease have been found in the vessel wall.

Symptoms.—The symptoms depend upon the vessels affected. In the case of the femoral artery, there may be severe pain in the course of the vessel with sometimes redness and swelling in the part affected. The pulse below is obliterated. The limb becomes pale and cold, and then livid. Gangrene may or may not follow; it depends upon the rapidity with which the vessel is blocked. In some cases where the onset is severe and the symptoms suggest that gangrene will follow, the circulation improves and colour returns to the limb. In other cases, several of the arteries may be infected at the same time, with high fever and symptoms of an acute infection. Some cases of cerebral thrombosis in which a young or middle-aged patient makes a good recovery and lives for twenty or thirty years without any other vascular catastrophes are probably of this type.

Prognosis and Treatment.—In acute arteritis treatment, other than rest and general and local measures for the relief of pain, is of little avail. The condition is a very severe one. If the artery involved is a large one, every effort should be made to avoid infectious gangrene, and in some cases a surprising return of circulation may be observed.

Chronic Arteritis

Ætiology.—Acquired syphilis is by far the most common cause of chronic arteritis, and less frequently congenital syphilis. Tuberculous endarteritis is not uncommon in the small pulmonary arteries and in the arteries of the brain in tuberculous meningitis. Endarteritis obliterans may also be caused by infection with pyogenic organisms of a subacute or chronic type. Moreover, changes in the adventitia of the small arteries are also found in polio-encephalo-myelitis and in encephalitis lethargica.

Pathology. — Chronic arteritis is a focal affection, and is found in muscular and elastic arteries of all calibres. It is common in the aorta and large elastic arteries, and it also frequently attacks the small arteries. The large muscular arteries, however, are but rarely affected by syphilis. Chronic inflammation of the arteries has been divided into—(1) Endarteritis, where the intima is affected; (2) mesarteritis; and (3) periarteritis, where the external coat is involved. In the great majority of cases of inflammation of the smaller arteries all coats are involved. The muscular and elastic fibres tend to be destroyed and this may result in direct rupture. The changes in the intima are very conspicuous. Its layers become very much thickened by inflammatory infiltration and proliferation. In the early stages round cells are seen, and later spindle-shaped fibroblasts, definite granulation being thus formed, while in cases of syphilis plasma cells and eosinophil leucocytes are often present. The result of this thickening in such small arteries is to narrow the vessel, and the condition is often termed endarteritis obliterans. The lumen may finally become completely blocked, leading in the brain to cerebral softening, and in other tissues to fibrosis. The adventitia is also greatly thickened in chronic syphilitic arteritis and consists of inflamed tissue infiltrated by lymphocytes, plasma cells, and occasional eosinophil leucocytes.

Syphilis of the aorta or *syphilitic mesaortitis* is a focal inflammation, but it may implicate almost the whole length of the aorta. The inflammation extends from the adventitia. The vasa vasorum proliferate and in most cases pass into the intima. About these vessels is a zone of granulation tissue, usually consisting only of plasma cells, lymphocytes, eosinophil leucocytes, and fibroblasts, but occasionally there are gummata with giant cells. Endarteritis of the vasa vasorum is found only in the more intense reactions. The elastic fibres of the media are completely destroyed in the areas of granulation tissue; occasionally the media is necrosed between areas of granulation tissue. The *Sp. pallida* has been demonstrated in the lesions. The intima of the aorta is usually thickened over the areas of inflammation, and this thickening has been in the past confused with the degeneration of the intima that we know as atheroma. The inflammatory thickening of the intima due to syphilis can, in its earlier stages, be distinguished by the naked eye from atheromatous thickenings by its sharper demarcation, pearly colour, rubber-like consistency, crenated outline, pitted surface, and freedom from fatty degeneration. The weakening of the vessel wall on account of the replacement of the middle coat frequently results in dilatations, varying in size from minute stellate patches to large aneurysms. The scarring and pitting are due to fibrous tissue replacing the inflamed media and are characteristic. In the later stages atheroma usually occurs

in the thickened intima over the areas of inflammation; also syphilitic mesaortitis and primary atheroma may co-exist, especially in later life.

The *coronary* circulation is often found affected in these cases, with the result that there are attacks of angina pectoris. Owing to the mesaortitis of the ascending aorta, the orifices of the coronary arteries become narrowed or blocked, but the disease does not spread far down the arteries, in this way providing a striking contrast with atheroma. It may cause extensive necrosis or fibrous patches in the myocardium, and the heart is not uncommonly enlarged. Frequently the aortic ring has expanded, or the aortic valves have become involved by the syphilitic inflammation, so that aortic regurgitation is a common sequel.

The *arteries of the brain* are frequently involved by syphilis, which causes endarteritis obliterans and consequent cerebral softening. This change is also present in syphilitic meningitis, where the syphilitic inflammatory reaction is more intense. The kidneys are but rarely affected, though occasionally gummata are found. The eyes are not infrequently attacked and a condition of syphilitic choroido-retinitis may be seen on ophthalmoscopic examination. In other organs, such as the liver and testicle, gummatous necrosis, followed by fibrous changes, is found. In rarer instances the trachea and lungs are affected.

Symptoms.—The symptoms that result from syphilitic vascular disease depend upon the organ affected.

In the aorta, aneurysm is a common result from syphilis. Aortic regurgitation, with its usual effect on the heart, is even more common. The symptoms of necrosis or fibrosis of the myocardium are severe anginal pains, often resulting in sudden death. Occasionally the heart muscle may give way, with the usual signs of chronic cardiac failure. If the brain is affected by arterial thrombosis, the symptoms depend upon the area affected; hemiplegia, aphasia, and hemianopia may all result. Albuminuria is quite uncommon in syphilitic vascular disease. Iritis may be present, and more commonly choroiditis, in which white patches surrounded by pigmented areas give a striking appearance to the fundus oculi. The optic disc is often white and atrophied. In syphilitic meningitis, œdema of the optic papilla is often present. The radial artery is practically always normal to the touch in cases of syphilitic vascular disease.

Course.—The course of syphilitic arterial disease is very variable. The symptoms resulting from endarteritis and subsequent thrombosis in medium-sized arteries such as the cerebral, are generally present in the acute secondary stage, from 2 to 5 years from the date of infection, but the vascular disease may exist with exacerbations all through life, and the important and characteristic cardiovascular changes in the first part of the aorta generally follow 15 to 25 years after the original infection.

Prognosis.—The prognosis in cerebral syphilitic vascular disease is on the whole good, if the condition be taken early enough and treated properly. It has to be remembered, however, that vascular syphilis is often complicated by parenchymatous syphilis, where the spirochætes are not only found in the walls of the vessels, but also in the cerebro-spinal tissues themselves, and this complication certainly increases the gravity of the condition. In the later cardiovascular syphilis the prognosis is bad unless the diagnosis is made early before any serious cardiac symptoms have developed.

Treatment.—Prophylaxis is of the greatest importance in syphilitic vascular disease. With regard to treatment, in the acute stages of syphilitic vascular disease it is generally thought that mercury is the best drug to use. Mercurial inunctions or soluble intramuscular mercurial injections should be given for 2 or 3 weeks before any intravenous injections are prescribed. Moreover, iodides should be given by the mouth, to absorb as far as possible the inflammatory products in the intima of the vessels. The indiscriminate use of arsphenamine and neoarsphenamine in the acute stages of syphilitic vascular disease has been followed by most disastrous results, their administration causing further swelling of the intima and further blocking and thrombosis of the small vessels. After mercury and iodides have been given for 3 or 4 weeks, neoarsphenamine, should be administered cautiously in small doses and gradually increased.

Thrombo-Angiitis Obliterans

This name was suggested by Buerger in 1908 for a disease characterised by acute inflammation of the deep arteries and veins, and sometimes by a migratory inflammation of the superficial veins in the extremities. Thrombosis develops and the vessels become occluded.

Ætiology.—The malady is found most commonly in middle-aged male Hebrews. The cause is unknown, but the pathological changes suggest that it is due to an infection. Syphilis is usually not present, the Wassermann reaction being negative. Excessive tobacco smoking has been suggested as a predisposing factor.

Pathology.—The deep vessels of the arms and legs, especially the latter, are occluded by thrombosis in various stages of organisation; their walls are traversed by vessels, and show a little inflammatory infiltration. In about a quarter of the cases this is associated with a migratory phlebitis in the superficial veins of the limbs. The condition is characterised by extensive progressive thrombosis, with organisation, with little inflammation of the vascular coats.

Symptoms.—The onset is gradual with pains in the feet and toes. The patient is unable to walk for more than a few minutes without severe cramp-like pain in the legs (intermittent claudication, see page 1041). The thrombi in the superficial veins, when they occur, are also very tender. Redness of the extremity, especially when in a dependent position, is often noted, while blanching occurs when the limb is raised. Diminution or loss of pulsation in the arteries, such as the radial or dorsalis pedis, is often present. In the later stages, the cramp-like pain becomes intense, and the disability in walking often leads to marked mental depression. Trophic changes appear in the skin, with gangrene, and fissures and ulcers may occur.

Diagnosis.—(1) Raynaud's disease more often attacks females; the upper extremities are most affected; and X-rays show marked atrophy of the bones of the hands. This is not present in Buerger's disease. (2) In erythromelalgia the limbs become red and flushed, but the arteries pulsate forcibly; gangrene does not occur. (3) In gangrene due to Mönckeberg's sclerosis, the calcified arteries may be well seen by means of the X-rays.

Prognosis.—The course of the disease varies. Some cases progress

rapidly, while others last for years. Gangrene may require high amputation of the limb.

Treatment.—As the cause is not known, there is no specific treatment. With regard to drugs, iodides and glyceryl trinitrate are used. Gentle massage is useful, and diathermy sometimes helps. Ultra-violet therapy has been tried. Buerger recommends *passive postural exercises*, and employs the following method: "The affected limb is elevated, with the patient lying in bed, to from 60 to 90 degrees above the horizontal, being allowed to rest upon a support for from thirty seconds to three minutes, the period of time being the minimum amount of time necessary to produce blanching or ischæmia. As soon as blanching is established, the patient allows the foot to hang down over the edge of the bed for from two to five minutes, until reactionary hyperæmia or rubor sets in, the total period of time being about one minute longer than that necessary to establish a good, red colour. The limb is then placed in the horizontal position for about three to five minutes, during which time an electric heating pad or a hot-water bag is applied, care being taken to prevent the occurrence of a burn. The placing of the limb in these three successive positions constitutes a cycle, the duration of which is usually from six to ten minutes. These cycles are repeated over a period of about one hour, some 6 to 7 cycles constituting a séance" (Leo Buerger, *The Circulatory Disturbances of the Extremities*). Others claim that the maintenance of a high venous pressure and stimulation of the heart are the most effective lines of treatment. Pain is relieved by rest in the recumbent position, and heat applied to the painful limb by electric pads or electric light baths is also useful. Ulcers of the legs should be treated surgically.

Polyarteritis Nodosa or Periarteritis Nodosa

Polyarteritis nodosa is a rare complaint characterised by prolonged fever and the occurrence of nodular swellings, and in some cases aneurysms of the medium-sized arteries. It may affect arteries in almost any part of the body, producing a very diverse symptomatology.

Ætiology.—Young adults are most commonly affected, and males more often than females. The cause is unknown. The Wassermann reaction is negative, but the pathological changes and course of the disease suggest an infectious agent.

Pathology.—The medium-sized arteries are usually affected, especially those of the heart, kidneys, and intestines. A remarkably focal acute inflammation extends through all the coats of the artery with hyaline or fibrinoid necrosis of the arterial wall, and within the lumen are often found thrombi, which may become organised. Aneurysmal dilatation is usually present. There may be many polymorphonuclear leucocytes and some mononuclear cells, lymphocytes, and plasma cells; eosinophil cells are a characteristic but inconstant finding. White or yellowish-white nodules, from the size of a pin's head to that of a pea, can be seen on the arteries. Owing to the alteration in the lumen of the vessels, necrosis and infarcts occur in the organs supplied.

Symptoms.—The disease may start in almost any way, even with bronchial catarrh or with epigastric pain. There is tachycardia and irregular fever, with marked prostration. Some cases may start as an acute illness, simulating nephritis or rheumatic carditis; in others long continued malaise is the main

presenting symptom. Acute abdominal pain may be caused by disease of the mesenteric arteries—indeed, even perforation of the intestine and peritonitis have followed. If the arteries of the heart are involved, evidence of myocardial disease will be present; and when the kidneys are affected, blood and casts appear in the urine. Occasionally bronchial asthma, cough and hæmoptysis have been noted. Later, in a small proportion of cases, nodular swellings, varying in size up to a pea, may be felt in the subcutaneous tissues of the abdomen, thorax, and limbs. Examination of blood shows the anæmia and a moderate leucocytosis. Blood cultures are sterile.

Diagnosis.—This is extremely difficult, owing to the variable symptoms displayed. In most cases, a pyrexial infection, of unknown origin, has its nature revealed only post-mortem. Rarely, however, where a node was felt in the subcutaneous tissues and excised during life, the diagnosis has been made before death. The diagnosis should now be made more often if it is suspected in any obscure and varied illness in which there is some evidence of arterial involvement.

Prognosis.—It has been said that in most cases death occurs within a few weeks to a few months after the onset of symptoms. Now, however, when more cases are recognised, it is found that many recover and that the disease may run an intermittent course for many years.

Treatment.—This is the same as that of any acute infection. Arsenic, mercury, and quinine should all be tried, though the results up to now have not been encouraging. In the main the treatment should be symptomatic as the parts involved are so varied.

DIFFUSE HYPERPLASTIC SCLEROSIS

The diffuse hyperplastic sclerosis of Jores and Evans, formerly known as arterio-capillary fibrosis of Gull and Sutton, is characterized by intimal hyperplasia, especially of the smaller arteries and arterioles, and hypertrophy of the media, particularly of the medium-sized arteries.

Ætiology.—Diffuse hyperplastic sclerosis is common in late middle age, and is by no means a senile change. In the great majority the causes are those of hyperpiesia (see p. 1065). The affection may also be due to gout and lead poisoning, and chronic nephritis. In rare cases associated with chronic interstitial nephritis, it may occur in young children. It is more common in males than in females. The inherited constitution is of great importance as shown by the high familial incidence in certain cases. Syphilis has no part in the causation of this condition, though, of course, it may be present in syphilitic cases.

Pathology.—The condition is widespread, frequently involving the whole arterial system. It affects the smaller arteries and the arterioles, and the medium-sized arteries. The kidneys and spleen are most commonly affected, especially the first; the next most frequently, the brain; while the pancreas, liver, suprarenal glands, stomach and intestines are less often implicated. The characteristic lesion consists of a cellular proliferation of the intimal cells and increase of hyaline material. At a later stage there is fatty degeneration in the arterioles alone. The thickening of the intima may lead to obliteration of the lumen of the vessels. There is hypertrophy of the media of the medium-sized arteries, *e.g.* the radials, with little or no

change in the intima. In the case of the smaller arteries and arterioles, a patchy ischæmic fibrosis of certain organs, *i.e.* the kidneys and brain, may take place. Hæmorrhages may also occur.

There may be co-existent atheroma, *e.g.* of the cerebral and coronary arteries, and, it may be, of the aorta, due to age or, in the opinion of some, the result of the hypertension.

Symptoms.—In diffuse hyperplastic sclerosis the vessel wall may be felt to be uniformly thickened—the so-called "whip-cord" artery. The degree of hardening of the arteries is found on palpation to vary at different times. The artery feels hardest when the vessel is most contracted and consequently smallest. As the muscular arteries are those chiefly affected, the radial, brachial, and temporal arteries are involved. The systolic blood-pressure in cases of simple hyperpiesia may be 160–240 mm. or more; it may reach even 300 mm. in cases associated with chronic interstitial nephritis. Symptoms of cardiac hypertrophy are common in the early stages, but in favourable cases they may not appear for years. In some cases cardiac hypertrophy is followed by dilatation, with its attendant symptoms. Headache, of a throbbing and bursting character, and generally in the occipital region, is an early symptom of arterial hypertrophy, and giddiness and fullness in the head are frequently complained of. Transient paralysis may occasionally be met with, and this has been attributed to spasm of the hypertrophied arteries. Later on, cerebral hæmorrhage may occur, with the production of hemiplegia. Albuminuria and casts in the urine may be found, while profuse renal hæmorrhage may occur. Uræmic symptoms do not occur frequently and then not till late unless the condition is secondary to chronic nephritis. Gastro-intestinal symptoms are often present. The patient may first complain of dyspepsia. A chronic diarrhœa without obvious cause in an elderly man should lead to a careful examination of the arteries and kidneys. Bronchitis and emphysema may mask a cardiovascular hypertrophy, and the enlargement of the heart may be overlooked unless there is a careful examination of the blood-pressure. The changes in the fundi are numerous and characteristic, and have been discussed in the section on hypertension (see pp. 1066, 1067). Intermittent claudication is not uncommon in these cases.

Prognosis.—The prognosis depends very largely on the degree of renal involvement. In hyperpiesia the condition may last for many years and only be terminated by hæmorrhage into the brain, the ischæmic fibrosis of the kidney, which accompanies it, being of no clinical importance. If, however, there is evidence that the cardiovascular hypertrophy and high blood-pressure are complicated by true nephritis, the condition is a grave one and uræmia may ensue; and when well-marked albuminuric retinitis is present death usually occurs within six months, though very rare cases have been recorded where a certain amount of ocular change has persisted for years.

Treatment.—The first indication is to remove the cause of the condition as far as possible. As a rule the most important thing is the regulation of the patient's life, the removal of anxiety and the reduction of his work and activity to a reasonable amount. The reduction of alcohol and tobacco is often needed, and it is the average daily consumption that counts in this direction. Any gouty tendencies should be corrected by the administration of alkalis and intestinal antiseptics, such as sodium benzoate. All sources of focal sepsis, whether in tonsils, teeth, nasal sinuses, or genito-urinary tract,

should be carefully sought for and, if found, removed. Moderation in food and drink, with regular exercise and care in promoting diaphoresis, is essential. Turkish and vapour baths may be given cautiously. The administration of a purgative pill once a week, and the use of a mild saline purgative each morning are indicated; while in acute crises the abstraction of one pint of blood from the arm has often saved life.

MÖNCKEBERG'S MEDIAL SCLEROSIS

This form of degeneration is accompanied by a deposition of lime salts in the middle coat.

Ætiology and Pathology.—The cause is undoubtedly a senile degeneration of the elastic tissue and the muscle of the large muscular arteries, and a deposition of masses of lime salts in the dying tissue. It has no relation to syphilis. This degeneration has been caused experimentally in animals by a great variety of toxins. In man the causation is obscure, but it is common in diabetes and in old people. The lime salt is deposited, more or less symmetrically, within the media in plaques, which encircle part or all of the lumen. The affection is very common in the arteries of the leg below the bifurcation of the femoral; occasionally the radial and ulnar arteries are affected; rarely the aorta.

Symptoms.—The symptoms are coldness and œdema of the legs, as the result of defective circulation through them, and finally, and not uncommonly, gangrene results, this form of degeneration being usually present in senile and diabetic cases. The arteries feel like pipe stems, and sometimes crackle when rolled beneath the finger. They can be well seen by means of the X-rays.

Prognosis.—This depends partly upon the amount of gangrene present and partly upon the associated conditions.

Treatment.—It is clear that if amputation has to be undertaken a local amputation is of little value, and the limb should be amputated above the knee, as the arterial degeneration almost aways extends to the bifurcation of the femoral artery.

FATTY DEGENERATION OF THE MEDIA

Fatty degeneration of the media occurs commonly in all arteries. *It tends to occur in cases of high blood pressure, and is consequently a common and important secondary complication of diffuse hyperplastic sclerosis.* It is probably the result of toxins or lack of nourishment, and is frequently present in cases of severe anæmia. It also occurs in old age, and is associated with cardiovascular hypertrophy. The muscle fibres become lost, being replaced by fibrous tissue. The vessel wall usually becomes weakened and is liable to rupture.

ATHEROMA

Synonyms.—Atherosclerosis; Degeneration of the Arterial Intima.

Definition.—Atheroma is a variety of arterial degeneration which affects

and is almost confined to the intima. It is characterised by the accumulation of debris, which is at first fatty and later becomes impregnated with lime salts. The Greek word was used by Galen to signify a swelling full of gruel-like material.

Ætiology.—There is no doubt that atheroma is found more frequently and is more widespread with advancing age. Long life is a question of the blood vessels, and it has been well said that a man is only as old as his arteries. The quality of the arterial tissue that has been inherited may be poor, and a tendency to the development of atheroma at about the same age is often seen in all the members of certain families, thus showing the influence of heredity in the production of the condition. Atheroma also results from the amount of wear and tear to which the vessels have been subjected. It appears as a secondary change in cardiovascular hypertrophy, so that it tends to be more frequent in patients with hypertension than in other subjects of the same age. The affection is much more common in men than in women, and in subjects who have hard and prolonged mental or physical work. Moreover, it is much more common in the aorta than in the pulmonary artery, and when it does occur here it is nearly always associated with high pulmonary pressure, *e.g.* in mitral stenosis and in pulmonary fibrosis. The severity of the disease increases with the length of time during which the high blood-pressure has existed. Over-eating and stress and strain of modern life are probably factors in the ætiology of the condition. It has been said that the most important cause of atheroma is chronic poisoning. Acute degeneration of the media has been found after typhoid fever in young people, and has been caused experimentally by the injection of bacterial toxins. Chronic lead poisoning and gout are also ætiological factors. On the other hand, syphilis has no connection with atheroma, though the condition of the aorta known as syphilitic mesaortitis was for a long time confused with the chronic intimal degeneration we now know as atheroma. Disease of the kidneys probably has no direct relation with atheroma, though the high blood-pressure of chronic interstitial renal fibrosis and of secondary contracted kidney is an important factor in producing atheroma in the large elastic arteries.

Pathology.—Atheroma occurs in the large elastic and muscular arteries. The condition is usually most marked in the aorta. The coronary, cerebral, retinal, radial, brachial, and temporal arteries are frequently affected. The peripheral arteries may be normal to the feel in cases where there is advanced atheroma of the coronary or cerebral arteries. In the slighter degrees, minute yellow flecks or patches on the aorta may be observed by the naked eye. In the later stages, yellow plaques or buttons are conspicuous, and under the microscope masses of large fatty crystals, with a covering layer of fibrous tissue, are to be noted. Atheromatous plaques may ulcerate and the contents be discharged into the aorta, and thrombi are often deposited on the surface of these atheromatous ulcers. As the atheroma may be associated with degeneration of the media, a general dilatation of the aorta is very common. On the other hand, circumscribed aneurysm due to severe medial degeneration very rarely occurs. The aortic valves are frequently affected by atheromatous degeneration, and aortic stenosis or aortic regurgitation may result. A yellow atheromatous patch is commonly seen on the anterior flap of the mitral valve. Atheroma often causes great narrowing of the

lumen of the vessels, and eventually a thrombosis may form and complete occlusion result; this is the most dangerous result of atheroma; it frequently occurs in the large divisions of the coronary arteries, especially in the anterior interventricular branch of the left, and is not uncommon in the vessels of the brain. With regard to the heart, atheroma has a most profound influence, owing to the fact that it is one of the commonest causes of fibrosis of the myocardium; but the chief danger is a sudden blockage of one of the coronary arteries, generally the anterior ventricular branch of the left coronary. In these cases, if death does not follow immediately, a sudden softening of the heart muscle (myomalacia cordis) may occur, and an aneurysm of the heart may result, and in certain rare cases actual rupture of the heart wall has followed—a broken heart. In the brain, atheroma results in cerebral thrombosis, and is the commonest cause of this condition in old people, and in middle-aged people who have not had syphilis. Very commonly, however, especially in those cases of atheroma where the blood-pressure is raised, hæmorrhage may occur. In most cases of atheroma the kidneys are not involved, though occasionally atheromatous plaques may be found on the branches of the renal artery. Should, however, one of these plaques be large enough to cause much narrowing of an interlobar artery, a wedge-shaped red area of fibrosis in the distribution of the artery will occur. The renal changes, however, are relatively unimportant, and they rarely lead to symptoms during life.

Symptoms.—The blood pressure is only raised if the atheroma happens to complicate cardiovascular hypertrophy. In the aorta a diffuse dilatation, with pulsation in the supra-manubrial notch, may be present. The radial, brachial, and temporal arteries are often irregularly thickened and tortuous and can often be seen pulsating beneath the skin, but this dilatation has none of the important effects that so often follow a saccular aneurysm. Atheroma of the coronary arteries frequently gives rise to cardiac failure, and more often to angina pectoris; and sudden death is not uncommon, owing to a sudden thrombosis of a large branch. In the brain, hemiplegia usually results from hæmorrhage and more rarely from thrombosis. Ocular symptoms are rare in atheroma of the retinal arteries, which may be seen with the ophthalmoscope to be irregularly swollen and tortuous, but swelling of the optic disc and retinitis are not present.

Prognosis.—The course and prognosis are extremely uncertain. Circulation through the diseased vessels may proceed fairly satisfactorily for a long time, but thrombosis may occur with alarming suddenness, and with the direst results, if a cerebral or cardiac artery is affected.

Treatment.—The treatment of atheroma is unsatisfactory. Prophylaxis exists in the removal of the cause when possible. Great attention should be paid to diet, and repletion should be studiously avoided. Alcohol and tobacco should be taken with greatest moderation, and attention should be paid to regular exercise, and the action of the skin should be assisted by warm baths. It is doubtful if drugs are of value in the treatment of atheroma; but small doses of potassium iodide seem to be of some use in absorbing the degenerative products and assisting in the circulation of the blood through the obstructed areas.

OTHER DEGENERATIONS ALLIED TO ATHEROMA

There are closely allied intimal degenerations, in which this accumulation of fatty debris is absent.

In *fibrotic degeneration*, muscle fibres and to a less extent elastic fibres disappear after little or no fatty degeneration, and the intima becomes fibrotic. This may be found in any artery, but is very common in the smaller arteries, for instance, the interlobular and afferent arteries of the kidneys, where atheroma is very rare.

Hyaline degeneration affects the ultimate arterioles in the kidney and other organs; the muscle and elastic fibres disappear rapidly, and the intima becomes swollen and hyaline, and usually fatty. It is common with high blood pressure, but is otherwise rare.

Both these forms of intimal degeneration are of importance, because intimal fibrosis is much less focal than atheroma, and both forms, in affecting arteries of small calibre, lead in the same way as atheroma to a narrowing of the lumen sufficient to cause ischæmic destruction of the tissues. They may therefore be considered together with atheroma in their clinical effects.

ARTERIAL INFILTRATION

The commonest form of infiltration is amyloid infiltration.

Ætiology.—Amyloid or lardaceous disease occurs in cases of long suppuration due to pyogenic organisms, and is frequently associated with the secondary pyogenic infections that occur in tuberculosis of the bones and joints, in chronic syphilitic ulceration, and in actinomycosis.

Pathology.—The amyloid substance is extracellular and is deposited beneath the endothelium of capillaries, the reticulum of adenoid tissue and the pulp of the spleen, and in the smaller arteries and veins, especially in their middle coats. The affected organs are firm to the touch and have a waxy appearance. The amyloid substance can be demonstrated macroscopically by pouring tincture of iodine on the affected organ, the waxy material being stained a deep mahogany colour. Microscopically, an iodine staining may be used, or a methyl-violet stain, which colours the amyloid substance pink and the parenchymatous cells blue. In the kidney, the small arterioles in the glomeruli, those around the convoluted tubules and those in the medulla, are first attacked. In the intestine, the arterioles in the villi stand out clearly. There are two forms of amyloid infiltration of the spleen: the diffuse waxy spleen, where the venous sinuses are outlined and the central artery of the Malpighian capsule is affected; and the sago spleen, where the Malpighian capsule is greatly enlarged by the amyloid infiltration—its central artery is untouched, but its branches into the capsule are greatly swollen by the waxy material. In all these organs the parenchymatous cells are unaffected directly by the amyloid infiltration, but in the later stages necrose, owing to interference with their nourishment.

Symptoms.—The patient is pale, but often has a waxy complexion with a bright colour in the cheeks. Chronic, profuse and painless diarrhœa is common. The urine contains a large quantity of albumin, and is usually fair in

amount and of low specific gravity. The liver and spleen are enlarged, and ascites and œdema of the legs are often present.

Prognosis.—If the chronic suppuration can be cured, the condition may sometimes disappear; but in the majority of cases this is not possible, as the septic condition is engrafted on to a chronic tuberculous or other granulomatous condition, which is almost always impossible to eradicate.

Treatment.—This consists in trying to remove the cause.

INTERMITTENT CLAUDICATION

So far the various conditions discussed have been classified according to the underlying pathology. Intermittent claudication is only a symptom, but it provides such a characteristic syndrome that it is best taken separately here. The term " intermittent limp " or claudication is applied to a condition in which severe pain, in one or both legs, comes on after walking for a certain distance.

Ætiology and Pathology.—In the large majority of cases this syndrome occurs in elderly men, who have well-marked calcification of the middle coat of the arteries of the lower limbs (Mönckeberg's degeneration, *q.v.*). In rarer cases it may be present in atheroma or diffuse hyperplastic sclerosis or thrombo-angiitis obliterans (*q.v.*). It may be associated with high blood pressure, gout, diabetes, syphilis, or excessive indulgence in tobacco.

The symptoms are due to the arteries of the leg being unable to supply the muscles with the increased flow of blood that the limb requires during walking. It is one of the earliest signs of partial impairment of the arterial flow.

Symptoms.—The characteristic pain comes on after walking a certain distance and is brought on more quickly by faster walking. It may be accompanied by cramp in the calves, and also by numbness or tingling sensations. It causes the patient to limp and finally to stop. After resting for a minute or two, he is able to continue walking, but the symptoms again recur after he has walked for a further period. Sometimes the pain may only be described as tiredness or may only be felt in the feet and unless a careful examination is made the pain may be attributed to flat feet. Often the patient may suffer from angina pectoris, the causation of the two conditions being very similar, or his anginal pain may seem to disappear as his intermittent claudication appears, really because he is no longer able to walk quickly enough to provoke the anginal pain. In nearly all cases of long standing there is absence of pulsation in the dorsalis pedis artery, or in the posterior tibial of the affected limb, which often shows signs of circulatory disturbance, being swollen, congested, and mottled, while the toes may be white and cold; but in early cases the arteries may still carry enough blood when the patient is resting so that it is more difficult to confirm the diagnosis. The amount of calcification in the arteries, which is often very extensive, may be determined by X-ray examination. In many cases dry gangrene of the limb has supervened.

Prognosis.—The prognosis is bad, but the attacks may persist for years before more serious results, such as gangrene, appear.

Treatment.—Exercise must be limited, and the patient warned to move

slowly and avoid hurrying in his walks. The production of intermittent venous occlusion may give helpful results. Diathermy has been used to relieve the pain. Heart muscle extracts and preparations of the pancreas given hypodermically have been tried, but without much success. Dry gangrene may require amputation of the limb, and when threatened may be relieved by removing the sympathetic nerves round the femoral artery.

ANEURYSM

Definition.—The word aneurysm is derived from the Greek to widen or dilate, and may be said to include any dilatation of an artery.

Aneurysms are generally divided into—

1. TRUE ANEURYSMS, in which the walls of the dilatation are formed by the coats of the artery. These may again be divided into—

(*a*) *Diffuse aneurysm.*—These are general dilatations of an artery. The dilatation is generally not great, and is of little clinical significance except that it indicates medial degeneration. The artery is sometimes tortuous in addition. The so-called cirsoid aneurysm is a very extreme example of this.

(*b*) *Circumscribed aneurysm.*—These are limited to a segment of an artery or to a part of its circumference.

(*c*) *Dissecting aneurysm.*—These are caused by the splitting of the coats of the artery, the blood having passed through the lumen into the wall of the artery, separating one coat from another.

(*d*) *Arterio-venous aneurysm.*—In these there is a communication between an artery and a vein; there are two varieties in this group—(1) aneurysmal varix, and (2) varicose aneurysm.

2. FALSE ANEURYSMS are those following a wound or rupture of an artery, with the formation of a diffuse or circumscribed hæmatoma, and are bounded by tissues external to the wall of the artery.

When a true aneurysm ruptures and gives rise to a false aneurysm the resulting structure is known as a mixed aneurysm.

Ætiology and Pathology.—The two main factors in the causation of aneurysm are—(1) loss of the muscular and elastic fibres in the wall of the artery; (2) strain. The latter is generally brought about by repeated and prolonged muscular effort, and high arterial pressure may sometimes be an additional factor. The importance of strain as a causal factor is borne out by the fact that aneurysm is much more frequent in men than women—about five to one—and occurs more frequently in the fourth decade of life than at any other period. It also occurs much more frequently in hard manual workers, such as dock labourers, soldiers and sailors. *By far the most common cause producing weakening of the large elastic arteries is syphilitic inflammation. In persons dying of aneurysm, examination of the aorta in the neighbourhood of the aneurysm will generally reveal mesaortitis* (see page 1031). In the first part of the aorta this is nearly always so, but as one gets farther away from the aortic valves an increasing number of aneurysms are due to atheroma and non-syphilitic degeneration of the media; in the abdominal aorta less than half are syphilitic. Small aneurysms may also result from erosion of the walls of the arteries in cases of septic endocarditis—the so-called mycotic aneurysm. Frequently these are multiple; they occur most often

in the cerebral arteries or in the peripheral arteries. Extensive growth of streptococci and septic granulations may be seen in the neighbourhood of the dilatations.

Aneurysm may also be the result of congenital defects in the media of the vessel, which is very commonly seen about the circle of Willis, at the junction of the anterior communicating artery with the anterior cerebral. The aneurysms vary from about the size of a pin's head to that of a pea, and not infrequently their rupture gives rise to a diffuse subarachnoid hæmorrhage, the origin of which is often overlooked unless careful search is made for the aneurysm. Congenital aneurysm has also been described in the aorta, at the point of insertion of the ductus Botalli, and in cases of coarctation of the aorta, in which condition there is great narrowing of the aorta just below the origin of the left subclavian artery.

Loss of support by surrounding tissues also appears to lead to the production of aneurysm, *e.g.* at the base of a gastric ulcer a small aneurysm often projects as a nodule and is liable to rupture. Peptic erosion may also be a cause of weakening the walls of such arteries. In the cavities of the lungs, occurring as the result of pulmonary tuberculosis, it is quite common to find an aneurysm on the walls of the arteries lying in such cavities.

It is very doubtful if external trauma alone is ever the cause of true aneurysm, but injury to the artery by penetrating wounds by knives or bullets may certainly cause it.

Slight medial degeneration leads to diffuse aneurysm, and severe medial degeneration may cause circumscribed aneurysm. It is the usual cause of circumscribed aneurysms of muscular arteries, such as the popliteal, but is a very rare cause of circumscribed aneurysm of the aorta. Atheroma itself does not lead to aneurysm, but it may be complicated by medial degeneration. Continued high blood-pressure is an important contributory factor in the formation of a diffuse dilatation of the aorta, but this has few clinical resemblances to saccular or even to fusiform aneurysm.

One of the most striking appearances in an aneurysm is the coagulation of blood in the sac itself. This does not occur in diffuse dilatation of the aorta, but in those cases of sacculated aneurysm where the wall has become roughened. The sac becomes lined with fibrinous deposits, and occasionally an aneurysm may be cured by the deposition of successive layers of fibrin, so that the sac becomes almost completely filled. On the other hand, thrombus in aneurysms may form emboli and so lead to infarcts. Again, in many fatal cases of aneurysm, rupture and hæmorrhage have taken place, the deposition of fibrin having failed to prevent the blood reaching the surface. Rupture may take place externally, or into any of the hollow viscera or the serous cavities. Rupture into the pleura is common, as also is rupture into the trachea or into the œsophagus. In these cases, death is usually sudden, though oozing may have taken place some time before the final rupture. When the hæmorrhage forces itself into the connective tissues or muscles, it takes place much more slowly, and in the cases of the limbs may allow time for treatment. An aneurysm often exercises pressure on the other organs and structures in its neighbourhood. The heart is displaced away from the aneurysm, and the blood vessels are often narrowed so that circulation through them is impeded. The trachea, the bronchus, the œsophagus, and the nerves passing near the aneurysm also suffer. When the aneurysm meets

bony tissues, absorption of the bone takes place and the vertebræ are frequently eroded in this way, the bone being absorbed more rapidly than the intervertebral cartilage. When the aneurysm presses against the anterior surface of the chest, the ribs and sternum are pushed forward and finally are absorbed and perforated.

I. ANEURYSM OF THE THORACIC AORTA AND ITS BRANCHES

These are two types—(1) The diffuse aneurysm, or general dilatation, which occurs in medial degeneration of the aorta ; and (2) the circumscribed, usually saccular, aneurysm, almost always the result of syphilitic inflammation.

General Dilatation of the Aorta (Diffuse Aneurysm)

Symptoms.—In general dilatation of the aorta the enlargement is extensive, but never reaches a very great size. The symptoms are generally due to atheroma and the medial degeneration that accompanies it. Very often there is interference with the coronary circulation, and this leads to diminution of the circulation of blood through the heart and consequently to cardiac pain. The aorta may sometimes be felt pulsating in the supra-manubrial notch, and the X-ray photograph will show general dilatation of the aortic arch. When the aortic ring is not stretched, the dilatation of the aorta beyond it may lead to the formation of a systolic murmur. Occasionally these patients die suddenly, on account of thrombosis of an atheromatous branch of a coronary artery. Provided there is no aortic regurgitation or coexisting coronary disease, patients with a dilated aorta may live for many years without serious discomfort.

Circumscribed Aneurysm

These are generally saccular but may be fusiform.

Symptoms.—Aneurysm of the Ascending Part of the Arch of the Aorta.—An aneurysm of the ascending part of the arch tends to grow forward and outwards, and to produce a pulsating tumour that is palpable and audible at the level of the second or third interspace ; hence it is often called the *aneurysm of physical signs*. It often erodes the ribs and sternum. The tumour is tender and is often the seat of pain, which may be constant but is increased by exertion. A soft systolic murmur may be heard over it. If syphilitic aortitis spreads to the aortic valve or if the part adjacent to the aortic valves is affected, the aortic ring may be dilated and aortic regurgitation will take place. There will then be hypertrophy and dilatation of the left ventricle, with an aortic diastolic murmur, and the symptoms of aortic regurgitation will be added.

The pressure effects produced by an aneurysm of the ascending aorta are as follows : The heart is displaced downwards and to the left. The superior vena cava is pressed upon ; this may result in cyanosis of the head and neck, and œdema of the arms, and enlarged veins may occasionally be seen coursing over the front of the thorax. Very rarely the aneurysm may rupture into the superior vena cava, in which case the symptoms noted may come on quite suddenly and are very marked. There is often a systolic thrill, and on auscultation a continuous murmur, which is increased during

systole, is of great diagnostic value. The aneurysm may press upon the right bronchus, causing a chronic cough, due to irritation of the bronchus and stasis of its contents, and deficient or absent breath sounds over the upper lobe of the right lung. It may occasionally press upon the pulmonary artery and in rare cases, actually open into it, causing great dilatation of the right ventricle and auricle. Such aneurysms may present themselves to the left of the sternum rather than in the usual place, the right. Aneurysm of the ascending aorta has been known to perforate into the right ventricle and much more frequently into the pericardial sac. When the aneurysm comes forward it may irritate the pleura; and in some cases a loud pleuritic rub, audible over the aortic area, may be one of the early signs. Not uncommonly this form may rupture into the pleura or sometimes externally.

ANEURYSM OF THE TRANSVERSE ARCH OF THE AORTA.—As the arch of the aorta passes from right to left it also passes from before backwards, and consequently aneurysms arising from the transverse and descending parts of the aortic arch are situated more deeply in the chest than those arising from the ascending portion. Aneurysms of the transverse and descending parts of the aortic arch have been called by Broadbent *aneurysms of symptoms*, because their presence has often to be inferred by the pressure symptoms that they produce, while a pulsating tumour is only present in the very late stages and may not appear at all.

1. *Pain.*—Pain is one of the commonest and earliest symptoms of aneurysm. It may often occur behind the sternum or across the back and pass down the left arm and be very severe: it then lasts longer than true anginal pain and is more liable to occur at night; this form of pain occurs when the ascending aorta is distended. When, however, the transverse arch is affected the pain is sometimes felt on the left side of the neck and even in the occipital region; it is probable that this pain in the neck is a reflected pain caused by abnormal afferent impulses reaching the cervical spinal cord as a result of the distension of the transverse arch. A boring, persistent pain in the chest is probably the result of direct pressure of the aneurysm. Sometimes there may be true angina pectoris owing to involvement of the mouths of the coronary arteries.

2. *Respiratory Symptoms.*—Dyspnœa is common in aneurysm, and apart from associated heart disease is usually caused by pressure upon a bronchus. There is often stridor, which in this case is heard both in inspiration and in expiration. Hæmorrhage also occurs as a result of leaking of an aneurysm through the bronchus. It may at first be slight, but often a huge gush of blood supervenes, causing death. It is said that reflex irritation of the vagi will occasionally cause bilateral adductor spasm of the vocal cords and marked dyspnœa. In this case the stridor is only heard with inspiration and disappears if a little chloroform is inhaled. Patients with aneurysm often have a ringing, rough, brassy cough. If the pressure on the bronchus has been gradual, secondary changes occur in the lung, and compression of the left bronchus in the early stages may produce over-distension of the left lung with diminished or absent breath sounds, so as to lead to a suspicion of pneumo-thorax; later on bronchitis occurs with dilatation of the bronchus with expectoration of purulent phlegm. Pressure on the trachea may occasionally be observed in cases of aneurysm of the aortic arch, the larynx being drawn downwards and backwards with each cardiac pulsation. A

physical sign described by Surgeon-Major Oliver is known as *tracheal tugging*. The patient should be placed in the erect position, and directed to close his mouth and elevate his chin. The cricoid cartilage should be grasped between the finger and thumb and gentle steady upward pressure be made upon it. If there is an aneurysm, the pulsation of the aorta will be distinctly felt transmitted through the trachea to the hand. This sign may occur in aneurysm before other symptoms are evident, but is not very reliable.

3. *Pressure on nerves.*—(*a*) The left recurrent laryngeal nerve.—This nerve courses round the arch of the aorta and passes up behind it, and is consequently often involved in aneurysm of the transverse arch. The abductor fibres of the recurrent laryngeal nerves succumb to the effect of pressure before the abductor fibres and consequently the vocal cord is at first in the position of adduction. During respiration, the right vocal cord moves up to and meets the adducted left vocal cord and respiration is unaffected. During phonation, the right vocal cord again comes up to and meets the left vocal cord, and the voice may be quite normal. It is therefore clear that a laryngoscopical examination may reveal the early stage of pressure on the left vocal cord before there has been any alteration in the voice. As the pressure increases, the adductor muscles are affected and the left vocal cord remains motionless in the cadaveric position half-way between full inspiration and full expiration. The voice is now hoarse, and it not uncommonly happens that hoarseness is the first symptom for which the patient presents himself. (*b*) The sympathetic nerve.—Pressure upon the sympathetic nerve causes first of all irritation and later on a paralysis of the cervical sympathetic fibres. When the sympathetic is irritated, the pupil on the same side is dilated, and there may be sweating and flushing of the same side of the face and ear. When the cervical sympathetic is paralysed, the pupil is smaller than on the opposite side, the eyeball may be sunken into the orbit, and there may be a slight degree of ptosis. Unequal pupils in aneurysm are, however, frequently found without any of the other symptoms of sympathetic irritation or paralysis, and in these cases Doctors Wall and Walker suggest that the difference in the pupils is due to the pressure of the aneurysm upon the arteries passing to the neck. They have shown that in a condition of low blood pressure the pupils are dilated, whilst in a condition of high blood pressure they are contracted, and that pressure upon one common carotid will cause dilatation of the pupil on the same side. They point out that under these conditions the dilated pupil is constantly on the same side as the smaller temporal pulse, and they consider that the dilated pupil and the small pulse are due to the same cause, namely, pressure upon the arteries supplying that side of the neck. Unequal pupils also occur as the result of syphilitic disease of the nervous system. We may get bilateral pin-point pupils, or the pupils may be unequal and irregular in outline. In both cases the reaction to light is lost, while the reaction to accommodation remains. (*c*) Pressure upon the intercostal nerves occasionally results from an aneurysm that presses backwards and erodes the vertebræ and posterior portions of the ribs. In these cases the pain is very severe along the affected nerves. In the distribution of the nerve itself the skin may be anæsthetic—the so-called *anæsthesia dolorosa*. (*d*) In some cases the aneurysm presses upon the brachial plexus, shooting pain occurring in the head and neck and down the right arm.

4. *Pressure upon the branches springing from the aorta.*—This is not uncommon, and may result in the absence of one radial or temporal pulse, or inequality between the two pulses. If the innominate artery is pressed upon, the right radial and temporal arteries may be small and imperceptible, while in an aneurysm of the transverse arch of the aorta, the left subclavian artery is compressed, in which case the left radial pulse may be affected. A sphygmographic tracing is often of value in demonstrating the difference between the two pulses, and a forced expiration, by increasing the intrathoracic pressure, will often accentuate the difference between the two sides. When the pulses are markedly unequal, the blood-pressure is also diminished on the side of the feebler pulse; a difference of pressure of over 30 mm. between the two sides is in favour of aneurysm provided it is not due to coarctation of the aorta.

5. *Pressure on the œsophagus.*—This may result in slight difficulty in swallowing but the dysphagia is very rarely important. Occasionally the aneurysm may ulcerate into the œsophagus so that death takes place from a sudden rupture.

Aneurysm of the Descending Portion of the Arch.—In these cases the sac frequently projects backwards and erodes the vertebræ from the third to sixth thoracic, causing great pain and occasionally compression of the spinal cord, resulting in paraplegia. Dysphagia is more common, and sometimes a tumour appears in the region between the scapula and the spine, and may attain a very large size.

Aneurysm of the Descending Thoracic Aorta may occur close to the diaphragm. Aneurysm of this form is frequently overlooked, pain in the back being the most prominent early symptom.

Diagnosis.—*Inspection.*—This is most essential. Abnormal pulsation should be looked for in the thorax, and can often be seen when the patient is seen obliquely in a good light. Posterior pulsation is generally observed to the left of the spine. Enlarged veins over the chest, suffusion of the face, and alteration in the pupil may be noted. The apex-beat is often displaced from its normal position, especially when the sac is large, this being due to pressure of the aneurysm on the thorax; the heart itself is seldom hypertrophied, unless there is a leakage through the aortic valves.

Palpation.—Palpation may reveal the area and degree of the abnormal pulsation. There may only be a diffuse impulse, but if the sac has perforated the chest wall, a forcible heaving and expansile impulse may be felt. Occasionally a diastolic shock is to be noted. This has been thought by some to be due to the forcible closure of the aortic valves producing an effect within the aneurysmal sac; another explanation is that the contraction of the heart draws in the ribs during systole at the point where they are adherent to the aneurysm and the diastolic shock is produced by the elastic recoil of the ribs and costal cartilages. Occasionally a systolic thrill may be felt.

Percussion.—A dull area may in some cases be made out in the second right interspace in cases of aneurysm of the ascending aorta. Much more rarely an aneurysm of the arch may press forwards and to the left, and produce dullness below the left clavicle. Pressure upon a bronchus may at one period result in hyper-resonance from lung distension, and later, owing to absorption of air in the lung, the percussion note may become dull.

Auscultation.—There may be no murmur, even in a large aneurysm, but a systolic murmur is not uncommon. When both systolic and diastolic murmurs are heard, aortic regurgitation is present in addition to the aneurysm. Accentuation of the aortic second sound is a most constant auscultatory sign of aneurysm, but it occurs with syphilitic aortitis before an aneurysm has developed.

Reference has already been made to alteration in the radial and temporal pulses. Exceptionally, in a large aneurysm of the descending aorta there may be absence of pulsation in the abdominal aorta and peripheral arteries of the legs, the dilatation of the thoracic aorta being sufficient to convert the intermittent into a continuous stream.

Examination by radioscopy is most important in every case where aneurysm is suspected and may give valuable information. The chest should be examined from the anterior, the posterior and the right oblique positions. The pulsation of the tumour and its relation to the aorta may actually be seen, but photographs should always be taken, both in the anterior-posterior and oblique positions, as much information is obtained from the density of the shadow cast by the aneurysm. If the latter is very dense, it can be reasonably inferred that deposition of the laminated clot has taken place within the sac.

Complications and Sequelæ.—The main complication causing death is rupture, which may take place either externally, into the pericardium, into the pleura, into the œsophagus, into the bronchus, or into the lung tissue itself. Pressure on the trachea, causing stridor and respiratory obstruction, is a very distressing complication. Bronchitis may occur during the course of the illness, and may be recovered from more than once. Broncho-pneumonia and gangrene of the lung not infrequently occur when there is pressure upon a bronchus, and empyema may occasionally result. Tuberculosis of the lung may coexist with aneurysm, but death from hæmoptysis, the result of perforation of a deep-seated aneurysm into the bronchus, has often been mistaken for the profuse hæmorrhage of tuberculosis. Cardiac failure is responsible for a large number of deaths. This may be the result of interference with the circulation through the coronary arteries, and in other cases it is due to the aortic regurgitation. Cerebral embolism sometimes occurs in cases of aortic aneurysm, a portion of the clot within the artery becoming displaced and passed up to the brain.

Course.—Most cases live from 2 to 5 years from the time when the first symptoms have appeared. Occasionally life may be prolonged for several years by treatment, provided the diagnosis is made early. Spontaneous cure may be obtained by deposition of laminated clots within the cavity of the aneurysm, but this is comparatively rare.

Diagnosis.—Intrathoracic aneurysm is sometimes difficult to diagnose from intrathoracic neoplasm. In both there may be an externally projecting tumour, but in aneurysm the pulsation may be seen to be expansile. The diastolic shock indicates an aneurysm. Systolic murmurs may occur in both conditions, but the ringing aortic second sound is of great importance, and is rarely heard in tumours. Tracheal tugging is in favour of aneurysm, while progressive wasting and enlargement of glands in the neck are in favour of neoplasm. Aneurysm, as a rule, occurs in apparently healthy men between 45 and 60 years of age, whereas malignant growth in the chest is associated

with emaciation and pallor. In aneurysm there is a greater likelihood of the pupils and pulses being unequal, while in neoplasm œdema of the upper extremities and chest wall is not uncommon. In all cases an X-ray examination should be made, and will nearly always clear up the diagnosis. Clinical evidence of infection by syphilis and a positive Wassermann reaction are obviously important.

A violently pulsating thoracic aorta, either in association with aortic regurgitation or with violent throbbing of the heart, may lead to the unfounded suspicion of an aneurysm.

In cases where an empyema is pointing on the left side in the region of the heart, the tumour may pulsate. The throbbing is usually diffuse and widespread, and there is a coexistence of a pleural effusion. Exploration with a fine needle will usually settle the diagnosis. It must, however, be remembered that occasionally an empyema may be the result of extension of septic trouble from a bronchus which has become compressed by an aneurysm.

Prognosis.—In aneurysm this is always difficult. Complete cure is very unlikely, although pain and other unpleasant symptoms and physical signs may give way to treatment. The presence of aortic regurgitation is unfavourable, while an aneurysm progresses much more slowly in people of a placid disposition and those who lead a quiet life. Even in cases where treatment has apparently been most successful and pain and dyspnœa have been apparently relieved, sudden death from rupture may occur.

Treatment.—The recognition that the main cause of aneurysm is the weakening of the wall by syphilitic mesaortitis has brought anti-syphilitic remedies into the forefront of modern treatment of aneurysm of the thoracic aorta. Mercurial inunctions and injections have been but little tried, but in many cases a good deal of benefit has been observed. The iodides have been given in aneurysm for many years—long before syphilis had been recognised as a cause of the condition. The most striking effect of iodide is the relief of pain, and this may be obtained by even small doses, such as 5 grains three times a day. In all cases, however, large doses, such as 20 grains three times a day, should be given a trial. Neoarsphenamine has been given intravenously in many cases with great success; it should always be tried when the diagnosis is made early enough, but should never be used if congestive failure or paroxysmal nocturnal dyspnœa have developed.

Efforts to produce clotting within the sac should be tried in early cases of aneurysm. Tufnell's method—that of a complete rest and restricted diet—is only of historic interest. The patient had to lie in a quiet and secluded room for several months. Few patients put up with such a rigid diet and rest. Secondly, the administration of lime-salts, such as the chloride or lactate of calcium, should also be tried, in an endeavour to promote clotting within the sac. The gelatin treatment has been abandoned.

Many patients with intrathoracic aneurysm do better if, after a preliminary rest with the treatment appropriate to their stage, they are allowed to follow their general vocations, provided their work be not too strenuous for body or mind. Nearly always it will be necessary for their activity to be curtailed. Patients should be cautioned to take things as easily as possible, to avoid alcohol, to eat with great moderation, and to avoid any sudden exertion. At least 10 hours should be spent in bed. A certain amount of tobacco may be smoked.

Special symptoms may have to be treated. For severe pain, cyanosis and dyspnœa, venesection will often give marked relief. Amyl nitrite and iodide of potassium are of great service in relieving the anginal pain of aneurysm. Severe paroxysmal dyspnœa is nearly always due to direct pressure on the trachea; both inspiratory and expiratory stridor are present. The inhalation of chloroform does not give relief, and tracheotomy is useless. In some very rare cases there may be a bilateral abductor spasm of the vocal cords, due to irritation of the vagi, and relief may be obtained by chloroform. Intubation of the larynx is preferable to tracheotomy, which should never be performed to relieve the dyspnœa of aneurysm.

Surgical Treatment.—This may be considered under four heads—(1) ligature of the vessels arising from the arch of the aorta; (2) the passage of wire into the sac with or without galvanism: (3) needling the sac; and (4) ligature of the neck of the sac. There are few cases where the outlook under medical treatment is so bad that the certain risks and uncertain benefits of surgical treatment can be advised with wisdom.

Ligature of vessels has been of little service in the case of aneurysm of the aorta. In aneurysm of the innominate artery, combined simultaneous ligature of the right common carotid and subclavian arteries may be tried, but even this may be insufficient to prevent the flow of blood through the sac. Moore's method of introducing silver or zinc wire into the sac through a cannula has been used, but the best results have been in cases of abdominal rather than intrathoracic aneurysm. Puncture of the aneurysm and scratching its wall with the point of a needle, as advocated by Sir William M'Ewen, has sometimes been partially successful. Ligature of the neck of the sac may be undertaken when it appears to be small, but suitable cases are very rare.

Aneurysm of the Innominate Artery.—This is not uncommon. It forms a pulsating tumour, which can sometimes be felt above the right clavicle, and nearly always produces marked diminution in the right radial and temporal arteries. In this form of aneurysm, paralysis of the right recurrent laryngeal nerve occurs not infrequently, the right vocal cord being paralysed instead of the left.

Aneurysm of the Carotid and Subclavian Arteries is mainly of surgical interest. It has been thought to be most frequent in the common carotid, especially in women, but in many of these cases there is really a kinked carotid artery, due to hypertension and athero-sclerosis, that simulates an aneurysm. Subclavian aneurysm is nearly as frequent as carotid aneurysm. Syphilis is found in nearly all cases near the aorta but trauma becomes more important towards the periphery.

II. ANEURYSM OF THE ABDOMINAL AORTA AND ITS BRANCHES

Aneurysm may occur in any part of the abdominal aorta, but it is much less common than aneurysm of the thoracic aorta. A forcible dynamic pulsation of the vessel is often mistaken for aneurysm and no case should be diagnosed as aneurysm unless a tumour can be grasped between the fingers. Often in true aneurysm there is evidence of syphilis and the Wassermann reaction is positive. A systolic thrill can sometimes be felt, and a systolic murmur is, as a rule, audible. The complications in abdominal aneurysm are

many. Death may result from complete obliteration of the lumen by clots, or by erosion of the vertebræ and compression of the spinal cord, resulting in paraplegia. Occasionally the superior mesenteric artery may become blocked by a clot and acute intestinal obstruction result. The commonest complication is rupture, which generally takes place into the retro-peritoneal tissues, with the formation of a large rapidly-growing tumour in the flank. More rarely death takes place from rupture into the peritoneum or duodenum.

Treatment.—The treatment of abdominal aneurysm is the same as that of thoracic aneurysm. In cases where medical treatment is unsuccessful after a fair trial, surgical measures should be undertaken and are more likely to be successful than in thoracic aneurysm.

ANEURYSM OF THE SPLENIC ARTERY is very rare. A tumour can be felt near the spleen and it may perforate into the colon. If the diagnosis can be made, removal of the aneurysm and of the spleen should be undertaken.

ANEURYSM OF THE MESENTERIC ARTERY, which is also rare, generally results in plugging of the vessel or its branches, with the result that acute intestinal obstruction takes place and death occurs from this cause.

ANEURYSM OF THE HEPATIC ARTERY is very rare.

ANEURYSM OF THE RENAL ARTERY has occasionally been noted, and in some cases successfully removed.

ANEURYSM OF THE BRACHIAL ARTERY used to be common, but is now rarely seen.

ANEURYSM OF THE FEMORAL ARTERY is much more common, and is most often traumatic.

ANEURYSM OF THE POPLITEAL ARTERY is one of the most common of the peripheral aneurysms. It has been suggested that this is due to the fact of the exposure to stress and strain to which the popliteal region is subjected during violent lifting efforts.

In all cases of peripheral aneurysm not due to trauma, a syphilitic basis should be invesigated; but the aneurysms of the muscular arteries of medium size are almost invariably due to medial degeneration, and a syphilitic aneurysm would be most unusual. The treatment is mainly surgical. Distal or peripheral ligature and excision have all been tried, and more recently Matas has suggested treatment by *Reconstructive Endoaneurysmorrhaphy*. After rendering the limb exsanguine, he freely opens the arterial sac and by a process of suturing reconstructs a channel between the afferent and efferent artery of the sac. This is theoretically the best treatment, but in practice it is often found impossible.

When the symptoms warrant surgical treatment, proximal ligature is probably the method most frequently used for a large artery and excision of the sac for a smaller one. Proximal ligature as close to the aneurysm as possible has been the classical operation since the time of John Hunter. It should be combined with distal ligature, as this does not increase the risk of gangrene and diminishes the risk of spreading infection or of an embolus becoming detached.

Until the War of 1914–1918 great care was taken to avoid injury to the vein, but it was found that proximal and distal ligature of the vein as well as of the artery reduced the risk of gangrene. This should therefore be the routine surgical treatment.

III. DISSECTING ANEURYSM

This may originate in an atheromatous ulcer. Very often the dissection of the coat is small, especially when the blood-pressure is not high. When, however, there is a very high blood-pressure and much degeneration of the media, an extensive dissecting aneurysm may occur. The degeneration of the media may cause a small split in the intima and the dissection separates the intima from the media, so that in some cases there may be a double tube instead of a single aorta. Extensive dissection frequently causes sudden death, but in other cases the patient may live on, and the association of a rapidly beating heart and a feeble pulse in the lower limbs has been suggested as a clinical sign by which the condition may be recognised. The immediate picture is very similar to that of a coronary thrombosis. If the dissection spreads up the common carotids, symptoms from interference with the cerebral circulation may follow and this soon after an attack, suggesting coronary thrombosis may reveal the diagnosis. Occasionally the patient makes a complete recovery and lives for years with the circulation through the new channel made by the dissection.

In many cases of extensive dissecting aneurysm of the aorta, due to medial degeneration, vascular hypertrophy is well marked, and consequently the blood pressure was high during life. Less commonly dilatation, rupture and the dissecting aneurysm of the aorta are apparently due to congenital weakness, histological evidence of degeneration or inflammation being absent.

IV. CIRSOID ANEURYSM

Cirsoid aneurysm is a condition in which an artery is dilated and tortuous. Occasionally it is due to medial degeneration of muscular arteries, particularly the splenic and temporal, but this form is of little clinical importance. More often it is due to defective development of the walls of arteries and their branches, and this form has been called serpentine angioma. The arteries, their branches, the capillaries, and even the efferent veins dilate progressively, causing destruction of the intervening soft tissues and erosion of bone. The superficial temporal, posterior auricular, and occipital arteries are most commonly affected. It also occurs in the brain, pancreas, orbit, and limbs. It is most common between puberty and 30 years of age. Although the condition is generally congenital it may develop greatly after some local injury such as a blow.

Pathology.—The arteries are dilated, thinned and very tortuous, and the disease tends to spread towards the capillaries and also along the arteries that feed the aneurysm. The skin over the aneurysm is often atrophied and may become ulcerated, leading to very dangerous hæmorrhage.

Symptoms.—There is an ill-defined pulsating tumour on the scalp, in which the tortuous vessels may be felt. In rare cases the tumour may be slow in its growth, but this is generally rapid and the skin over it ulcerates, leading to hæmorrhage.

Treatment.—This is very difficult. In limited cases the tumour may be excised. Generally, however, ligature of the peripheral arteries of the growth is more satisfactory. Electrolysis and injections of perchloride of iron into the

mass have been tried, with some success. Occasionally spontaneous cure follows some infection.

V. ARTERIO-VENOUS ANEURYSM

Arterio-venous aneurysms, in which an artery and a vein communicate, are of two kinds: (1) aneurysmal varix, where the two vessels anastomose directly; and (2) varicose aneurysm, where the sac separates the connecting vessels.

(1) ANEURYSMAL VARIX.—The aneurysm is usually traumatic in origin and used to be frequent at the elbow, as the result of venesection. The artery is wounded at the same time as the vein and they become connected, the result being that the vein becomes markedly dilated and tortuous.

The varix forms a soft, compressible, ill-defined tumour, which pulsates. Pain in the tumour is not uncommon. A marked thrill can often be felt and a loud briut may be heard over the tumour. If the limb is raised the tumour shrinks, while it becomes large and congested if the limb is held downwards. The limb below the tumour is often œdematous.

In some cases the aneurysm remains stationary, and all that is required is an elastic support. If, however, it tends to increase in size, the artery should be ligatured above and below its communication with the vein, and the vein should also be ligatured.

An intrathoracic aneurysm may become adherent to a vein and perforate into it. The most common site is when an aneurysm of the ascending arch of the aorta perforates the superior vena cava, but even this is rare. The latter vessel becomes greatly distended and an arterio-venous aneurysm is formed. There is often a sudden onset when the lumen of the two vessels becomes connected; there is congestion of the head and neck and upper limbs, great distension of the veins, and often œdema. On auscultation over the tumour, a continuous humming murmur is heard, with marked accentuation during systole.

(2) VARICOSE ANEURYSM.—This occurs when an artery and vein are simultaneously wounded. A false aneurysmal sac is formed in the tissues and communicates both with the artery and vein. The symptoms are similar to those of an aneurysmal varix, but in addition there is a pulsating tumour, which can be distinguished from the dilated vein. This form of aneurysm should be excised by open operation combined with four-fold ligature of the artery and of the vein. It is not often seen in civil life but is fairly common in war-time, mainly as a result of gun-shot wounds.

ARTERIO-VENOUS ANEURYSM OF THE ORBIT OR PULSATING EXOPHTHALMOS.—This is a form of aneurysm by anastomosis, due to a communication having formed between the cavernous sinus and internal carotid artery as it passes through it. It is generally the result of a fracture of the base of the skull. It is usually unilateral, but may be bilateral, and the communication may take place immediately after the fracture, or evidence of the lesion may only appear days or weeks after the injury.

The main symptom is protrusion of the eyeball, the globe being displaced outwards and downwards. It may be seen to be visibly pulsating, but if not, slight pressure upon the globe of the eye will bring out pulsation. A loud bruit, either continuous or increased during systole, may be heard anywhere

over the head ; this roaring sound is generally very distressing to the patient. There is great dilatation of the veins around the eyelids, conjunctivæ, and fundus. Headache is common

The condition may last for years, and in a few cases spontaneous recovery has taken place.

The treatment is either compression or ligature of the carotid artery. The great danger in ligaturing the carotid artery is the occurrence of cerebral softening and hemiplegia. To avoid this, it is better to ligature the artery temporarily and see if any cerebral symptoms tend to develop ; if they do, the ligature should be removed after 24 hours ; but if they do not, the ligature may be tightened and the artery completely occluded.

DISEASES OF THE PULMONARY ARTERIES

The pulmonary artery is much less frequently the seat of disease than is the aorta, but it is liable to be affected by pathological changes of a similar character to those that are found in the systemic arteries.

Ætiology and Pathology.—Four main pathological changes are generally recognised, namely.

1. HYPERTROPHY.—This condition is associated with an increase in the blood pressure in the lesser circulation and is found in cases of disease of the lungs, such as emphysema, pulmonary fibrosis, and bronchiectasis, and also in disease of the heart, such as mitral stenosis. The intima of the pulmonary arteries hypertrophies and is prone to degeneration, so that patches of fatty change (atheroma) appear in the hypertrophied tissue. This form of intimal degeneration is superimposed upon hypertrophy, which is the result of obstruction to the lesser circulation and is independent of inflammatory change.

2. INFLAMMATION.—There is no doubt that *syphilitic* inflammation may attack the pulmonary arteries as well as the aorta. The larger trunks may be affected by mesarteritis, and saccular aneurysms of the main branches have been described, but are rare. The smaller arteries and arterioles in the lungs may also be affected by syphilitic arteritis, with endarteritis obliterans. The endarteritis, either by itself or in combination with thrombosis, may lead to complete occlusion of the lumen. Ayerza and his pupils have emphasised the importance of syphilis as an ætiological factor in the production of cyanosis and congestive heart failure in the absence of the usual causes of these conditions, such as emphysema and fibrosis of the lungs, or mitral stenosis. Fatty or calcareous changes may occur as secondary changes in the walls of the inflamed arteries.

Tuberculous inflammation of the branches of the pulmonary arteries is also common. Tuberculous endarteritis obliterans is frequent in phthisis. Tuberculosis of the lung or a bronchial gland may extend through the wall of a large artery to its intima, giving an intimal tubercle which when softened can lead to a general dissemination. The wall of a pulmonary artery exposed in a tuberculous cavity is frequently weakened by tuberculous or pyogenic invasion from without, and an aneurysm results. The profuse hæmoptysis found in the latter stages of chronic pulmonary tuberculosis results from the rupture of one of these aneurysms.

3. Degeneration.—Degeneration of the intima secondary to intimal hypertrophy or to inflammation has been described above. Slight primary intimal degeneration, or atheroma, is not uncommon in elderly subjects. C. F. Coombs and others have described cases of a severe atheroma of the pulmonary artery in young subjects, in whom there was no evidence of syphilis or of pulmonary or cardiac lesions, and suggest that in these cases there is an inherited tendency to intimal degeneration.

4. Congenital Malformations.—In the majority of cases a pulmonary stenosis is present, but in rare instances dilatation of the vessel has been found. These conditions are described under congenital heart disease (*q.v.* p. 968).

Symptoms.—The symptoms of disease of the pulmonary artery are those of obstruction of the lesser circulation.

Dyspnœa is often an early symptom, and may occur on exertion or in nocturnal paroxysms. In the later stages it becomes constant, with attacks of orthopnœa. Cyanosis is one of the most characteristic manifestations, but it varies in intensity and also in the stage of the disease at which it appears. Cyanosis is due to an imperfect oxygenation of the blood passing through the lungs at each cardiac cycle. It will, therefore, be most marked in those cases in which only a small proportion of the blood passes through the lungs at each beat, as in congenital pulmonary stenosis, or those in which the capillary area in the lungs has been so reduced by emphysema or the lung itself has been so damaged by fibrosis that the circulating blood is imperfectly oxygenated. In mitral stenosis the degree of cyanosis is remarkably variable and probably depends as to whether secondary changes in the lungs have developed. In Ayerza's disease (syphilitic inflammation of the pulmonary arteries) the cyanosis may be extreme and the patients may have almost a black appearance (cardiacos negros). This may be due to the endarteritis obliterans of branches of the pulmonary artery, or to a coexisting syphilitic obliterating bronchitis, or a syphilitic pneumonia causing fibrosis of the lung.

Hæmoptysis may occur before cyanosis has become established or in the later stages. It may be slight or profuse, and may be associated with attacks of pulmonary artery thrombosis. Cough, with mucopurulent expectoration, is common, and attacks of vertigo may occur. Somnolence is not infrequently found when marked cyanosis is present. The fingers are not clubbed, except in cases resulting from bronchiectasis or fibroid lung.

The pulse is usually regular and the heart is much enlarged, especially the right ventricle. If mitral stenosis is present diastolic murmurs may be heard at the apex. There are no constant physical signs in the lungs, but if emphysema, fibrosis, or bronchiectasis has been the determining factor, the physical signs characteristic of these conditions will be found. Œdema is often present and may be extreme and the liver enlarged. The spleen is not palpable. The blood shows an increase in the number of red cells, up to 8,000,000, the number varying with the degree of cyanosis.

The radioscopic findings are characteristic. The right ventricle is enlarged, the pulmonary artery often dilated, and the branches of the pulmonary artery show more clearly than usual and can be followed into the lung and in some cases can be seen to pulsate. The electrocardiogram shows a marked right ventricular preponderance and alterations in the *P* wave, suggesting right auricular hypertrophy.

Diagnosis.—Cases of pulmonary artery affections secondary to pulmonary or cardiac disease can be distinguished by the presence of the symptoms and signs of the underlying lesion. There is no sure method of diagnosis between syphilitic and non-syphilitic cases. In syphilitic pulmonary arteritis the patients are usually between 30 and 50 years of age and may give a history of syphilitic infection. The Wassermann reaction in the blood is positive.

Course.—There may be a history of pulmonary symptoms, such as cough and dyspnœa, for many years. Later the intense cyanosis may develop, and this may last for 4 or 5 years. Some of these patients die in their sleep, but in others myocardial failure, with advanced anasarca, is the cause of death. Others die of complications, such as broncho-pneumonia.

Prognosis and Treatment.—The outlook depends on the causative factor. In early cases in which syphilis has been established as the cause of the inflammation of the pulmonary artery, anti-syphilitic treatment will retard the progress of the disease. In paroxysms of cyanosis, venesection gives marked relief. The usual treatment for congestive heart failure must be adopted, when this has supervened.

PHLEBITIS

Phlebitis or inflammation of the veins may be sharply divided into two great classes—(1) non-suppurative or plastic, and (2) suppurative. The terms endo- and peri-phlebitis have been used to indicate inflammation of the internal and external coats. Peri-phlebitis results from invasion of the veins by inflammatory processes outside it, or from injury. It may extend inwards towards the lumen of the vein, and result in endophlebitis and generally clotting of the blood within the vein. Endophlebitis is usually the result of poisons or microbes circulating within the vein. Inflammatory changes of a plastic type occur in the endothelium, and in consequence a clot or thrombus is set up within the vein. The clot may adhere to the vessel wall and completely obliterate it. Organisation of the clot by fibrous tissue may occur, the vein being transformed into a hard fibrous cord. In other cases the clot may become softened and broken down, and the circulation may be resumed through the vein. In certain cases changes in the composition of the blood may lead to clotting in a vein, and the presence of this clot itself may give rise to a plastic phlebitis; this is sometimes called *thrombo-phlebitis*. In other cases the vein and contained clot may become invaded by pyogenic organisms, and leucocytes will enter the clot and cause it to break down into a purulent fluid.

Plastic Phlebitis

Ætiology.—(1) Traumatic phlebitis; (2) the formation of a non-infective clot—thrombo-phlebitis; (3) gouty phlebitis may accompany an attack of gouty arthritis or may occur independently; (4) typhoid fever not infrequently causes phlebitis and thrombosis; (5) in pneumonia and influenza phlebitis is not an uncommon complication; (6) post-operative phlebitis is not at all uncommon in cases of operation on the lower abdomen and the

bladder; and (7) puerperal phlebitis or phlegmasia alba dolens frequently follows parturition.

Phlebitis may attack any vein, but is most common in the lower limb, particularly in the saphena vein.

Symptoms.—Phlebitis is accompanied by pain and tenderness in the course of the affected vein, which can be felt as a hard cord. The skin may become reddened over the superficial veins, and the limb is often œdematous when thrombosis has taken place. There is usually more or less febrile disturbance. In gouty phlebitis, the pain is often severe, the areas of inflammation are often multiple; there is a great tendency for more than one vein to be attacked at once, and, in opposition to most forms of phlebitis, the disease may be symmetrical.

Complications and Sequelæ.—The complications and sequelæ of plastic phlebitis are those of the thrombosis that accompanies it, and will be described under thrombosis.

Prognosis.—This is generally good apart from the risk of embolism or of the thrombosis spreading towards the large veins, such as superior or inferior vena cava. Treatment must be carefully carried out to minimize the risk of this.

Treatment.—Patients with phlebitis should be put to bed, and the limbs elevated and wrapped in cotton wool. All sudden movement, friction, or handling should be avoided. The bowels should be freely opened, as chronic constipation and stasis in the colon may impede the circulation in the iliac veins. In gouty phlebitis, the diet should be restricted to fish and light farinaceous foods, but when patients are marasmic and anæmic, the diet should be as liberal as their digestive powers will permit. In all cases of phlebitis foods containing much lime-salts, such as milk, should be limited. Potassium or sodium citrate with carbonate of ammonia and liquor ammonii acetatis are of service. Glycerin of belladonna smeared over the inflamed vein appears to ease the pain.

Suppurative Phlebitis

Ætiology.—Suppurative phlebitis is the result of infection of the walls of the veins with pyogenic organisms. The micrococci may be in the circulating blood, as in some cases of puerperal phlebitis, or they may reach the veins from a focus of suppuration around it, as in facial carbuncle, middle-ear disease, or inflammation of the portal veins—suppurative pylephlebitis.

Pathology.—The coats of the vein are infiltrated with leucocytes, the clot which has formed within the vessel breaks down into yellow pus, and abscesses are not infrequently found along the course of the vein. Not uncommonly the septic inflammation spreads along a vein, splitting up the coats.

Symptoms.—There is a throbbing, smarting pain in the region of the affected vein, and the part drained by it is œdematous. Not infrequently the septic process spreads along a vessel. There is often fever, a rapid pulse, a dry tongue, and delirium, and in many cases a succession of rigors indicates the development of pyæmia.

Complications and Sequelæ.—These depend upon the situation of the vein and the occurrence of emboli, owing to breaking away of the softened

clot. (See Thrombosis.) When the vein is superficial the diagnosis is easy, but when a deeply-seated small vein is affected the only symptoms may be those of the pyæmia to which it gives rise.

Treatment.—The prevention of this disease by asepsis is one of the great advances in modern surgery. As soon as the disease is recognised, a ligature should be placed upon the vein between the affected area and the heart, the inflamed vein should be thoroughly laid open, the septic clot removed and the cavity thoroughly cleansed. In some cases where numerous abscesses are formed, amputation is the only means of arresting the general infection.

Thrombosis of the portal vein is commonly the result of septic conditions within the abdomen, most often suppuration in the region of the appendix. The condition is not always acute. Peptic ulcers may lead to portal thrombosis, and tubercular glands along the course of the portal vein have been found to cause clotting within the lumen of the vessel. Dysenteric ulcers resulting from bacillary dysentery may also give rise to septic portal thrombosis, but typhoid ulceration very rarely does so.

The effect of portal thrombosis is to produce a portal pyæmia, portions of the clot passing into the liver and causing abscesses within the radicles of that organ. Occasionally the portal vein itself becomes converted into a sac containing pus, and the liver is then riddled with abscesses along the course of the portal branches. This condition is known as *portal pylephlebitis*.

Symptoms.—The symptoms of septic portal thrombosis are the occurrence of fever and of rigors. The liver becomes enlarged and tender, and jaundice of a slight degree is quite common.

As the condition is such a generalised one, recovery very seldom takes place, even if treatment is adopted.

Treatment.—This consists in removing the cause and incising any liver abscesses.

MAURICE CAMPBELL.

THROMBOSIS AND EMBOLISM

Thrombosis is the name applied to the coagulation of blood within living vessels, whether in the heart, the veins or the arteries.

Embolism is the process whereby a portion of clot or other substance, such as parasites, fat globules, masses of bacteria or particles of tumour, is carried from one part of the circulation to another, and is impacted when it arrives at a vessel too narrow for its further progress. An infarct is the degenerated or necrosed condition of the tissues due to interference with the circulation of blood within it, and can be caused by embolism, thrombosis, endarteritis, endophlebitis or strangulation of veins. An infarct is generally wedge-shaped in outline, with the base towards the periphery of the organ affected. As seen post mortem, it is either yellowish-white in colour (the white infarct), or blood-red in colour (the hæmorrhagic infarct).

In the case of the white infarct the tissue deprived of its blood supply becomes permeated with lymph from the surrounding living tissue, and coagulative changes take place in it. In the case of the kidney or spleen, the

coagulable material is sufficient to render the infarct hard. In the case of the brain, less coagulable lymph is poured out, and the area of the brain affected becomes softened. In the early stages there is often a zone of congested vessels around a white infarct; this is a reaction on the part of the surrounding living tissues to the presence of the dead material. Later the infarct becomes invaded by fibrous tissue and a scar results.

In hæmorrhagic infarct, coagulation and necrosis also take place, but to this is added hæmorrhage, by diapedesis of the red blood cells from vessels of the collateral circulation. A hæmorrhagic infarct is commonly seen in the lung; a cone-shaped area of lung tissue becomes hard and dark-red in colour. Should the embolus, instead of being aseptic, contain living micro-organisms, a septic process is set up within the infarct and an abscess results. Such purulent abscesses are commonly seen in the lungs, as the result of septic phlebitis, and occasionally in the systemic system, as the result of septic endocarditis.

THROMBOSIS

Ætiology.—The causes of thrombosis are—(1) altered conditions of the blood or increase in its coagulability; (2) slowing of the current of the blood within the vessels; and (3) a lesion of the lining membranes of the vessel or cavity of the heart. Thus, thrombosis may occur in cases of anæmia or after infections or operations, where the blood is more coagulable than normal; in the appendages of the dilated auricles of the heart where the movement of blood is feeble or in peripheral vessels or in the lungs when the circulation as a whole is feeble, *e.g.* with a failing heart; and it may result from inflammation of the lining of the vessel or degenerative changes in its endothelium, especially when there is atheroma associated with much narrowing of the channel obstructing the circulation.

(1) Intra-Cardiac Thrombosis.—This is one of the commonest forms of thrombosis and is very important. It occurs in the left auricle, when it has become extremely dilated as the result of mitral stenosis. The ante-mortem clot generally begins to form in the dilated appendix of the left auricle, but may extend by the deposition of excessive layers of fibrin to invade the auricle itself so that a large ball thrombosis be formed within the cavity. Portions of the ante-mortem clot may break away from the thrombus, and may be carried into the left ventricle and into the general circulation, and embolism may occur in the brain, spleen, kidneys, intestines and the main arteries of the limbs. This danger is mainly to be feared in the first few weeks after the deposition of the thrombus, but may of course recur as fresh thrombi form.

Ante-mortem clot is occasionally deposited among the meshes and cavities of the dilated left ventricle. In cases of cardiac fibrosis and myelomalacia cordis, the result of disease of the coronary arteries, and especially after coronary thrombosis and cardiac infarction, the lining of the heart may become affected and fibrinous deposits occur within either ventricle. Lastly, in septic endocarditis, large vegetations, consisting of clot and masses of micro-organisms, may occur. Inflammation of the ventricle and of the auricle may also be present, and ante-mortem clot may be deposited on these roughened surfaces. Portions of this clot may leave the ventricle and pass into the

general arterial circulation, where the effect produced will depend upon whether the emboli are aseptic or contain micro-organisms.

Thrombosis in the right auricle occurs in many conditions where there is gradual cardiac failure and dilatation of the right side of the heart. Portions of ante-mortem clot form in the right auricular appendix, and parts may break away and pass into the lungs and an embolism of the pulmonary artery result. If the embolus is sufficiently large to cause blocking of the artery or of one of its main branches, sudden death ensues, but if only one of the smaller branches is affected, a pulmonary infarct results. Much more rarely ulcerative endocarditis occurs on the right side of the heart, and portions of the valves or affected clot reach the lungs in the same way.

(2) ARTERIAL THROMBOSIS.—Arterial thrombosis is rarer than venous thrombosis. It is sometimes due to arterial embolism, but is also the result of trauma or disease of the arterial walls, such as atheroma or endarteritis.

Thrombosis of the coronary arteries is a very important condition, since it is a frequent cause of sudden death and of serious cardiac disability. It has already been described (pp. 991–994). The usual artery affected is the anterior interventricular branch of the coronary artery. Atheromatous plaques are constantly found within the thrombosed vessel, and sometimes atheroma has occluded the orifice of the artery. In cases where the circulation has been slowed and greatly diminished before the final clotting, changes in the wall of the left ventricle are very common. Syphilitic mesaortitis sometimes occludes the orifices of the coronary arteries but this is much less common.

Thrombosis is very frequent in the small cerebral arteries, especially when they have become narrowed as the result of disease. In early middle-age this narrowing is usually the result of syphilitic endarteritis, but most patients are older and then the arterial lumen is diminished by atheromatous changes in the wall of the vessel.

Thrombosis of the main artery of a limb usually results in gangrene; the limb becomes first white and pallid, later mottled in appearance, and finally black. If the patient survives the immediate shock and the disease to which the thrombus owes its origin, a line of demarcation will form between the vital and devitalised tissues, and the limb should be amputated well above this level.

Thrombosis of the retinal artery is more common than embolism. There is a sudden painless loss of sight in one eye, and generally the blindness is permanent and complete. Within a short time there is opacity of the central parts of the retina, and the macula shows up by contrast as a bright cherry-red spot.

(3) VENOUS THROMBOSIS.—*Thrombosis of the lateral sinus* occurs in disease of the middle ear. The mastoid cells become infected with pyogenic organisms and the disease spreads to the petrosal or sigmoid sinus. The clot in the vein becomes softened by pyogenic organisms, and particles break away and are conveyed to the lungs, in which pyogenic abscesses are formed.

The symptoms of septic thrombosis of the lateral sinus—and its continuation of the jugular vein—are infiltration of the tissues of the neck, with a cord-like induration of the vein itself, with some restriction of the movements of the head. There is a history of a chronic and often offensive discharge from the ear of the same side. A high temperature and rigors,

due to flooding of the circulation by poison, occur when a portion of the septic clot is dislodged. In these circumstances the jugular vein should at once be ligatured below the clot, in order to prevent further portions of the clot gaining access to the blood stream. A radical mastoid operation should also be performed, the sinus opened and its septic contents removed.

Thrombosis of the longitudinal sinus of the brain occurs as the result of injuries and infected wounds of the skull. It is a common war injury, the vertex of the head having been injured by a bullet as the soldier passes along the trench. Thrombosis of the cranial sinuses also occurs in marasmic patients, but it is usually agonal.

In many of these cases, owing to the vertical position of the leg areas in the brain, a paraplegia is produced, while the arms are not affected. The condition should be treated by trephining and draining the cranial cavity. Occasionally the longitudinal sinus becomes thrombosed in septic conditions in children and also in chlorotic anæmia in adults.

Thrombosis of the cavernous sinus is not infrequently the result of the extension of a chronic suppurative process of the sphenoidal cells at the back of the nose. The cavernous sinus is also affected by septic processes on the face; a small boil on the nose or a mosquito sting on the face may produce a septic thrombosis of the angular vein; this vein communicates with the ophthalmic vein, and the septic clot may extend along the latter into the cavernous sinus. As the venous plexuses of the pterygoid and zygomatic fossæ communicate through the foramina in the middle fossa and by the inferior ophthalmic vein, purulent inflammation of the jaw and of the teeth sockets is sometimes a cause of cavernous thrombosis. The result is that a marked degree of exophthalmos and swelling of the lids, and œdema of the optic disc and extensive retinal hæmorrhages occur. Not infrequently the septic condition of one cavernous sinus spreads to that on the other side through the circular sinus, and the exophthalmos may be double. Death from pyæmia or meningitis results. Owing to the position of the sinus, operation is impossible.

Thrombosis of the central retinal vein is common in elderly patients with athero-sclerosis and high blood pressure. The loss of sight is not so sudden or complete as in blockage of the artery. There is often albuminuria. Glaucoma often develops, but if the thrombosis is in a tributary vein the degree of recovery may sometimes be fairly good.

Femoral thrombosis is perhaps the commonest form of thrombosis. It frequently occurs after parturition and in anæmic and marasmic states. It is met with after infectious fevers, especially after typhoid fever, more rarely after influenza and pneumonia. It also follows operations, especially if a septic condition has been dealt with, or results from the operation. The thrombosis generally occurs in the femoral vein, and there is often some rise of temperature and a slight rise in pulse rate. It is most common on the left, because of the pressure of the right common iliac artery on the left common iliac vein. The limb affected becomes œdematous and a hard cord is found in the course of the vein.

In other cases thrombosis of the veins may also occur in marasmic conditions secondary to carcinoma, tuberculosis and tertiary syphilis.

Complications and Sequelæ.—Collateral circulation is usually satisfactorily accomplished in femoral thrombosis. In cases where the arteries

as well as the veins are involved gangrene may occur. Occasionally the thrombosis may spread up into the iliac vein and into the inferior vena cava, in which case both legs may become swollen and œdematous. Even in cases where the inferior vena cava has become thrombosed, recovery may take place, collateral circulation being established by means of veins passing up from the legs into the axillæ. If, however, the clot reaches the entrance to the renal veins, death nearly always results from renal thrombosis. Embolism is not at all uncommon in femoral thrombosis, the clot passing into the right auricle, and then into the right ventricle and pulmonary artery.

Treatment.—Complete rest for at least 3 weeks, as a precaution against embolism, should be insisted upon. Limitation of foods containing quantities of lime salts, such as milk, and the administration of citrates and salts of ammonia will materially help in the treatment of the case. The leg should be elevated and wrapped in cotton wool and kept warm.

EMBOLISM

Embolism may occur in three main situations, namely—(1) in the systemic circulation; (2) in the pulmonary circulation; and (3) in the portal circulation.

Emboli in the systemic circulation are derived from ante-mortem clots in the left auricle and left ventricle. These clots are formed in cases of mitral stenosis and more rarely in mitral regurgitation, and also when the left ventricle is greatly dilated and hypertrophied. In these cases the emboli are aseptic. Systemic emboli also occur in septic endocarditis, when portions of the valve break away or masses of fibrin and micro-organisms pass into the general circulation. These emboli are septic, and when they reach their destination usually form abscesses.

Emboli in the pulmonary circulation may have their origin in clots formed within the right auricle and right ventricle, or more rarely from septic endocarditis of the tricuspid and pulmonary valves; they may also come from any part of the systemic venous system. A very important form of pulmonary embolism is met with after abdominal operations and after childbirth. About the tenth day after an apparently successful abdominal operation or an uneventful parturition, a pulmonary embolism may occur with appalling suddenness. Death may take place at once, or hæmoptysis and pleurisy supervene. The clot forms in the common iliac vein, at the junction of the internal and external iliacs. Not only may a clot pass along the veins, but we also get droplets of fat in fat embolism, air bubbles in air embolism, and masses of parasites in parasitic embolism.

Two recent studies, one of autopsy cases of hæmorrhagic infarct of the lung and one of post-operative cases of thrombosis and embolism, support the view that embolism is much the most common cause of pulmonary infarction (87 per cent.) and that this generally comes from a venous thrombosis. In 14 per cent. of the autopsy cases a massive pulmonary embolism was the main diagnosis and most of these were after operations or fractures. In 47 per cent. heart disease with the accompanying stagnation of the blood stream appeared to be a predisposing factor. A potential source for the

embolus was found in 75 per cent., most often in the pelvic or leg veins. Massive embolism was more likely to occur on the tenth day but was not infrequent at any time in the first fifteen days; it was independent of sepsis and depended on the stagnation of the blood stream, either from the state of the heart or more often from the mechanical conditions of rest. Smaller infarcts were more closely associated with sepsis (which suggests that the embolism is more often due to the breaking off of a small part of the thrombus) and more erratic in the time of their appearance.

In embolism in the portal circulation portions of clot in the radicles of the portal vein are finally arrested in the liver.

Symptoms.—1. Embolism of the Cerebral Arteries.—The onset is sudden, and the left side of the brain is rather more often affected than the right. Hemiplegia or aphasia is produced; consciousness is lost only for a few minutes during the attacks.

2. Embolism of the Splenic Artery.—The onset is sudden, with pain in the left side and sudden enlargement of the spleen, which is very tender. During the next few days, the spleen diminishes in size, but it often remains permanently enlarged.

3. Embolism of the Renal Arteries.—Sudden pain in the back is produced, and blood and a little albumin are present in the urine. The hæmaturia may last for a day or two, or longer if a larger branch was involved.

4. Embolism of the Superior Mesenteric Artery.—The patient is seized with sudden, violent abdominal pain and distension. The collateral circulation, in spite of the numerous vascular arteries that supply the intestine, fails, and gangrene of the small intestine results. There is a complete intestinal obstruction, and blood finds its way into the stools and into the peritoneal cavity. Operation should be undertaken at once, but owing to the large amount of bowel affected recovery is very rare.

5. Embolism of the Central Artery of the Retina.—This is not an uncommon event in cases of mitral stenosis and in septic endocarditis of the aortic and mitral valves. The patient is seized with pain in the eye and becomes suddenly blind on one side. The optic disk becomes pale and the retinal vessels small. Occasionally only a single branch of the vessel is affected. The same picture is found more often as a result of arterial thrombosis in elderly patients with athero-sclerosis or high blood pressure.

6. Embolism of a Large Artery in a Limb.—This sometimes occurs. There is acute pain in the limb, followed by numbness and loss of power. The pulse is imperceptible below the seat of the embolism, and gangrene results.

7. Air Embolism.—Air may enter the veins during operation on a large vein, or during intravenous injection of saline or other solutions, or after distension of the bladder and the urethra with air. Air embolism is undoubtedly capable of causing death, but a small quantity may enter a vein without any effect whatever, or, if some disturbance should arise, without fatal termination. The exact way in which air embolism causes death is doubtful; it may be due to arrest of the pulmonary circulation or to cerebral anæmia.

The diagnosis is not difficult; the respiratory embarrassment, convulsions, the feeble pulse and the characteristic sound upon air entry into the veins are usually sufficient.

Treatment consists in immediately occluding the vein into which the air has entered. Stimulants should be administered hypodermically and nitrite of amyl inhaled. Venesection may be used to relieve the embarrassment of the heart.

8. Fat Embolism.—Fat may reach the blood vessels in cases of fracture of bones and in cases of hæmorrhage into or rupture of the liver. The fracture is usually situated in the long bones, generally in the tibia or femur, and occasionally in the ribs. Fat embolism may occur within a few hours of fracture of the bones.

The fat droplets first lodge in the capillaries of the lungs. Occasionally they are forced on through the lungs into the general circulation, and the glomeruli of the kidney may be plugged with fat cells, and they may also lodge in the brain or spinal cord.

The patient becomes cyanosed, and crepitations from œdema of the lungs may be heard at the bases. The temperature remains normal. Cerebral complications, such as delirium, coma and rarely localised paralysis, may be found. The urine should always be examined, as oil drops have been detected by staining with osmic acid, and also the retinæ, as in one case the fat drops were recognised in the retinal vessels before death.

When fat embolism occurs within a few hours of fracture of the bones, it has to be diagnosed from the general shock of the accident. It is doubtful whether fat embolism in the lungs can alone cause death; more probably this is due to the disturbance of the kidneys or lesions of the brain.

The indication for treatment is to sustain the heart. Nitrite of amyl is often useful, and inhalations of oxygen should be given to lessen cyanosis.

9. Paradoxical Embolism.—In certain cases of venous thrombosis, emboli occur not only in the lungs but also in the systemic arteries. It has been shown that in these cases the embolus has passed from the right auricle to the left auricle through a patent foramen ovale. These crossed or paradoxical emboli are often preceded by pulmonary embolism, which causes a rise in pressure in the right auricle and a fall in the left auricle, so that the embolus can pass from the right to the left side of the heart.

Maurice Campbell.

ARTERIAL BLOOD PRESSURE

HYPERTENSION

In hypertension the systolic and diastolic blood pressure readings are persistently—not necessarily permanently—above certain levels, from whatever cause. Authorities differ somewhat as regards these levels, for the limits of normal variation are fairly wide, and, moreover, it is now practically universally believed that the blood pressure does not normally increase with advancing age as much as was previously thought to be the case; but it is generally agreed that persistent readings above 150 and 90, or at any rate 160 and 90, in adult males, and 170 and 100 in the elderly are pathological.

It is important to note that a transient increase in the blood pressure

readings, especially of the systolic, may occur with nervous excitement, such as is not infrequently incidental to a medical examination.

The late Sir Clifford Allbutt introduced the term *hyperpiesia* to denote a clinical condition in which there is a persistently raised blood pressure independent of renal disease. Some writers use the term *essential* or *primary* hypertension, or *hypertensive cardiovascular disease* (Janeway). The increased blood pressure is the essential or primary condition. Any changes which may be in the walls of the blood vessels, the heart, the kidneys or other organs are either a secondary result of the hypertension, or co-existent with it, and in the latter case may or may not be due to the same cause as is the hypertension.

Ætiology and Pathology.—The ætiology and pathology of hyperpiesia is obscure, and constitutes one of the most important and difficult questions in clinical medicine.

An inherited constitution is an important factor, as revealed by the high familial incidence in certain cases. The malady is more common in late middle life; in those who tend to worry, to be over-anxious, to take things too seriously, or are of an excitable disposition; in those whose manner of life involves continued mental or emotional stress or strain; and in the obese. It may be the result of poisons circulating in the blood, which act as pressor substances, such as occurs in endocrine disturbances, for example, at the female menopause, in tumours of the adrenal cortex or medulla, with Cushing's Basophilism Syndrome (pituitary basophilism), and in acromegaly; in focal sepsis; and in chronic alcoholic excess and excessive smoking. The general consensus of opinion is that a high protein diet intake in itself is not a cause, but in my view it is.

With regard to the pathogenesis of hyperpiesia, it is generally agreed that the immediate cause of the condition is an increased resistance to the passage of blood through the smaller arteries, especially the arterioles, at first due to hypertonus on their part. If the latter does not cease, either spontaneously or because of therapeutic measures, then, sooner or later, cardiac hypertrophy, especially of the left ventricle, and diffuse hyperplastic sclerosis supervene (see page 1035). The latter gives rise to actual narrowing of the lumen of the blood vessels, which may even be great, and a resultant further increase in the resistance to the passage of blood.

The cause of the initiation of the hypertonus of the arteries cannot yet be explained.

It is to be noted that some now consider that hyperpiesia is primarily of renal origin. Among the reasons adduced for this view are that some cases, in the course of time, develop into what is termed "malignant" hypertension. It may here be observed that this only occurs in a small proportion of cases. The matter will be dealt with further later on. Again, experimentally produced renal ischæmia in dogs, the result of the gradual narrowing of the renal arteries by means of clamps, will give a condition similar to hyperpiesia in man. With regard to this, it may be pointed out that pressor substances circulating in the blood from any source, including the kidneys, will have a like effect.

By far the general consensus of opinion—which I myself share—is that it is not possible to explain hyperpiesia as being due to structural changes in the kidneys, in which connection the following observations may be

made. (1) In hyperpiesia the blood pressure becomes normal under ether anæsthesia, and is diminished during sleep. (2) Hyperpiesia and diffuse hyperplastic sclerosis may occur independently of any renal lesion. (3) While in hyperpiesia and diffuse hyperplastic sclerosis the kidneys generally become involved secondarily, it may be in marked degree, with consequent increased obstruction to the circulation and an increase in the hypertension, in a large proportion of cases there is generally little or no impairment of renal function, which is one of the most characteristic features of hyperpiesia, and less than 10 per cent. die from renal failure. (4) There is frequently an absence of hypertension in polycystic and tuberculous disease of the kidney, occasionally in acute nephritis, and rarely in chronic nephritis. (5) In chronic nephritis changes may take place in the renal vessels of an almost exactly similar nature to those in diffuse hyperplastic sclerosis, leading to hypertension and similar cardiovascular accidents. But there the vascular changes are secondary to the nephritis.

Hypertension is not by any means only the result of kidney disease. There are many other causes. Indeed, it may even be asked whether in some cases of hypertension and diffuse hyperplastic sclerosis, and chronic nephritis, the former may have been the cause of the latter? Or, again, may both be the result of a common cause?

While the great majority of cases of hypertension are of the nature of hyperpiesia, the condition may also be due to diffuse hyperplastic sclerosis (see page 1035), chronic and acute nephritis, polycystic disease of the kidney, increased intracranial pressure, *e.g.* intracranial hæmorrhage, and polycythæmia vera. With regard to the first, however, the condition is rather the result than the cause.

Symptoms.—In hyperpiesia the patient is often well nourished and may be plethoric. There may be a complete absence of subjective symptoms for some years, and the condition may be discovered accidentally, *e.g.* during an examination for the purpose of life assurance.

Usually the onset of symptoms is insidious. The most common early symptoms are a feeling of fullness and it may be of throbbing in the head, transient giddiness, tinnitus aurium, flushing, insomnia, palpitation, languor and early fatigue, the latter especially on mental effort, headache, of a dull aching or it may be of a throbbing character, particularly in the occipital region and especially in the morning, impairment of memory, mental irritability and diminished emotional control. The blood pressure readings are above those mentioned in the first paragraph.

The condition may subside, either spontaneously or the result of therapeutic measures. If not, the blood pressure readings usually increase, and the systolic may reach 240 mm. or even more. Consciousness of the action of the heart may become more prominent. Sooner or later, there is evidence of hypertrophy of the heart, especially of the left ventricle, and of diffuse hyperplastic sclerosis (see page 994). The walls of the radial, the brachial and temporal arteries may be felt to be uniformly thickened—the so-called "whip-cord" artery. The degree of hardening of the arteries is found on palpation to vary at different times. The artery feels hardest when the vessel is most contracted and consequently smallest. The character of the pulse is that of high-tension. The retinal arteries are often thickened, and on ophthalmoscopic examination may show a glistening light along their

course—the so-called "silver wire" arteries, due to reflection of light from the thickened vessel. Even more important is a visible irregularity in calibre of the arteries best seen near the disc. Further, at the arterio-venous crossings there may be seen an obstruction to the flow of blood through it, leading to distension of the peripheral part of the vein and also to deviation of the vein where it crosses the artery.

The subsequent clinical picture and course exhibit considerable diversity.

The cardiac symptoms are by far the most common. The most frequent are shortness of breath, palpitation and precordial discomfort or pain, referred to exertion. Later, cardiac failure, usually left-sided but it may be involving both sides, may supervene (see page 857). Acute left-sided failure may occur (see page 857). Angina pectoris is not very infrequent. There is occasionally coronary occlusion. For further particulars, the reader is referred to page 857.

Various gastro-intestinal symptoms are often present. There may be hæmorrhages from the nose, the stomach, the intestines and other mucous membranes, the kidneys, the conjunctiva, and occasionally the retina, which are sometimes flame-shaped. There may be tingling, numbness and cramp of the limbs, and occasionally intermittent claudication. Hypertensive encephalopathy (see page 1607) may occur. Cerebral hæmorrhage may be a terminal event.

Not infrequently there is albuminuria, generally slight and not constant, and there may be polyuria and nocturnal micturition, and hyaline and granular casts. There is usually no or little impairment of renal function. Uræmia is rarely a terminal event.

There is a small group of cases of hypertension in which, instead of the symptoms being mild or moderate, the course slow, and little or no renal insufficiency, the symptoms are severe, the course is progressively rapid, and the patients die from renal failure. The former, which constitutes the great majority, is called benign and the latter "malignant" hypertension. There are also intermediate forms between the two groups. The renal changes in malignant hypertension are described as malignant nephrosclerosis, and those in benign hypertension may be termed benign nephrosclerosis. It may be remarked, however, that the term malignant is not altogether an appropriate one.

Malignant Hypertension.—There appear to be two forms of this, namely: (1) In a case of benign hypertension of a varying number of years' duration, the symptoms suddenly become severe and the malady pursues a rapid course. (2) In an individual who has not been aware that he had hypertension, from the outset there are severe symptoms in association with hypertension and the course is rapid. The second usually occurs at an earlier age than the first.

There are the same changes in the kidneys as in the benign form, and, in addition, those which are believed to be characteristic, *i.e.* acute necrosis of the walls of the arterioles and also often of the root of the glomeruli, and it may be resultant thrombosis of the glomeruli. While acute necrosis is most marked in the vessels of the kidneys it is also found in those of other organs. There has been much discussion among pathologists regarding the interpretation of the distinctive changes in the kidneys. In the opinion of some, they are an intensified result of the ætiological factor of the changes

in the walls of the arteries in the benign form; while others think they are due to a special toxin. Again, some are of opinion that malignant hypertension is merely a severe or extreme phase and a terminal result of the benign variety, whereas others think that it is a separate entity.

In malignant hypertension, the blood pressure, especially the diastolic, is usually materially higher than in the case of the benign form, being generally over 200–120, and may be very high and may become extreme. There is lassitude, anorexia, frequently loss of weight, severe headache and anæmia. Changes in the retina occur earlier and are more marked, hæmorrhages being more evident and retinopathy is frequent if not usual. There is polyuria and nocturnal micturition. The urine is of low specific gravity, and contains hyaline and granular casts, a variable amount of albumin and often red blood cells. As the disease progresses, there is evidence of renal impairment. Death occurs from uræmia, cardiac causes or cerebral hæmorrhage.

In hyperpiesia it is probable that more than half the patients die from cardiac causes—in the great majority from congestive failure, not infrequently from angina pectoris, and occasionally from coronary occlusion; in a fair proportion of cases, cerebral hæmorrhage is a terminal event; in less than 10 per cent. uræmia; while in the remainder the cause of death is some intercurrent disease.

Diagnosis.—Hypertension is recognised by persistent blood pressure readings above those mentioned in the first paragraph of this article.

The diagnosis between hyperpiesia and malignant hypertension may readily be made from a consideration of the respective clinical features described above. That between malignant hypertension and chronic glomerular nephritis may be difficult.

Prognosis.—Hyperpiesia usually pursues a slow course. It is probable that the duration of life after the beginning of symptoms is ten to fifteen years, or even more. The outlook is chiefly affected by the blood pressure readings, particularly the diastolic, the state of the heart and of the arteries, and the patient's manner of life. See also page 996. The duration of life in malignant hypertension is usually at the most two years.

Treatment.—As regards the treatment of hyperpiesia, the first indication is a thorough review of the ætiology. Then, the question as to whether a preliminary rest and, if so, how much is advisable should be considered (see page 862).

Hyperpiesia is an excellent example of the value of treating not only the disease but the patient. He should be reassured and encouraged. It is inadvisable to let him know the exact blood pressure readings at any time.

In no cardiovascular malady, excepting perhaps in angina pectoris, is the manner of life of so great consequence.

The cardinal indications are that, while the patient's activities should not be unnecessarily curtailed, they should come within the limits of his strength and even keep something in reserve; there should be a sufficiency of rest in his life; and all causes of mental and emotional stress should be carefully avoided. With this object in view, inquiry should be made regarding the patient's environment, the nature and hours of his work, his habits, the question of sleep and other relevent matters, while his temperament should be taken into consideration.

Each patient should be in bed for at least ten hours each night, rest physically and mentally for at least half an hour after the midday meal and have a quiet day each week. If the blood pressure is more pronounced, he should be in bed for at least twelve hours, rest for at least an hour after lunch, and stay in bed on one day a week with, it may be, a diet limited to vegetables, fruit and milk. In addition to an annual holiday of good length, several shorter ones during the year are advisable, in each case with a sufficient element of rest. As indicated, physical exertion and mental effort should be within the limits of the patient's strength (see page 863), with something in reserve. With this proviso, walking in the open air, riding a non-pulling horse, golf and mild bicycling are suitable forms of the former. The patient should be encouraged not to worry, or be over-anxious, or to take things too seriously; to avoid all excitement and other forms of emotional stress; and cultivate the art of "relaxing," physically and mentally.

If the patient tends to worry, or be over-anxious, or to take things too seriously, sedatives (see page 863) are often of special value. The matter of sleep is also of particular importance, and if there is insomnia, it should be treated on the lines laid down on page 863. Again, any obesity should, without fail, be corrected.

The amount of fluid with meals should be diminished, while an ample quantity should be taken between meals. Some prefer the mildly alkaline waters. The benefit of a regulated diet of moderate latitude may be considerable. Its amount should preferably be rather less than is needed. Those articles of food which especially stimulate the cardiovascular system should be reduced and proportionately to the degree of hypertension. The quantity of beef and mutton should be diminished, while twice-cooked meat, salted and preserved meat, liver, kidney, brains, sweetbreads, meat soup, and gravies, and meat extractives are better avoided altogether. Fish, poultry, game (not high), rabbit, vegetables, salads and fresh fruit are suitable. Ruthmol may be used as a substitute for table salt with meals. Moderation in the use of tobacco, tea and especially of coffee should be enjoined. Alcohol is better avoided altogether.

Strict attention to the condition of the bowels, preferably by a saline each morning, and a mercurial preparation at bedtime once or twice weekly are indicated.

Cold and hot baths are contra-indicated; but a warm bath, the temperature of which is gradually lowered, may be taken daily. A Turkish bath once or twice a week may be helpful. Patients often derive much benefit from a course of treatment at a Spa where different kinds of baths are used, on account of the rest, the change of air, the regular mode of life and exercise, the careful dieting and other factors, and in such cases periodic visits are to be recommended.

Iodine, in some form, in small doses appears to be occasionally of help. The same perhaps applies to the nitrites, such as a combination of sodium nitrite, erythrityl tetranitrate and mannityl hexanitrate, when symptoms are present. I have been disappointed with the results of the administration of mistletoe, liver extract, and potassium and sodium thiocyanate.

Diathermy, high frequency currents and other forms of physiotherapy are employed by some.

When the blood pressure is very much raised, particularly if there are

SECTION XIV

VASOMOTOR NEUROSES (ANGIO-NEUROSES)

INTRODUCTION

UNDER this heading are described several diseases in which vasomotor disturbance is the prominent symptom. Sensory, secretory and trophic disturbances may also be present. These diseases differ from each other both in regard to the nature and location of the vasomotor changes. Thus in Raynaud's disease there is a spasm of peripheral arteries. In erythromelalgia there is vaso-constrictor paralysis or excitation of the vaso-dilator nerves. In angio-neurotic œdema there is disturbance of capillary permeability, and perhaps of capillary tone. These diseases are described as vasomotor neuroses because a lesion of structure is not an essential part of their pathology, and because a considerable functional element is generally present. Thus they are common in persons who have an unstable nervous temperament, and emotional disturbance and fatigue play a not unimportant part in their ætiology. It has been thought in the past that these diseases were primarily due to disorder of the involuntary or vegetative nervous system. Lewis, however, has shown in the case of Raynaud's disease that a local fault of the vessels rather than a disordered vasomotor impulse determines the spasm of the digital vessels, and he finds the explanation of Raynaud's disease in terms of vasomotor dysfunction unconvincing. Too little is known of the ætiology of acroparæsthesia, erythromelalgia and Milroy's disease to throw light on this aspect but whatever the basic pathogeny of these conditions may be, vaso-dilatation is a prominent feature of erythromelalgia.

It is important that as far as possible a distinction should be drawn between these diseases occurring as neuroses and similar syndromes complicating recognised pathological states, such as lesions of the spinal cord or brain (tabes dorsalis or hemiplegia), lesions of peripheral nerves (peripheral neuritis), and lesions of vascular channels, or local pressure effects, such as may result from a cervical rib. But they are not separated by a rigid line from slighter manifestations of vasomotor instability, such as are frequent in women at the climacteric, and in clinical disorders resembling exophthalmic goitre. They are undoubtedly akin to such common symptoms as flushings, cerebral hyperæmia, facial congestion, angio-spasm in all its varieties, tachycardia (in some of its forms), anginal attacks, migraine, vertigo, tinnitus aurium, universal or circumscribed hyperidrosis, and gastric disorders of certain forms of functional gastric dyspepsia.

Lewis's studies on the local vascular reaction to irritation of the human skin have thrown much light on these diseases. He showed that there are three components in the reaction: (1) a primary dilatation of capillaries—the *red line*; (2) an increased permeability of these capillaries, producing the *wheal*,

which is independent of the nerve supply; and (3) the *flare*, which depends on the integrity of the sensory nerve fibres in the neighbourhood. All these phenomena can be produced by an intradermal injection of histamine, and he attributed them to the liberation of this or some similar chemical substance to which he gave the name of "H-substance." It has been suggested that local liberation of histamine may play a part in producing the vesicles in herpes and the rash in erythema nodosum. It is of special interest that these reactions are partially dependent upon and partially independent of the nervous system. Some of the angio-neuroses are therefore so closely related to allergy that a general description of that condition is called for here.

ALLERGY

Idiosyncrasy has been defined as an unusual physiological personal equation, and allergy is a chemical idiosyncrasy, which expresses itself as an urgent attempt on the part of the cell to conserve its chemical identity. The tendency to allergy is inborn, whereas anaphylaxis is an acquired sensitivity. All the phenomena of allergy can be reproduced by histamine. The question is, how does this substance, which is toxic to everyone, become liberated in the tissues of certain people in answer to stimuli which are quite harmless to everyone else? Normally there are two antagonists to histamine, adrenalin and the special ferment histaminase. It has therefore been suggested that the chemical basis of allergy is a congenital lack of histaminase, aggravated by an intermittent deficiency in adrenalin. The reaction is usually excited by foreign proteins, but a similar idiosyncrasy may be shown to various drugs.

The manifestations of allergy express themselves chiefly (*a*) in *the respiratory system*, by asthma, hay fever, paroxysmal rhinorrhœa, recurrent catarrhs; (*b*) in *the skin*, as urticaria, purpura and eczema, particularly of the infantile type; (*c*) in *the alimentary canal*, by diarrhœa and vomiting, or spastic colon; and (*d*) by *effusion into joints*. There are many other conditions which with more or less show of reason might be added to this list. Certainly some cases of migraine seem to be of this order. It will be noted that several of these manifestations could be interpreted as a violent attempt to expel the invader, at any rate from the vital organs.

Most allergic manifestations are worse at night, because of the prominence of vagus control then, so that there is a relative insufficiency of the sympathetic nervous system, and therefore in the supply of adrenalin. The principal conditions produced by allergy are described under their appropriate headings.

ANGIO-NEUROTIC ŒDEMA

Synonym.—Quincke's Disease.

Definition.—A paroxysmal affection, characterised by the appearance of circumscribed œdematous swellings of the skin and subcutaneous tissues of transient duration. The mucous membranes are often affected.

Ætiology.—Heredity is an important factor. Osler reported the case of a family in which five generations had been affected, involving 22

members. The condition is more common in men than in women, and generally affects the young. Those attacked are usually of a nervous disposition. Garrod reported a case in which each recurrence of periodic hydrarthrosis was attended by circumscribed œdema, either of the lips or eyelids. The attacks may coincide with menstruation. The exciting cause is generally difficult to determine. It may be emotional strain, exposure to cold, or trauma. Local trauma sometimes determines not only the onset but the site of an attack, as in a case recently reported in which riding provoked an attack on the inner aspect of the thighs and knees.

Pathology.—In the absence of a known pathology various theories have been advanced to explain the condition. Local venous spasm, a direct nervous influence on capillary walls, as a result of which the permeability of the vessels is increased, and, more recently, the local action of a circulating toxin on the capillary walls, are theories which have obtained support. With regard to the last named, Garrod drew attention to the joint swellings that frequently accompany erythematous and urticarial rashes resulting from known toxic causes. Such conditions form a part of the clinical picture of serum sickness, or may occur after taking certain articles of diet, or as the result of stings of insects or nettles. Lewis has shown that a modification of the same toxin may produce a dermolysin or a hæmolysin. In the former instance œdema; in the latter purpura results. Thus, *B. welchii* may produce either condition, depending on the intensity of the infection. This thesis illustrates the present view of angio-neurotic œdema as being a local expression of the presence of a circulating toxin, prone to occur in persons of nervous temperament, rather than a disease *sui generis*. The patients often show other signs of allergy, especially in their sensitiveness to foreign proteins.

Symptoms.—The complaint takes the form of acute circumscribed swellings of the skin and subcutaneous tissues, 1 to 4 inches in diameter. The swellings are rounded, painless, rarely itch, and are generally pale or sometimes redder than the surrounding skin, from which they stand out prominently. They may develop simultaneously in different parts of the body, and disappear in a short time. They may recur repeatedly, or only after a period of years; the recurrence is occasionally periodic. They occur most commonly in the eyelids, lips, cheeks and backs of the hands, and are asymmetrical. The whole side of the face, one side of the scrotum, the penis, a whole limb, or in fact any part of the skin, may be involved. The pharynx, tongue and conjunctivæ may be implicated. Œdema of the glottis is rare, and has proved fatal. Swelling of mucous membranes may lead to symptoms of gastro-intestinal disturbance, such as nausea, vomiting and colic. Cases in which hæmorrhage from mucous membranes, stomach, bronchi, bladder, etc., occurred have been reported. Hæmoglobinuria has been observed; in such a case a Wassermann test is indicated. The attacks are generally afebrile, and there is no constitutional disturbance, unless the stomach or intestine is involved.

Course.—This is variable. Recurrence is frequent, often at intervals of 3 to 4 weeks, but sometimes after long intervals. It is rarely periodic.

Diagnosis.—The complaint is so characteristic, in the sudden onset and rapid subsidence of asymmetrical rounded swellings, that it is hardly likely to be confused with other affections. The condition is nearly allied to

urticaria, from which it is distinguished by the circumscribed and deep-seated nature of the swellings and the absence of itching. No distinction is made between angio-neurotic œdema and giant urticaria.

Treatment. — The general health must receive first attention, and a saline purge is indicated. Both arsenic and quinine have been advocated. It is advisable to avoid any particular protein in the food which is found to excite attacks. When the attacks occur after a particular meal of the day, a capsule containing 1 to 2 grains of peptone half an hour before that meal appears to have an effect in temporarily desensitising the body against foreign protein. This, combined with 5 to 7½ minims of tincture of belladonna and 10 to 15 grains of calcium lactate after meals, has prevented recurrences in several cases. The former drug diminishes the vagal hypersensitiveness, and the latter increases the viscosity of the blood. One of the most useful forms of treatment for the relief of the paroxysm is a subcutaneous injection of 3 to 7 minims of liquor adrenalinæ hydrochloridi. This excites the antagonistic action of the sympathetic. For the same reason half a grain of ephedrine orally administered may be tried. When the tongue is involved the patient should be given one or two of Armour's suprarenal tablets to suck. Pituitary (posterior lobe) extract injections have also been recommended. Bromide is often helpful as an additional measure when the symptoms are marked. In severe cases the intravenous injection of small doses of peptone might be considered. Autohæmotherapy has proved decidedly useful in some cases. Vitamin K is also worthy of a trial.

Intermittent Hydrarthrosis, which is described under "Diseases of the Joints" (p. 1367), presents some interesting affinities with the vasomotor neuroses, particularly in its association with angio-neurotic œdema.

RAYNAUD'S DISEASE

Definition.—"Intermittent pallor or cyanosis of the extremities brought on by cold, with the skin a normal colour between attacks" constitutes Raynaud's phenomenon, which may occur however in conditions other than Raynaud's disease.

Ætiology.—The cause of this malady is unknown; it almost exclusively affects young women, and symptoms may begin any time between adolescence and middle age. The diagnosis of Raynaud's disease in a man is nearly always wrong. Jonathan Hutchinson preferred to speak of Raynaud's phenomenon, regarding it not as an entity but as a syndrome occurring in many different conditions. As he first suggested, a few cases are due to syphilis, congenital or acquired. It has occasionally been observed after acute infections.

Pathology.—Lewis has shown that there is an abnormality of the digital arteries, which expresses itself in a hypersensitiveness of these vessels to relatively low temperatures. It seems therefore that the fault lies primarily in the vessel wall rather than in the nerve supply to the muscle fibres. In advanced cases there is endarteritis, with partial occlusion of the lumen of the artery.

Symptoms.—The patients complain of attacks of pallor, blueness or numbness of the fingers, brought on by contact of the hands with anything

cold. Keeping the palms of the hands in cold water (15° C.) for 15 minutes in a cool room (18° C.) is usually sufficient to induce an attack. The body temperature is just as important, if not more so, than that of the hands in determining the onset of cyanosis. When such patients feel chilly in themselves their hands go blue on the slightest provocation, *e.g.* when sitting in a draught; when walking, cycling or driving a car in cold weather; or when swimming. When the body is really warm it is impossible to induce an attack no matter how cold the hands are. Emotion also may bring on an attack. In this connection it is interesting that an injection of adrenaline may have a similar effect. The attacks vary from slight pallor of one finger-tip to cyanosis and numbness of all the fingers of both hands. The cyanosis begins as a light-bluish tint, and later becomes a deeper blue. It always starts at the finger-tips, and spreads proximally to the base of the fingers and perhaps to the palm; rarely, if ever, does it reach above the wrist. If the attack persists for long, a secondary waxy pallor replaces the cyanosis. The hands remain blue or pale until they are warmed. They feel cold to the observer's touch. When the hands are warmed (40° C. for 3 minutes), or when the body temperature rises, the blueness begins to pass off, and irregular red blotches appear in its midst "like the spots on a plaice." Some of these appear and fade away, but in the end they coalesce until the dorsum of the hand and the palm are fiery-red or scarlet. Gradually this redness spreads up each finger from base to tip.

Throughout the period of cyanosis the patients complain of a "tingling" or of a "feeling of numbness" in the fingers; some of an "uncomfortable sensation"; some of a "slight pain"; severe pain is unusual. When warmth is applied in any form—hot air in front of a fire, or by friction—the fingers quickly recover their normal colour. During this stage there are paræsthesiæ, "pins and needles," etc. In only a few patients is sweating of the hands a marked feature during attacks. Swelling of the fingers is rare. In a severe attack local pressure on a finger leaves an indentation which takes longer to disappear than when the circulation is normal. While the hands remain cold the radial pulses are of smaller volume and the veins less prominent than when warm. If a finger is accidentally cut when cold it does not bleed; "only a little dark blood oozes out." If symptoms occur in the feet they are usually less severe than in the hands. Nutritional changes at the extremities are rare in true Raynaud's disease. But in the later stages, when secondary arterial changes in the arterial walls have occurred, small areas of superficial necrosis at the finger-tips may be found, which leave small depressed tender scars.

Diagnosis.—This has been considerably clarified by John Hunt. The first question to be answered is: Is the complaint "Raynaud's phenomenon"? *i.e.* Is there *intermittent* cyanosis of the extremities, brought on by cold, with the skin a normal colour between attacks? The following conditions with their vascular phenomena are eliminated by this simple definition, many of them because their symptoms are continuous and not intermittent: chilblains; frost-bite; acrocyanosis; erythrocyanosis; clubbed fingers and cyanosis of the fingers and toes due to lesions of the heart and lungs; enterogenous cyanosis; incipient gangrene from arterial thrombosis (in advanced arteriosclerosis, thrombo-angiitis obliterans, or ergotism); arterial embolism; diseases of the nervous system

(neuritis, poliomyelitis, syringomyelia, pyramidal lesions, and hysterical paralysis), cervical rib. If true Raynaud's phenomenon is present then the other conditions in which this phenomenon occurs must be considered:

(1) *Hereditary cold fingers.*—Many healthy young people find that their fingers go white and numb on exposure to cold. This is the commonest cause of Raynaud's phenomenon, and is local syncope in its simplest form. The onset is usually during childhood up to about the eighth year. Both sexes are affected, as are often members of the same family. These three points clearly differentiate the condition from Raynaud's disease.

(2) *After local injury or infection of the hands or feet, and in workmen using vibrating instruments*—pneumatic chisels, hammers, riveters, road drills, etc.

(3) *Scleroderma.*—This is diagnosed from Raynaud's disease by the following points: The fingers soon become stiff, and the stretched shiny skin cannot be picked up from the underlying tissues. Nutritional changes in the finger-tips are frequent. It is not confined to the extremities, and is much more rapidly progressive, painful and depressing than Raynaud's disease.

(4) *Syphilitic Arteritis.*—This may be diagnosed when Raynaud's phenomenon is associated with severe necrosis of the nose and ears, and when hæmoglobinuria is present. A blood Wassermann may be positive.

(5) *Other rare causes of Raynaud's phenomenon.*—Erythræmia is one.

Treatment.—Cold in any form should be avoided. The temperature of the body as a whole is almost more important than that of the hands and feet, and warm clothing is essential. The temperature of a living-room should be about 20° C. (68° F.). Cold water should be banned, and gardening in cold weather left to others. Gloves should be loose and long, overlapping the coat-sleeves. For people who work with their fingers, mittens are invaluable. A muff, a small hot-water bottle, or an electric heater in a handbag or pocket may be recommended. Cracks at the ends of the fingers may be covered with a collodion preparation, or with narrow strips of elastic adhesive plaster. The skin of the fingers may be kept soft by applying liquid paraffin. Care should be taken to avoid minor injuries to the fingers, and when these occur they should be treated at once. Boots or shoes should be of stout construction, allowing plenty of room for the toes, and stockings or socks should be thick and soft; two thin socks often keep a foot warmer than one thick one. Tight suspenders should be avoided. Bedsocks and hot-water bottles are helpful at night.

The number of drugs that have been recommended to relieve symptoms indicates how few are really valuable. Thyroid, calcium lactate or gluconate, potassium iodide, and belladonna are perhaps the favourites. In some patients physical therapy is needed to give relief: postural exercises; radiant heat, taking special care to avoid burns; contrast baths; intermittent venous occlusion by alternating positive and negative pressures; and galvanic baths. Sympathectomy is indicated when the attacks of cyanosis are causing definite distress or recur so frequently as to interfere with work, and when temperature tests suggest that there is a considerable degree of vasomotor tone. The immediate results of the operation are excellent; but after some months, perhaps two years or more, slight symptoms may return. In spite of this disappointment the great majority

of patients insist, even several years after the operation, that their hands are better than they were before it. The relief of major symptoms is due to removing from the vessels the burden of their normal vasomotor tone. The local fault in the vessels remains untouched, for on this the operation has no effect.

ACROPARÆSTHESIA

Definition.—A vasomotor neurosis, characterised by paræsthesiæ of the hands, especially affecting the finger-tips.

Ætiology.—The condition is usually observed in women, especially at the climacteric. It rarely occurs before the age of 30. It is frequently associated with a neuropathic diathesis and a lowered vitality due to any cause. General causes include inanition, anæmia and pregnancy. Local causes are exposure to cold, particularly cold water, or to alternate hot and cold water as experienced by washerwomen.

Symptoms.—The onset is insidious and the symptoms are almost entirely subjective. The affection is often limited to one hand or certain fingers, the toes rarely being affected. The patient complains of numbness, tingling, formication of the fingers or tenderness of the finger-tips. There may be slight loss of sensibility in the finger-tips and occasionally evident pallor.

Diagnosis.—The condition is readily distinguished from Raynaud's disease by the absence of local asphyxia. It is important to exclude any affections of the spinal cord, such as tabes dorsalis.

Prognosis.—The complaint tends to be continuous and persistent. The outlook regarding recovery is not good, unless the condition is due to a recognisable and removable cause. There are, however, no complications.

Treatment.—This is directed to the removal of the cause, and improvement of the general health and of the local circulation. Sodium salicylate and bromides are often helpful, and radiant heat and massage are of value.

ERYTHROMELALGIA

Definition.—A rare condition characterised by pain, redness and swelling of the toes and feet, and less often of the hands.

Ætiology.—Little is known of the ætiology of the disease. Men are more often affected than women. The condition may occur in the course of a disease of the central nervous system, such as hemiplegia, disease of the cauda equina, and disseminate sclerosis. The swelling and pain are aggravated by standing and by warmth.

Pathology.—Disease of the peripheral arteries—a chronic endarteritis—has been described in three cases by Batty Shaw. Changes in the peripheral nerves have been held responsible, and Weir Mitchell found marked degeneration of the fine nerve branches in one case. Others regard the malady as an angio-neurosis, allied to acroparæsthesia and Raynaud's disease. Lewis prefers to regard erythromelalgia as a special instance of a condition he designates as *erythralgia*, which he maintains has nothing to do with abnormality of the vasomotor system, but always results from a local process.

There is a release into the skin of an unknown substance not histamine, which lowers the threshold of the pain nerve endings.

Symptoms.—The first case was described by Weir Mitchell, and was that of a sailor, aged 40, whose first complaint, following an African fever, was of "dull, heavy pains at first in the left, and soon after in the right foot. There was no swelling at first. When at rest he was comfortable, and the feet were not painful; after walking the feet were swollen. They scarcely pitted on pressure, but were purple with congestion; the veins were everywhere singularly enlarged, and the arteries were throbbing visibly. The whole foot was said to be aching and burning, but above the ankle there was neither swelling, pain . . . nor flushing."

Pain is generally the first symptom, soon followed by redness and swelling, most marked in the terminal phalanges of the toes or fingers. The pain is generally severe; at first it occurs only in the evening, but later it becomes chronic or remittent and may be agonising. The redness may increase to cyanosis. The swelling is more marked in the latter part of the day, and is aggravated by standing, walking, dependence of the limb and by heat. These symptoms are relieved by cold and recumbency. Hyperidrosis of the affected part is not uncommon. The condition may be complicated by general weakness, vertigo, headache, palpitations and tachycardia. Its complication with erythræmia has been described. Pellagra has been mistaken for erythromelalgia.

Prognosis.—The complaint is intractable, and tends to persist, with exacerbations and remissions, for many years.

Treatment.—The affected part should be elevated and immobilised. Faradism and cold have been recommended. Analgesics are required for the relief of pain, which may even necessitate amputation (Shaw). Sympathectomy is contra-indicated and should never be performed for this condition.

ERYTHROCYANOSIS

This condition occurs, as its full name, Erythrocyanosis Crurum Puellarum Frigida, implies, chiefly in the legs of young women. The feet and legs are cold, and the back of the leg and ankle is swollen and blue, especially at the insertion of the tendo Achillis. Chilblains are often present, and ulceration may occur where the swelling is most severe. The condition is due to vascular spasm, in which the modern fashion of inadequately protected extremities is presumably a factor. Treatment includes warmer stockings, with silk ones outside to gratify the usual desire for appearance, and the loosening of all tight bands above and below the knee. Exercises, such as walking and skipping, with local massage should be ordered, and elevation of the heel may give some relief. Calcium gluconate, vitamin D and small doses of thyroid have been advocated, and daily subcutaneous injections of acetyl choline bromide, beginning with $\frac{1}{4}$ c.c. and gradually increased to 1 c.c., have given good results. After a fortnight the injections may be administered less frequently, and at the end of six weeks discontinued. Bilateral lumbar ganglionectomy has been recommended, but should not be considered unless thorough medical treatment fails. It may improve the colour of the skin and promote healing of any ulcers, but it does not diminish the swelling.

CAUSALGIA

This is a form of neuralgia usually following injuries in the neighbourhood of certain nerves, particularly the median and sciatic. It is probably due to irritation of the peri-arterial sympathetic fibres. On account of the burning character of the pain, Stopford has suggested the name *thermalgia*. The malady is fully described under lesions of the median nerve.

MILROY'S DISEASE

Synonym.—Hereditary Œdema.

Definition.—In 1892, Milroy described a persistent œdema of the legs, occurring in the absence of any of the known causes of œdema, affecting members of the same family in successive generations.

Ætiology.—The disease has occurred in six generations of the same family, but the percentage of incidence in the families has varied greatly. It is apt to appear in neurotic families. Both sexes are affected about equally, and the œdema may either appear soon after birth, or its onset may be delayed till puberty or even till adult life. Thirty-five years after his original description, Milroy found that the disease was tending to die out in the family in which he first observed it.

Pathology.—Nothing is known of the pathology of the condition. There is no evidence of venous or lymphatic obstruction.

Symptoms.—Only the legs are affected, and these to a variable extent. Thus the swelling may be limited to the ankles; it usually does not extend beyond the knees, but may reach the thighs in long-standing cases. It never extends above Poupart's ligament. Gradually the affected part becomes hard and brawny. The swelling increases in the standing posture, and, once established, it is permanent. There is no pain or redness, the veins are not enlarged, and the general health is not affected.

In some cases there are acute attacks accompanied by fever and pain. During this phase the condition resembles erythromelalgia.

Diagnosis.—This is made on the familial incidence, and the absence of all other recognised causes of œdema. A group of cases in which there is swelling of the feet, ankles and legs without albuminuria or discoverable organic disease to account for the swelling, has recently been recognised by Osman. The patients the writers have seen have been women in the third decade. The swelling is pale, brawny, and does not pit on pressure. This type may respond to rest in bed and intensive alkali therapy.

Prognosis.—The affection does not tend to shorten life.

Treatment.—The affected parts should always be kept bandaged with crepe, as by this means the swelling can be kept under control, and the patient remains able to lead an active life; but if such measures be not employed the œdema gradually extends. Acute attacks may require opium internally, and evaporating lotions locally.

W. Langdon-Brown.
Geoffrey Evans.

SECTION XV

DISEASES OF THE RESPIRATORY SYSTEM

THE PHYSICAL SIGNS IN THE CHEST IN HEALTH AND DISEASE

ACCURATE diagnosis in diseases of the air-passages and lungs depends largely upon careful observation and record of physical signs, especially in their relation to subjective symptoms. Unfortunately, there is no strict uniformity in regard to the nomenclature of physical signs. It is, therefore, desirable to define explicitly the sense in which the various technical terms used in this section are employed. At the outset, it is well to emphasise the importance of a careful and methodical examination in every case. The magistral sequence of inspection, palpation, percussion, auscultation and mensuration has more than the sanction of tradition to commend it. Unless confined to bed, the patient should be examined both in the erect and recumbent positions in all cases of difficulty.

INSPECTION.—The patient being placed in a good light, the configuration of the chest, the range and character of the respiratory movements and the position of the cardiac pulsations should be carefully noted. Most of the terms used in this connection, such as flattening, retraction, recession of intercostal spaces and diminished movement are self-explanatory.

The respiration may be unduly slow (bradypnœa), rapid (tachypnœa) or distressed (dyspnœa). Dyspnœa may be inspiratory, expiratory or spasmodic. A peculiar periodic disturbance of the respiratory rhythm is that referred to as Cheyne-Stokes breathing. In this condition, the respiratory movements wax and wane in short periods of dyspnœa, each followed by an interval of apnœa or cessation of respiration lasting up to 30 or 40 seconds. It is due to deficient aeration of the blood and is met with in respiratory, cardiac and renal disease, and also in cerebral lesions and after some poisons.

A variety of grouped breathing is Biot's breathing, sometimes seen in tuberculous meningitis. The hyperpnœic period consists of a few breaths, deep or of increasing depth, followed by apnœa without the waning.

Certain abnormal forms of chest configuration are described: The *alar*, phthinoid or pterygoid type of chest is long, narrow and flat, with winging of the scapulæ; the subcostal angle is narrow and the upper interspaces are wide. The *emphysematous* or barrel-shaped chest is broad and rounded, the angle of Louis is prominent, the subcostal angle is wide, and the movements are restricted. The *pigeon breast* is characterised by prominence of the sternum, with sloping anterior thoracic walls. The *funnel breast* is

the converse of this, with depression of the lower end of the sternum and of the cartilages attached to it.

PALPATION.—Vocal fremitus or tactile fremitus is the vibration felt over the lung when the hand is placed flat upon the chest-wall without pressure and the patient says "ninety-nine" or some other resonant syllables. Vocal fremitus may be increased, decreased or absent in disease.

Tussive fremitus.—The similar vibration felt during cough.

Rhonchal fremitus.—The vibrations communicated to the chest-wall by sonorous rhonchi in bronchitis, and felt by the hand.

Friction fremitus or pleural fremitus.—A rubbing sensation communicated to the palpating hand in certain cases of dry pleurisy. A similar fremitus is occasionally felt in pericarditis.

PERCUSSION.—This consists in tapping the chest-wall over the lung and observing the note produced and the sense of resistance felt. Percussion may be *direct* on to the chest-wall or *mediate*, when the tap is made on to a finger or an instrument placed on the chest. The applied finger or instrument is called the pleximeter, the tapping finger or instrument, the plessor. Percussion should always be light, except over very muscular parts of the chest.

Normal resonance is the note obtained over healthy lung tissue.

Hyper-resonance is an increased resonance, with diminished sense of resistance obtained over emphysematous lung tissue.

Dullness is diminution or loss of resonance, with increase in the sense of resistance. Various degrees of dullness are described, such as impaired percussion, slight dullness, flat, wooden or stony note.

Tympanitic resonance—a hollow drum-like note.

Skodaic resonance—a clear, high-pitched note intermediate in character between the hyper-resonant and tympanitic notes.

Cracked-pot sound—or *bruit de pot fêlé*—a hollow note with a slight jingle added to it, obtained by smart percussion over a fair-sized cavity. It is also heard on percussion of a crying baby.

AUSCULTATION.—The breath sounds should be listened to first, then the adventitious or added sounds, and lastly the vocal resonance.

(*a*) BREATH SOUNDS.—The following varieties of breath sounds may be differentiated:

Vesicular breathing.—The normal respiratory murmur or faint rustling sound audible during inspiration and expiration, the former phase being two or three times as long as the latter. The pause between inspiration and expiration is short.

Cog-wheel, jerky or interrupted breathing is a form of vesicular breathing in which inspiration waxes and wanes, or is divided into two or more parts.

Harsh, exaggerated or puerile breathing.—An intense form of vesicular breathing heard in children and in some forms of emphysema.

Vesicular breathing with prolonged expiration.—There is no alteration in the intensity or pitch of inspiration, but expiration is more prolonged and often harsher.

Absent, diminished, weak and suppressed breathing are self-explanatory.

Bronchial breathing.—The pitch of both inspiration and expiration is raised. Expiration is as long as inspiration and is separated from it by a distinct pause.

Broncho-vesicular and vesiculo-bronchial breathing are incomplete forms of bronchial breathing in which inspiration or expiration respectively assume the bronchial type.

Tubular breathing is a peculiar form of high-pitched bronchial breathing of whiffing character, sounding as if produced close under the stethoscope. This term is often used as if synonymous with bronchial breathing, but should be restricted to breathing of the type just described, which is only heard in consolidation from lobar pneumonia and broncho-pneumonia and in collapse of the lung.

Cavernous breathing is bronchial in type, but both inspiration and expiration have a peculiar hollow character. Expiration is more hollow and more prolonged than inspiration.

Broncho-cavernous breathing is incomplete cavernous breathing, inspiration being bronchial, while expiration is cavernous.

Amphoric breathing.—An intense form of cavernous breathing, often having a very hollow metallic sound.

(*b*) ADVENTITIOUS SOUNDS.—These were formerly divided into dry and moist. The former are now called rhonchi, the latter râles.

Rhonchi are musical sounds produced by the passage of air over mucus or muco-pus in the bronchi. Those arising in the larger tubes are called sonorous rhonchi, those in the smaller tubes sibilant or whistling rhonchi.

Râles are bubbling or crackling sounds produced in the bronchi or alveoli by the passage of air through fluid exudate or secretion. They are usually divided into bubbling and crackling râles. Bubbling râles are heard when the lung tissue is still spongy. Crackling or crepitant râles are produced in consolidated or softening areas of lung. Both varieties are arbitrarily subdivided into fine, medium and coarse râles. Crepitant râles are sometimes referred to as "creps"; this practice may lead to confusion with crepitation and is better avoided. Crepitant râles were formerly called consonating, bubbling râles non-consonating. Gurgling râles are coarse, low-pitched râles, usually heard over a cavity, especially after a cough.

Crepitations are fine "hair-like" crackling sounds. They may be produced either in the pleura or in the lung. In the latter they occur only in pneumonia, broncho-pneumonia, collapse and œdema. They are heard chiefly with inspiration and may be increased in number and intensity by coughing. A coarse variety heard in resolving pneumonic lung is called redux crepitation.

Pleural crepitations are fine sounds of similar character occurring in the early or dry stage of pleurisy. They are heard rather towards the end of inspiration and are usually unaffected by cough.

Friction is a coarse rubbing, creaking or grating sound heard in pleurisy when there is rough exudate on the pleural surfaces. It may occur with either inspiration or expiration or with both.

Stridor is a loud, coarse sound, heard chiefly during inspiration in cases of obstruction of the larynx, trachea or main bronchi. It is louder and lower pitched than a rhonchus.

Post-tussive suction is a hissing sound, audible directly after cough. It is heard only over a cavity, and is caused by the influx of air to replace that expelled by cough.

Veiled puff of Skoda is a puffing sound heard towards the end of inspiration. It is said to indicate small and sacculated bronchiectatic dilatations.

Metallic tinkling and amphoric echo are terms used to describe the quality of certain sounds produced near a very large cavity or a pneumothorax, in breathing or coughing, or by the heart's action.

Succussion splash is a splashing sound produced in a hydro- or pyopneumothorax by shaking the patient, or getting him to shake his thorax. If a gastric splash can be excluded, it is pathognomonic of a pleural or subphrenic hydro- or pyopneumo-thorax.

Bell sound or *bruit d'airain.*—A ringing sound heard on auscultation over a pneumothorax or any large cavity when a coin placed flat on the chest-wall over the air-containing space is tapped by a second coin. A similar sound is often audible on flicking with the finger and thumb over the chest-wall under similar conditions.

Voice Sounds or Voice Conduction.

Vocal resonance is the muffled sound on listening over normal lung when the patient articulates " ninety-nine " or some other resonant syllables.

Bronchophony is an increase in the intensity of the normal vocal resonance.

Pectoriloquy is conduction of the articulate voice sounds which are clearly heard as if spoken into the stethoscope. It is best appreciated by auscultating the whispered voice, and is then called whispering pectoriloquy.

Ægophony denotes a peculiar bleating or nasal modification of the voice sounds, sometimes heard on listening to them through fluid in the pleural cavity.

Physical examination of the chest includes mensuration, estimation of vital capacity and examination by the X-Rays when these are necessary.

Vital capacity is determined by a spirometer, which measures the amount of air which can be expired by a full expiration after the deepest possible inspiration. The average for an adult man is about 3600 c.c. The vital capacity is diminished in many diseases of the respiratory system, notably in acute pneumonia, pulmonary tuberculosis and in attacks of asthma.

R. A. Young.
G. E. Beaumont.

DISEASES OF THE NOSE

ACUTE CATARRHAL RHINITIS

See The Common Cold, p. 133

CHRONIC CATARRHAL RHINITIS

Ætiology.—Simple chronic rhinitis appears to result from frequently occurring attacks of coryza, or even from the persistence of a single acute attack. Predisposing causes of this persistence are deficient resistance, local irritation, auto-intoxication from the gastro-intestinal tract, and reflex vasomotor disturbance. Thus we find chronic catarrh associated with

anæmia, stuffy and over-heated rooms, occupations involving inhalation of irritating dust or vapour, excessive smoking, snuff-taking (a commoner habit than is generally realised among shop-assistants and clerks who are prevented from smoking during working hours), dyspepsia and constipation, alcoholism, sexual excess and masturbation. Nasal obstruction is an important factor in keeping up chronic catarrh by preventing ventilation of the passages, allowing mucus to collect and encouraging the growth of micro-organisms. In children the presence of adenoids is the commonest cause of catarrh.

Symptoms.—The symptoms are nasal obstruction and excessive secretion, which may be watery or muco-purulent, and may come forwards to the nostrils or pass backwards into the throat ("post-nasal catarrh"). Secondary results, from the extension of the inflammation, include catarrhal and suppurative otitis media, pharyngitis, laryngitis and bronchitis.

The nasal mucosa may be reddened, but often has a pale, sodden appearance. The turbinals are swollen and are at first quite soft, but later, when definite thickening has occurred, they feel firmer, and no longer shrink after the application of cocaine or adrenaline. At this stage the condition may be called "hypertrophic rhinitis," and the mucosal thickening, most marked over the two ends of the inferior turbinals and over the lower margin of the middle turbinal, may form large lobulated masses.

Diagnosis.—The diagnosis, in cases of hypersecretion, can only be made after excluding by rhinoscopic examination all other causes, such as a foreign body, mucous polypus, syphilitic, tuberculous and lupoid ulceration, and, more especially, suppuration in any of the accessory sinuses; in the latter, the discharge is not scattered over the nasal passages, but emerges in a localised stream from one or other of the ostia and reappears in the same situation after being removed. The discharge of chronic rhinitis is bilateral, and, though often muco-purulent, is never true pus. The diagnosis from vaso-motor rhinorrhœa is often difficult; the symptoms of the latter come and go with great suddenness, often as a result of definite causes such as going into a hot room, and there is complete absence of symptoms between the attacks. A bacteriological examination is often helpful.

Treatment.—General treatment, directed to the predisposing causes mentioned above, is necessary if a good result is to be obtained. Next, nasal obstruction must be removed, and operative treatment is called for if the cause be adenoids, deviation of the septum, or great hypertrophy of the extremities of the inferior turbinal bodies. For details, the reader is referred to surgical works; but it must be emphasised that the valuable secreting surface of the nasal mucosa must not be recklessly sacrificed, and that large portions of inferior turbinal must on no account be removed, nor should every slight deviation of the septum be submitted to operation, for it is rarely quite straight. When the turbinal enlargement is soft and shrinks after the applications of cocaine, the galvano-cautery should be used under local anæsthesia to draw one or two lines along the length of the inferior turbinal, the result of which is to produce a scar binding the mucosa to the bone. When the case has not gone on to definite hypertrophy, the most valuable form of local treatment is cleansing of the nasal passages. The lotion must be warm, about 90° F., and quite unirritating; for this reason it should have approximately the same specific gravity as serum, and

normal saline solution does very well. A mildly antiseptic and alkaline lotion is usually preferred, of which Dobell's solution is the type, such as sodium bicarbonate, grs. 3; sodium chloride, grs. 3; phenol, gr. 1; glycerin, min. 45; water, fl. oz. 1. A convenient instrument for the purpose is a small rubber ball of a capacity of 2 oz. with a blunt nozzle moulded in one piece, which is slowly emptied into the nostril, while the patient breathes deeply through the mouth and inclines the head forward over a basin; in this way the palate is raised and the lotion passes through the naso-pharynx and out by the other nostril. The nose must not be violently blown afterwards, nor must any force be used during syringing, or fluid may be injected into the Eustachian tubes. Occasionally syringing causes headache, in which case the lotion may be used in a coarse spray-producer. Chronic nasal catarrh is, however, in certain cases notoriously resistant to treatment, especially under the conditions of civilised town life; indeed, many sufferers found themselves better in the wet and exposed conditions of life in the trenches during the War of 1914–1918. Vaccine therapy is uncertain in its effect, but gives good results in a proportion of cases; an autogenous vaccine should be prepared from the patient's nasal secretion.

ATROPHIC RHINITIS

Synonym.—Ozœna.

Ætiology.—Cases usually first come under treatment between the ages of 15 and 18, but its insidious beginnings date from an earlier age, and a history of nasal discharge through childhood is often obtainable. It affects females at least three times as often as males. A peculiar physiognomy is to be noticed in nearly half the cases; the skull is brachycephalic, the nose wide and flat, and the nostrils broad and so directed forwards as to be more than usually conspicuous. The affection is sometimes unilateral, in which case the septum is deflected and the disease occurs on the wider side. Occasionally it is found among several members of a family, which might be the result of contagion, but it is also inherited in circumstances where contagion cannot apply, and this may be due to inheritance of the disease or merely of the predisposing physiognomy. It is more often seen in the poorer than in the more well-to-do classes and, in England, it has become much rarer during the last twenty or thirty years. Of the many bacteria found in association with the affection, the most important are the Klebs-Loeffler bacillus, the *Cocco-bacillus fœtidus* of Perez, and the *Cocco-bacillus mucosus* of Beeritz, but the consensus of opinion is that they are secondary, and, though helping to produce the fœtor, are not the primary cause of the disease. The condition occurs at too early an age to be the final stage of hypertrophic rhinitis, nor is it usually due to accessory-sinus disease, which can be excluded in the majority of cases. It is probably the sequel of prolonged purulent rhinitis in childhood, which results in the replacement of the ciliated by squamous epithelium, and thus destroys the principal agent for the removal of secretion; the undue width of the nasal passages promotes this retention by diminishing the force of the expulsive current of air, by drying the secretions and by unduly admitting dust and micro-organisms. In this way crusts of dried mucus are formed and decompose, and the resulting inflammation prevents the

development of the turbinals and thus further increases the width of the nasal fossæ.

Pathology.—There is a chronic inflammation resulting in sclerosis and atrophy of the mucosa; the ciliated epithelium is replaced by squamous, the mucous glands are degenerated and the venous sinuses have disappeared. These changes are most marked over the inferior turbinals; the middle turbinals are frequently large and œdematous. The discharge is not pus, but mucus precipitated by evaporation, mixed with shed epithelial cells and teeming with micro-organisms. This collects and dries into large greenish-black crusts which give rise to the peculiar sweetish and horribly offensive odour. There is never true ulceration nor necrosis of bone.

Symptoms.—The symptoms are chiefly those of the nasal discharge and the offensive stench; the latter is rarely perceptible to the patient, who usually, in established cases, has complete anosmia. There are also obstruction from the crusts, dryness of the throat and cough, and often some degree of ill-health from toxic absorption.

The inside of the nose is full of crusts; the inferior turbinals are reduced to mere ridges, the mucosa is pale and thin, and through the widened nasal passages the body of the sphenoid and the wall of the pharynx are plainly visible.

Complications.—Infection of an accessory sinus may result by extension from the septic nasal cavities, but is not very common; conversely suppuration of the sphenoidal or a posterior ethmoidal cell is a possible, and has been considered by some authorities as the usual, cause of the affection. The lymphoid tissue of the throat is conspicuously absent; there is often a dry pharyngitis and laryngitis, and sometimes the crusting extends to these parts, or even down the trachea. Catarrhal and suppurative otitis are common, and the disease is thought by many to predispose to pulmonary phthisis.

Prognosis.—As the ciliated epithelium can never be replaced, the affection is not truly curable, though regular treatment can keep it in an inoffensive condition, and it is common to see a suggestive degree of atrophy of the turbinals in young people with rhinitis completely disappear under treatment. Also, the crusting tends to become less troublesome as time goes on and ultimately to cease, a state of things which is difficult of explanation.

Treatment.—The nose must be kept clean by regular syringing with a mild alkaline antiseptic lotion, of which a large quantity should be used with a Higginson syringe provided with a fine nozzle which cannot block the nares. An oily, stimulating or emollient application, such as oleum eucalypti 15 minims to 1 ounce of paraffinum liquidum may be applied as a paint or spray, or a 25 per cent. solution of dextrose in glycerin as a paint. The crusting can be prevented by excluding the air and, when syringing is insufficient, this should be done by introducing a plug of gauze or cotton wool loosely into the anterior nares, which should be changed twice a day by the patient. After some weeks of treatment the packing may be omitted, but resumed in the event of a relapse. When the surgeon removes the plug the discharge is seen to be a clear mucus; if pus be found, it must be traced to its source in an accessory sinus. Paraffin wax may be injected under the mucosa, to narrow the nasal passages, but it is liable to slough out, and a piece of costal cartilage has been implanted with the same object. A plastic operation

has been devised to shift the antro-nasal wall inwards and has given encouraging results. The treatment of anæmia is important; good food and an open-air life, especially at the seaside, are beneficial.

EPISTAXIS

Ætiology.—The causes of epistaxis may be classified as follows:

Local causes.—Traumatism, including blows on the nose, fracture of the base of the skull, surgical operations and foreign bodies; the small septal erosion of rhinitis sicca, which is the commonest of all causes; malignant disease; angio-fibroma, or "bleeding polypus," of the septum; multiple telangiectasis, a curious hereditary affection characterised by numerous minute dilatations of the capillaries on the face and mucous membranes of the nose, mouth and throat; the general congestion caused by adenoids; and syphilis, lupus and the rarer granulomata, though in these the bleeding is usually an insignificant symptom.

General causes.—High blood pressure, as in arterial disease, chronic nephritis, cirrhosis of the liver, violent exertion, extremes of heat and cold, congestion at the menstrual period or "vicarious menstruation"; venous congestion, as in mitral stenosis, tumours in the thorax or root of the neck, emphysema, bronchitis and whooping-cough; toxic blood conditions, as pernicious anæmia, leukæmia, purpura, scurvy, and all the acute infectious fevers, especially in the prodromal stage. To these may be added rarefaction of the air, as in aeroplane ascents and mountaineering, and poisoning by some drugs, especially salicylates and quinine.

The *source of the bleeding* is, in the large majority of cases, in a region called Little's or Kiesselbach's area, situated on the front and lower part of the septum just beyond the vestibule.

Treatment.—Epistaxis, of sufficient severity to call for the attention of the doctor, should always be treated, though it is of comparatively little importance in healthy young people; in older patients with high blood pressure the loss of blood may be beneficial, but the occurrence is so distressing and alarming to the patient that other means to lower the pressure should be adopted.

The source of the bleeding is usually so far forward that a pledget of wool introduced for less than an inch into the naris, and held by compressing the nostril, will generally control it temporarily. To arrest it and prevent recurrence the bleeding spot must be found, started if necessary with a probe, controlled by application of cocaine and adrenaline on a plug of wool, and sealed by the galvano-cautery at dull-red heat. The use of an emollient ointment during the separation of the scab is advisable. In obstinate cases the bleeding may recur from another spot or from the opposite naris, when the treatment must be repeated. As in other forms of hæmorrhage, a rapid excited heart's action, associated with restlessness and fright, is often present, and an injection of morphine is of great value. Calcium lactate is often recommended and may be given in 20-grain doses three times a day for 2 or 3 days; or colloidal calcium may be injected subcutaneously. If the bleeding is from the usual situation, formal plugging of the nose is seldom called for; but sometimes the bleeding proceeds from farther back in the nose, or is so

profuse that its situation cannot at first be determined. In such cases the naris should be evenly packed with ribbon-gauze introduced on forceps under inspection. The older method of plugging the posterior nares is seldom required, and carries the risk of causing otitis media. Nasal plugs quickly become septic, and should ordinarily be removed in 24 hours; but they may be kept sweet for several days, should it be necessary to retain them, by moistening them frequently with peroxide of hydrogen.

MUCOUS POLYPUS

Ætiology and Pathology.—Nasal polypi are rare before puberty and are somewhat commoner in men than in women. They never grow from the septum, inferior meatus or inferior turbinal, but only from the ethmoidal region and interior of the accessory sinuses. They are not neoplasms, but are essentially due to a local œdema of the mucous membrane; the swelling thus produced is acted upon by the expulsive forces of the nose, and, being so pulled down and elongated, the return flow of its blood vessels and lymphatics is further impeded and a greater degree of œdema results. All stages of polypus formation may be found, ranging from an œdematous fringe along the border of the middle turbinal to enormous pedunculated masses which block the nose and expand its bony walls. In the majority of cases the œdema is due to inflammatory infiltration of the muco-periosteum of the ethmoidal labyrinth and is often associated with inflammation in the ethmoidal cells; sometimes, however, the cause is vasomotor disturbance, for polypi are found in cases of hay fever and paroxysmal rhinorrhœa in the absence of true inflammation. There is also another form, the so-called "choanal polypus," in which a large single polypus hangs into the naso-pharynx from a long pedicle attached within the antrum and passing through the ostium into the nose.

Symptoms.—The cardinal symptoms are nasal obstruction and discharge, which is profuse and watery. The symptoms are worse in damp weather. Cough, headache and asthma are not infrequent, and a loss of the power of mental concentration often occurs.

Polypi are smooth, shiny, white, translucent bodies, pedunculated and extremely soft and movable to the probe; their appearance is so characteristic that they cannot properly be mistaken for anything else. If they project into the nostril they become pinker and more opaque.

Treatment.—The best method of removal is in most cases with a wire snare, a process which can be rendered quite painless with skilful manipulation and the application of cocaine. Any polypoid mucosa in the neighbourhood should be removed with punch-forceps, but the application of caustics or the cautery only does harm. Recurrence is common, but becomes less rapid if the new polypi are removed at regular intervals before they have grown large. Inflammatory disease in the ethmoidal cells and other sinuses must, of course, receive treatment. In the worst cases, the polypi are so numerous and return so rapidly that the snare cannot deal with them adequately; in such they should be removed with a ring-knife or suitable forceps under general anæsthesia, together with the softened ethmoidal tissue, and any suppurating sinuses be opened at the same time.

PAROXYSMAL OR VASOMOTOR RHINORRHŒA

Synonym.—Allergic Rhinitis.

In this condition fits of sneezing are associated with a profuse watery nasal discharge, irritation of the nasal and conjunctival mucosa, nasal obstruction, and often marked depression and prostration. The discomfort is usually worse in the morning, in overheated rooms, or on going out into the cold. The rapidity with which the attacks come and go is sufficient to distinguish them from an ordinary coryza. The affection usually shows itself in early adolescence and tends to improve with advancing age; it is distinctly hereditary and is often associated, either in the patient or in his relations, with other symptoms of allergy, such as asthma, urticaria or chilblains. Males and females are equally affected, and it is most frequent among the cultivated classes; a mental shock is sometimes the starting-point of the attacks.

Of these cases, *hay fever* is the best known and most marked variety, and is due to specific susceptibility to a proteid substance contained in the pollen of certain grasses; in this country, attacks begin about the end of May and terminate in August. Hay-fever subjects are affected by very minute quantities of this toxin, whereas ordinary people are completely immune. Other individuals are susceptible to the pollen, seedlets or scent of other plants and flowers, and others again to the emanations from horses, cats, dogs and other animals; and researches show that asthma, urticaria, eczema or rhinorrhœa may be variously produced by many kinds of proteid substances, including common and uncommon articles of diet, such as eggs or lobsters, in certain people who are specifically susceptible to these substances.

Treatment.—The determining factors, which should receive attention, are heightened irritability of the nervous system, occasionally some intranasal abnormality which increases the sensitiveness, and the specific irritant. Nervine tonics, strychnine, arsenic and valerian, are indicated, and attention to the general health. Hay-fever patients are better in a locality as free as possible from pollen; some remain comparatively well at the seaside, others only on board ship, while some have to spend the best days of the year in a darkened room. Occasionally great benefit results from the removal of some nasal abnormality, a polypus or a sharp spur impinging on the turbinal, but the result of operative treatment is uncertain. In most cases the nares are normal, and in many of these a light cauterisation of the most sensitive areas is very helpful; the sites usually chosen are on the upper anterior part of the septum, and on the anterior part of the inferior turbinal. Ionisation of the nasal mucosa with sulphate of zinc is also employed. True hay-fever patients may have their susceptibility to pollen lessened by inoculation with dilute extract of pollen; the use of these extracts gives excellent results in a proportion of cases, and, more recently, the attempt has been made to test susceptibility to, and to immunise against, other proteid poisons.

ACCESSORY-SINUS SUPPURATION

Ætiology.—In the large majority of cases infection reaches the accessory sinuses from the nasal cavity, and may result from a simple coryza or from

one of the acute infectious fevers. Influenza is especially liable to produce disease of the sinuses, which may also be caused by measles, scarlet fever, erysipelas, enteric, pneumonia or small-pox. In addition, antral suppuration is caused by infection from the teeth, particularly the second bicuspid and first two molars, whose sockets are in closest proximity to the antral floor. The discharge from one sinus readily enters and infects another, so that disease of several cavities often coexists.

Symptoms and Diagnosis.—If the ostium of a suppurating sinus be occluded the pus is secreted under pressure, and the local symptoms are severe, whereas if the secretion can escape freely there may be no symptoms except discharge. The former class of case has been called "closed" and the latter "open" empyema. The difference between the two is, however, only relative, and many cases are alternating, the severe symptoms being relieved by periodical discharge. As the pressure of the pus in the cavity depends on the rapidity of its secretion, and the degree of occlusion of the ostium by inflammatory swelling, it follows that the closed and open cases correspond generally to acute and chronic suppuration; acute suppuration is usually fairly obvious, but some chronic cases with scanty secretion are only to be detected after very careful examination and may be for long the undiscovered cause of post-nasal catarrh, pharyngitis or chronic toxæmia.

The symptoms, then, are swelling, pain, tenderness and discharge, together with the secondary effects of the suppuration. Swelling is rare; the bony walls are not bulged by an empyema, and this is a point of distinction between it and a tumour or cyst, but occasionally spread of the inflammation causes periostitis, or a fistula in the bone is formed leading to an abscess outside the sinus. Thus, in frontal sinusitis a swelling may appear at the junction of the inner and upper walls of the orbit, displacing the eye downwards and outwards, or an abscess may form here and, after opening, leave a fistula. Similarly, ethmoidal disease may produce a swelling farther back on the inner wall of the orbit, displacing the eyeball outwards. In antral empyema, a little œdema of the cheek, or slight swelling in the canine fossa, may be found, but a swollen cheek is more likely to be due to dental periostitis, while any definite bulging of its bony walls is an indication of a tumour. Pain is often severe in acute cases, and in chronic suppuration there may be considerable neuralgic pain. Pain of an intermittent character, relieved by a sudden gush of discharge from the nose, is highly characteristic of sinus disease, as also is a peculiar periodicity, for it tends to begin regularly at the same time every morning and to get better during the afternoon. The pain may be of a local inflammatory character, or may be of a neuralgic type and referred to various parts. In antral suppuration it is over the cheek, or may be referred to the teeth or frequently to the supra-orbital region. The pain of frontal sinusitis is over the cavity or along the supra-orbital nerve; that of ethmoidal disease is over the nasal bridge, behind the eye or in the temple, and in sphenoidal suppuration, in the middle of the head, behind the eye, on the vertex or in the occipital region. Tenderness can usually be elicited in frontal empyema by percussion over the anterior wall, and especially by pressing upwards against the floor of the cavity; it is less marked in antral disease, in the canine fossa. Discharge into the nose is the most important, and often the only, symptom. A localised stream of pus in the nose, which reappears after removal, is, in the absence of a foreign body, conclusive

evidence of suppuration in an accessory sinus. The differentiation of the affected sinus is made by following the pus to its source with a probe and, in the case of the antrum, by tapping with a trocar and cannula. The antrum, frontal and anterior ethmoidal cells open into the middle meatus, and the posterior ethmoidal and sphenoidal into the superior meatus. Further assistance is afforded by transillumination and skiagraphy. Fetor, both subjective and objective, is often present, and a serious degree of anæmia and ill-health frequently results.

Complications.—These include pharyngitis, laryngitis, bronchitis, and otitis media; the swallowed pus causes various forms of gastric and intestinal disorder, including appendicitis. Acute septicæmia, and pyæmia are rare, but symptoms of chronic poisoning are common, and include anæmia, arthritis, fibrositis, and even mental aberrations. A very important series of complications results from extension of the inflammation to surrounding parts: orbital abscess or cellulitis, osteo-myelitis of the frontal bone, cerebral abscess, thrombosis of the cavernous sinus, paralysis of the oculo-motor nerves and, from the sphenoidal sinus, papillœdema and optic atrophy.

Treatment.—This, in acute cases, consists in rest in bed, hot fomentations to the affected part, aperients, a light diet, and a few doses of aspirin. Inhalations of mentholised steam at frequent intervals are of value, and may be prepared by adding 10 drops of 25 per cent. solution of menthol in spirit to a pint of steaming water in an inhaler. In recent cases of antral suppuration, the cavity should be tapped with trocar and cannula and washed out with a warm saline lotion; this should be repeated daily or every two or three days, according to the severity of the disease, and will effect a cure in a large proportion of cases in an early stage. Frontal sinusitis has a greater tendency to spontaneous cure; the anterior end of the middle turbinal may be amputated and occasionally a cannula can be passed and the cavity washed out. Cases which fail to recover under such treatment, and those of chronic suppuration, must be submitted to operation.

SYPHILIS

Congenital Syphilis

The *early form* appears at any time within 3 months after birth, usually within the first few weeks. The symptoms, frequently called "the snuffles," are those of nasal discharge and obstruction; the former may be thin and ichorous, or purulent and bloodstained, and is often associated with cracks and excoriations about the nostrils, upper lip and angles of the mouth; the obstruction may cause attacks of choking and frequently prevents the baby from taking the breast, and so produces wasting and malnutrition. These symptoms are not pathognomonic of syphilis, but may also be caused by catarrhal and purulent rhinitis, therefore the diagnosis must be established by the concomitant lesions.

The *late form* appears usually about the period of puberty, but may occur at any time after the age of about 5 years. It is characterised by a slow destructive gummatous infiltration and ulceration, and the symptoms are those of nasal catarrh and obstruction, frequently with fetor and crusting;

this chronic rhinitis destroys the ciliated epithelium, and may thus cause a true atrophic rhinitis which persists after the syphilis has become quiescent or cured. Congenital syphilis is apt to produce a very characteristic "saddle-back" flattening of the bridge of the nose.

Acquired Syphilis

Primary chancre is very rarely seen on the ala of the nose, and is accompanied by bubo of the submaxillary and pre-auricular glands, and by much induration and swelling.

Secondary syphilis does not produce noticeable symptoms in the nose; there may be rhinorrhœa and obstruction associated with hyperæmia of the mucosa.

Tertiary syphilis occurs usually in the form of a diffuse gummatous infiltration and ulceration, which may proceed to necrosis of any of the bony or cartilaginous walls of the nose; there is profuse purulent discharge, often bloodstained, which tends to dry into greenish-black crusts, the odour of which is extremely offensive. A localised gumma may occur on the septum, where it forms a smooth round swelling projecting into both nostrils which, by its contraction after healing, produces a steep depression of the bridge just below the nasal bones. Syphilitic ulceration sometimes attacks the external parts of the nose, causing perforation of the ala, or destruction of the columella with a characteristic depression of the nasal tip.

Diagnosis.—This seldom presents much difficulty; the form with crusting and ozæna imitates atrophic rhinitis, but in the latter there is never necrosis or decided ulceration—indeed intranasal necrosis may be considered pathognomonic of syphilis. A septal gumma has an appearance identical with that of a hæmatoma, but without the sudden onset and history of traumatism. Syphilitic perforations nearly always involve the bone, whereas those due to rhinitis sicca or lupus never do. Some cases of diffuse infiltration resemble lupus; but in the latter there is no necrosis or offensive odour, the characteristic nodules are usually to be seen at the edges of the lesion, and other patches of lupus may be found on the skin or in the fauces. The chief difficulty of diagnosis lies between severe syphilitic infiltration and malignant disease, but it can usually be determined by the clinical appearance, especially by the characteristic edge of the syphilitic ulcer, by the examination of an excised portion, by the Wassermann reaction, and by the results of anti-syphilitic treatment.

Treatment.—General treatment must be very prompt and energetic to prevent irremediable deformity, and should ordinarily be begun with the injection of arsphenamine or of one of its congeners. Of local treatment, the lesions should be kept clean by frequent syringing with a saline lotion, to which lysol, sanitas or listerine may be added when the odour is offensive; any necrosed bone must be removed as soon as it is loose.

LUPUS AND TUBERCULOSIS

Ætiology.—With the exception of the rare occurrence of tuberculous ulceration as a terminal infection in advanced phthisis, the lesions produced

in the nose by lupus and by tuberculosis are indistinguishable; it appears that the tubercle bacillus finds in the nasal mucosa a medium unsuitable for its development, its virulence is diminished, and it can only produce the modified lesions known as lupus. It is possible, also, that this modification of the bacillus by sojourn in the nose is the ordinary cause of lupus; at any rate it is frequently primary in the nares, whence it spreads to the fauces and larynx and on to the face and hands. The disease begins most often between the ages of 15 and 30, is twice as common in females as in males, and is usually seen in badly nourished people of the poorer classes.

Symptoms.—The early lesions are found on the antero-inferior part of the septum, the nasal floor and the front end of the inferior turbinal, within reach of the finger-nail, which probably conveys the infection. The characteristic "apple-jelly" nodules are seen, with or without ulceration, the latter with rounded slightly raised margins, and tending to spread in some directions and cicatrise in others. The lesions are covered by small adherent scabs, and perforation of the septal cartilage is common. The alæ often become involved with destruction of the margin or with perforation, and the nostrils may be much narrowed and deformed by scarring, while the lachrymal duct is frequently involved. The progress of the disease is extremely slow and may continue over many years. The subjective symptoms are nasal obstruction with a slight sticky discharge.

Diagnosis.—The nares should be examined in all cases of cutaneous lupus, for, if the disease remain unhealed in the nose, relapses will continually occur. In the majority of cases of nasal lupus the diagnosis is cleared up by the presence of lesions or scars on the face, fauces or larynx. The difficulties of diagnosis are from rhinitis sicca with perforation, and from syphilis. The typical brownish nodules are pathognomonic and can always be found by careful examination when the lesions are progressing; they can be made more conspicuous by blanching the mucosa with adrenaline. The scabbing of rhinitis sicca quickly clears up under simple emollient treatment, while the lesions of syphilis are more rapidly progressive and tend to involve bone.

Treatment.—The affected areas are defined by the application of adrenaline and thoroughly and carefully scraped away with a sharp spoon, a general anæsthetic being employed if the lesions are extensive; small lesions and recurrences are destroyed with the galvano-cautery. Nascent iodine by Pfannenstiel's method may be employed; sodium iodide is given in 7-grain doses six times a day, while the nose is packed with gauze kept moist with peroxide of hydrogen, 10 volume strength, with 5 per cent. of acetic acid added; when a marked reaction has been obtained this solution should be diluted to half its strength, the iodide being continued as before; the treatment may have to be persisted in for several months. Radium is still under trial, and tuberculin has not established its value in this affection.

Of general treatment, arsenic in full doses, fresh air, cod-liver oil and fattening foods are of value. Lupus does not show the same tendency to spontaneous cure in the nose as in the larynx; it is easy to obtain improvement, but complete cure is difficult.

TUMOURS OF NOSE

Papilloma occurs on the skin lining the vestibule and differs in no respect from cutaneous warts elsewhere. On the nasal mucosa it is excessively rare occurs usually on the septum, has a narrow pedicle, a rough red or greyish surface, and bleeds readily when touched; occasionally the growths are multiple and, when large, are difficult to diagnose from a malignant growth, but they do not erode bone; they tend to recur locally after removal.

Fibroma, similar to the naso-pharyngeal fibromata, occurs, though rarely, as a smooth pink growth attached to the posterior region of the nares. It bleeds readily and spontaneously and demands great caution in removal.

Angio-fibroma, or "bleeding polypus of the septum," is less uncommon. It varies from the size of a pin's head to that of a filbert, is red or purple, smooth or finely lobulated, sessile or pedunculated, and grows from the anterior part of the septum. The prominent symptom is epistaxis, for the tumour bleeds freely and spontaneously. When pedunculated, it may be removed with the snare and the base cauterised; when sessile, it should be stripped off the underlying cartilage with an elevator. Recurrence is common.

Osteoma and *enchondroma* are extremely rare, usually grow from the ethmoid region and produce obstruction and deformity.

Cysts.—Mucous polypi are occasionally cystic; the so-called "ethmoidal cyst" is an enlarged cell in the anterior part of the middle turbinal pressing on the septum and causing obstruction and headache. True cysts are sometimes seen on the anterior part of the nasal floor, and arise from the roots of incisor teeth. When small, they may be treated by intranasal removal of part of the wall; when large, they should be dissected out from the gingival fold. *Mucoceles* are cystic dilatations of the antrum, frontal sinus, or an ethmoidal cell.

Malignant tumours occur in all varieties: carcinoma, sarcoma, and endothelioma. Though they sometimes appear on the septum or nasal floor, the usual site of origin is the ethmoidal region. They tend to expand the bones of the face, producing a characteristic frog-like deformity, and they frequently invade the antrum and expand its walls, constituting a common variety of tumour of the upper jaw. The facial, palatine and orbital walls of the antrum may each be bulged outwards, the latter with displacement of the eyeball, and egg-shell crackling can sometimes be elicited. Sanious discharge and free spontaneous hæmorrhage are prominent symptoms and important for diagnosis. Surgical excision produces permanent cure in only a small proportion of cases; better results, especially in endothelioma and sarcoma, are obtained by the implantation of radium. According to the situation of the growth, access is gained by opening the antrum through the canine fossa, by lateral rhinotomy, or for the lower part of the nose by an incision in the gingivo-labial fold from the molar teeth of one side to the other.

HAROLD S. BARWELL.

DISEASES OF THE NASO-PHARYNX

ADENOIDS

Ætiology.—By this term is implied a chronic enlargement of the lymphoid tissue of the naso-pharynx, the "pharyngeal tonsil." This is normally present in childhood and disappears by the age of 20 or thereabouts, but if chronically enlarged may remain up to any age. The precise stage at which the enlargement becomes pathological can only be determined by the symptoms which it produces; these usually become manifest between the ages of 3 and 8, but occasionally show themselves at or soon after birth. The incidence of adenoids is universal, but they are most common in damp temperate climates, and chronic or recurrent nasal catarrh is the principal factor in the causation; the infectious fevers, particularly measles, scarlet fever, and diphtheria, are also a frequent cause of the hypertrophy.

Pathology.—The adenoid, as it should really be called, or enlarged pharyngeal tonsil, is a mass of lymphoid tissue of definite anatomical shape; it is thickest above and tapers away below, and presents a series of ridges which radiate from below upwards and slightly outwards. In older patients the mass is firmer and more fibrous, and the ridges are often adherent in places, leaving deep clefts and furrows in which secretion can collect and decompose.

Symptoms.—The symptoms of adenoids are many and various, and include those due to nasal obstruction, those caused by infection and by the extension of inflammation, and reflex processes attributable to irritation and lowered vitality. In infants the nasal obstruction interferes with sucking and a serious degree of malnutrition will result unless the baby be carefully spoon-fed. Older children snore at night, breathe heavily in the day, and either bolt their food or eat very slowly owing to the necessity of breathing through the mouth. Owing to lack of oxygen the patients sleep restlessly, wake unrefreshed and often suffer from a peculiar inability to concentrate the attention sometimes called "aprosexia." Persistent nasal obstruction during the period of growth mechanically produces permanent deformities of the jaws and face which narrow the nasal passages, prevent the mouth from closing naturally and thus perpetuate mouth-breathing. When the mouth is habitually held open, the alæ nasi are pulled downwards with the cheeks, and become narrow and slit-like and fall in like valves with each inspiration; this "alar collapse" is an important cause of obstruction in neglected cases of adenoids. The palate is narrow and highly arched; the dental arch is narrow and V-shaped, so that the upper incisors, crowded and prominent, look outwards rather than forwards, and are not covered by the short upper lip; the lower jaw retains its infantile obtuse angle, and the lower incisors lie behind the upper; the chin is receding and, in the worst cases, when the molar teeth come into contact on biting, the incisors cannot meet. Only a proportion of cases of adenoids show these deformities, and there is, indeed, considerable uncertainty as to the importance of adenoids in their ætiology; undue softness of the bones, such as occurs in rickets, is doubtless an additional factor, and also in the causation of the malformations of the chest which result from the obstruction to the entry of air. The long

narrow unexpanded chest with acute costal angle and prominent scapulæ is the commonest deformity. Harrison's sulcus, a transverse depression corresponding to the attachment of the diaphragm; pigeon-breast, a prominent sternum with depressed costal cartilages; and funnel-breast, a sharp depression at the lower end of the sternum, are also encountered.

Various infective processes result from the spread of inflammation and, if the naso-pharynx be large, are not necessarily associated with nasal obstruction. The terribly common catarrhal and suppurative affections of the ear in children are, in an overwhelming majority of cases, the result of adenoids. Blepharitis and phlyctenular conjunctivitis are also associated with adenoid vegetations. Feverish attacks, often with tender enlargement of the cervical glands, are caused by infection of the pharyngeal and faucial tonsils, and tuberculous disease of the glands is usually due to passage of the bacilli through these portals; in such cases the tonsils and adenoids may remain unaffected or may themselves show tubercles under the microscope. Chronic or recurrent bronchitis frequently results from the infection spreading to the lower air-passages. The mucus secreted by the adenoids is swallowed in large quantities, and produces derangements of stomach and intestines with failure of growth and general health. Finally, mouth-breathing predisposes to dental caries. The irritation of these vegetations, and their effect on respiration and the general health, account for numerous reflex and nervous disturbances. Among them may be enumerated laryngitis with spasm called "laryngitis stridula," spasm of the glottis without laryngitis or "laryngismus stridulus," stammering, reflex cough, asthma, night terrors and nocturnal enuresis; it should be stated that the latter disorder is by no means always to be cured by removal of the concomitant adenoids, and that in general too much stress must not be laid upon the presence of adenoids as the causative factor in all these reflex disturbances.

Diagnosis.—In the majority of tractable children a view of the naso-pharynx can with patience be obtained with a good light and a very small rhinoscopic mirror, when the upper part of the septum and the concavity above it are seen to be occupied by an irregular convex mass. Where this is impossible a rapid digital examination may be required; this is extremely unpleasant to the little patient, and may be postponed, in those cases where the tonsils are sufficiently large to call for removal, until the child is anæsthetised. Similarly, in very frightened, intractable children, if the symptoms point strongly to adenoids it is wiser to give an anæsthetic for examination, being prepared to remove the vegetations if present. In the mongolian type of idiocy the tongue is large and the mouth persistently open, and in microcephaly the extremely undeveloped naso-pharynx causes nasal obstruction; cases of both these types of maldevelopment are often brought to the doctor in the hope that removal of their adenoids will cure their "backwardness," and care should be taken not to fall into the error of performing a useless operation, though if a well-marked adenoid be present it should be removed under a guarded prognosis. On the other hand, adenoids can be present and produce serious secondary effects without causing nasal obstruction or any appearance of the typical "adenoid facies."

Treatment.—The normal naso-pharyngeal tonsil becomes swollen during a coryza, and such temporary swelling should not be diagnosed as "adenoids," by which term chronic hypertrophy is understood, and does not call for

removal provided that it subsides promptly, does not frequently recur, and is not associated with otitis media or other important complications. In such cases, and when the only symptom is a mild catarrh, the regular use of a simple warm saline lotion with a rubber ball-syringe (see p. 1086) will often effect a cure; in children below the age of 5 or 6 syringing is apt to be difficult and the lotion may be used in a spray, while in infants it is best to drop it into the nostrils from a small pipette like the filler of a fountain-pen. This treatment should be combined with open air—if possible a change to the seaside or a bracing country district—cod-liver oil, iodide of iron, or arsenic. Breathing exercises are of great value in these slight catarrhal cases, but only do harm where there is marked obstruction.

When the enlargement frequently recurs or has gone on to chronic hypertrophy, operative removal is the only treatment, and this is especially called for when any aural symptoms supervene, or when cervical adenitis is present. After operation the general treatment referred to above is valuable, but the nose should on no account be syringed until healing is complete, as this encourages aural complications. If the alæ nasi are collapsing, or the chest narrow, breathing exercises are of use, but healthy open-air occupations are more useful still. In patients in their teens, or upwards, turbinal hypertrophy has not infrequently resulted; the surgeon should be prepared to snare off enlarged posterior ends of the inferior turbinals at the time of the operation, and intranasal cauterisation may be required later.

TUMOURS

Innocent tumours in the naso-pharynx are exceedingly rare; the so-called "choanal polypus" is a variety of nasal mucous polypus which hangs into the naso-pharynx from a long pedicle attached within the naris.

Fibroma of the naso-pharynx, or naso-pharyngeal polypus, occurs usually in males between the ages of 10 and 25, grows by a broad pedicle from the periosteum of any part of the walls of the naso-pharynx, usually from the basi-sphenoid, and forms a smooth, rounded, pink mass which fills the naso-pharynx and sends prolongations into the nasal cavities. The palate is pushed downwards, the bones of the face expanded, and the eyeballs separated and displaced, producing the "frog-face" deformity. The cardinal symptoms are nasal obstruction and discharge, with headache and severe epistaxis; aural complications may follow, or the eyes may be involved, with diplopia, exophthalmos and compression of the optic nerve; and, finally, death results from exhaustion, hæmorrhage, sepsis or cerebral invasion. Histologically the tumour is composed of fibrous tissue containing numerous thin-walled blood vessels and a variable admixture of round or fusiform cells, so that in some cases it might be described as a fibro-sarcoma; but it is not truly malignant, for it neither involves the glands nor becomes disseminated, though there is a tendency to local recurrence after removal.

Radium has proved of considerable value in reducing the size and vascularity of these growths, as a preliminary to operation.

Malignant tumours are not common in the naso-pharynx, but epithelioma, sarcoma and endothelioma all occur. The early symptoms are chiefly pains of a neuralgic character and those produced by Eustachian obstruction;

later, epistaxis, nasal obstruction, secondary involvement of glands and affections of the eye and cranial cavity may appear. Surgical removal is rarely feasible, but sarcomata and endotheliomata in this region sometimes yield remarkably to treatment by radium.

HAROLD S. BARWELL.

DISEASES OF THE LARYNX

ACUTE CATARRHAL LARYNGITIS

Ætiology.—The affection ordinarily occurs as part of a coryza, or cold, the inflammation spreading downwards from the nose or naso-pharynx. It is also caused by over-use of the voice, especially with faulty voice-production, and frequently a slight catarrh is made worse by using the voice during a cold. It occurs in many infectious fevers, *e.g.* influenza, measles, scarlet fever, typhoid and small-pox, and it is occasionally a result of traumatism, instrumentation, or the inhalation of irritating fumes in chemical works or of the gases used in warfar. Predisposing causes are chiefly those factors which favour attacks of coryza, such as nasal obstruction or discharge, sedentary occupations and overheated rooms; apart from local tuberculous lesions, consumptives are very subject to laryngeal catarrh.

Symptoms.—The symptoms consist of hoarseness or aphonia, local discomfort varying from dryness or tickling to a burning sensation or actual pain, and irritable cough. There is little expectoration, unless the trachea and bronchi are involved. At the onset there may be slight feverishness and malaise. The degree of hoarseness is by no means proportionate to the objective appearances; the voice may be quite good in cases of decided hyperæmia, and may be completely lost when little abnormal is to be seen. This depends largely on the neuro-muscular tone; a muscular man will retain a strong voice with a degree of inflammation which would render a weakly woman completely aphonic—indeed some women lose the voice with every slight cold, so that it becomes difficult to differentiate between laryngeal catarrh and "functional aphonia." On the other hand, in some voice-users redness of the cords appears to be the normal condition and causes no interference with function. This variable effect on the voice is to be observed in all forms of laryngeal disease. In children, acute laryngitis is a serious affection. They show a far greater tendency to œdema and to spasm, and as the glottis is not only absolutely but relatively smaller than in adults, a dangerous dyspnœa may ensue with great rapidity. The larynx is reddened, and this is most obvious on the parts usually pale—the epiglottis and vocal cords, the vessels on the former being unduly prominent. The cords may be red, pink, yellowish, or merely have lost their bright pearly lustre. A small amount of mucous secretion is generally present, but no large accumulations or strings of mucus, such as are seen in chronic laryngitis. There is often a little swelling of the cords so that, on phonation, their edges come into contact at the centre; this explains how singers' nodules are caused by use of the voice during a laryngitis.

Treatment.—People suffering from the slighter degrees of laryngitis

rarely apply for treatment, unless they are professional voice-users. The patient should remain in a warm (65° F.), well-ventilated room, preferably in bed, and must not attempt to use the voice. The coryza, if present, should be treated at the same time. Steam inhalations are of value and may be used from an inhaler or from a jug round the mouth of which a towel has been wrapped in the shape of a cone. The water should be at a temperature of 130° to 140° F., and one of the following medicaments may be added in the proportion of one drachm to the pint: Compound tincture of benzoin (Friar's balsam) fl. oz. 1, with or without menthol, grs. 10–15; or benzoic acid, grs. 3, kaolin, grs. 12, tincture of tolu, min. 18, and water to fl. oz. 1, these being sedative, while oleum pini sylvestris, min. 40, magnesii carb. levis, grs. 20, water to fl. oz. 1 is mildly stimulating. Steam inhalations should only be ordered when the patient can remain in a warm room; when he is not confined to the house, or in a later stage, an oily solution from an atomiser is preferable, such as menthol, grs. 7, camphor, grs. 3, chlorbutol, grs. 5, liquid paraffin, fl. oz. 1. Internally, expectorants are indicated; tincturæ ipecacuanhæ, min. 10, or vinum antimoniale, min. 5, potassium iodide, grs. 2 or 3, ammonium carbonate, gr. 4—singly or in combination—or ammonium chloride, grs. 5, or oil of cubebs, min. 5 in syrup, every 4 or 6 hours. If cough is severe it should be restrained; a lozenge of morphine and ipecacuanha is useful, or a linctus containing diamorphine hydrochloride, gr. $\frac{1}{24}$, or liquor morphinæ, min. 2 to 4 to each drachm.

The acute laryngitis of children calls for prompt treatment. One or two grains of calomel may be given every 3 hours until the bowels have acted freely, after which it may be continued in $\frac{1}{2}$-gr. doses three times a day. Hot fomentations to the neck and a steam-kettle are advisable, and in acute febrile cases, 1 minim each of tincture of aconite and vinum antimoniale every 3 hours. If dyspnœa occurs, an emetic dose of ipecacuanha often gives prompt relief; 60 minims of the tincture followed by 30 minim doses every half-hour until vomiting occurs: in very young or weakly children, 15 minims every quarter-hour is to be preferred.

SPASMODIC LARYNGITIS

Synonym.—Laryngitis Stridula.

This is simply catarrhal laryngitis with spasm of the glottis as a marked feature. It is a disease of childhood and is predisposed to by general ill-health, rickets and adenoids. The onset is that of an ordinary cold, with slight feverishness, hoarseness and a frequent cough, and during the evening or night the respiration becomes embarrassed. There is inspiratory stridor, recession of the epigastrium and lower ribs and, in some cases, an alarming degree of asphyxia. The symptoms tend to subside towards morning and, though they may recur on the next few nights, it is usually with diminishing severity. The condition should be distinguished from laryngismus stridulus, in which there is no hoarseness or other symptoms between the attacks. The evanescence of the symptoms serves to distinguish it from œdematous laryngitis and from diphtheria, in which the attacks become increasingly severe. The general health requires attention, and adenoids, if present, must be removed after recovery has taken place.

ŒDEMATOUS LARYNGITIS

Synonym.—Œdema of the Larynx.

Ætiology.—Œdema of the larynx is not a disease but a pathological condition due to a variety of causes. Non-inflammatory œdema may be mentioned here for the sake of completeness; it occurs, though rarely, as part of the general anasarca of renal and cardiac disease. Angio-neurotic œdema sometimes occurs in the larynx, in which event it produces rapid and sometimes fatal dyspnœa (see p. 1074). The swelling which occasionally results from administration of potassium iodide in susceptible subjects may be placed in the same category.

Inflammatory œdema seldom results in adults from a simple catarrh, but it may do so in children; it more often occurs as part of an acute septic infection of the pharynx, trachea and bronchi, "acute fulminating laryngo-tracheo-bronchitis." Œdema may follow various forms of traumatism, the drinking of corrosive poisons, inhalation of irritating vapours, such as the poison gases of warfare, the lodgment of foreign bodies, or rough or unduly prolonged bronchoscopy. Scalding, from attempts to drink from a kettle-spout, is a common cause among children. In other cases it is a sequela of typhoid fever, pneumonia, scarlet fever or small-pox, and is a local complication of syphilitic, tuberculous, cancerous or traumatic ulceration.

Symptoms.—If part of a septic pharyngo-laryngitis, the general symptoms are severe. The chief local symptom is dyspnœa with inspiratory stridor and the associated symptoms of asphyxiation; there is hoarseness or aphonia, local discomfort and tenderness, and sometimes dysphagia. The arytenoepiglottidean folds are enormously swollen, appearing as pale or purple translucent flask-shaped masses; if the epiglottis be œdematous it forms a sausage-shaped swelling of the same appearance. The mucosa of the vocal cords is too adherent to permit much swelling, and "œdema of the glottis" is therefore a misnomer. The subglottic region is lax and may become swollen; indeed, the œdema may be confined to this region and then appears as a red swelling below each vocal cord. In children œdema may be inferred from the steadily increasing dyspnœa without the rapid increase and decrease typical of spasmodic laryngitis.

Treatment.—In slight cases, the swelling may be reduced by sucking ice and by the application of an ice-bag to the neck; the latter is inadmissible in young children. A spray of adrenaline, 1 in 1000, may be used. Hypodermic injections of pilocarpine, gr. $\frac{1}{8}$, are recommended and, for the œdema produced by iodides, large doses of bicarbonate of soda. Free scarification of the œdematous tissues at the upper aperture should be practised without undue delay; in adults this should be done with a laryngeal lancet under guidance of the mirror, but in children it is best performed with a curved bistoury guarded to near the point with strapping and passed down along the left forefinger as a guide. If this does not give quick relief, or if the dyspnœa be severe, tracheotomy should be performed without delay. Intubation is not suitable for cases of œdema of the upper aperture of the larynx, though it may be employed for subglottic cases, provided that skilled attention be immediately available should the tube be coughed out. Angio-neurotic œdema should be treated by a spray of adrenaline, and the same

drug, or a colloidal preparation of calcium, may be injected hypodermically; tracheotomy may here also be required.

MEMBRANOUS LARYNGITIS

The formation of false membrane in the larynx is nearly always part of an attack of diphtheria, which is discussed elsewhere, but by the term "membranous laryngitis" is implied a formation of membrane of non-diphtheritic origin. Apart from traumatic cases, due to irritating chemicals and scalds, inflammation of the larynx accompanied by membrane may be caused by streptococcal infection. The affection occurs especially in children between the ages of 2 and 8 years. The first symptom is hoarseness, soon followed by a brassy cough and the signs of dyspnœa; the patient is restless and the temperature rises rapidly to 103° or 104°. In some cases, however, the disease takes a subacute form, the attacks of dyspnœa being worse at night and abating towards morning. The diagnosis from diphtheria is only possible by bacteriological examination, and pending the report the case should be treated with antitoxin; but it may be noted that the pharynx is nearly always involved in diphtheria, whereas in membranous laryngitis the disease is often primary in the larynx. The prognosis is grave, worse than that of diphtheria since the introduction of antitoxin. An emetic dose of ipecacuanha should be given, and a steam-tent and hot fomentations to the neck are advisable. Calomel treatment is recommended; 1 or 2 grains every 3 hours until the bowels have acted freely, and subsequently 1 grain three or four times a day; the sulphanilamide group of drugs will doubtless be of value in this, as in other streptococcal infections. Tracheotomy or intubation must not be delayed when there is serious dyspnœa.

CROUP

Croup is an expression which dates from a period when the diagnosis of diseases of the throat was less exact than now but, as it is still in occasional use, it may well receive a definition in this place. The term can be used to cover any respiratory obstruction or obstructive dyspnœa, especially in children, but is usually limited to acute affections and therefore does not ordinarily include such conditions as multiple papillomata, congenital web or cicatricial stenosis. Croup may thus be caused by various inflammatory affections such as œdematous laryngitis, membranous laryngitis (both diphtheritic and non-diphtheritic), spasmodic laryngitis and retropharyngeal abscess, or by such reflex disturbances as laryngismus stridulus and spasm of the glottis, and is in fact descriptive of a symptom rather than of a disease.

CHRONIC LARYNGITIS

Ætiology.—The causation is similar to that of acute catarrhal laryngitis; indeed, chronic laryngitis is often the result of recurrent or persistent acute catarrh. The principal factors which predispose to chronicity are nasal

obstructions and discharges, dusty occupations and lack of fresh air, over-use of the voice and faulty voice-production, and the abuse of alcohol or tobacco; consumptives are particularly liable to non-specific catarrhal laryngitis, and oral sepsis must not be omitted. Almost any cause of general ill-health may be included among the predisposing causes, such as gout, rheumatism, anæmia, and gastro-intestinal, cardiac and hepatic disorders.

Symptoms.—The only constant symptom is impairment of the voice, which is hoarse, easily tired or even, though rarely, completely aphonic; it is sometimes weakest when tired in the evening, but is often at its worst on rising in the morning or after a rest. There is frequently a sensation of aching, dryness, tickling or of a lump in the throat, and there is usually some cough, but little expectoration unless the trachea and bronchi are involved.

The objective appearances vary with the severity of the affection. The larynx generally is of a deeper red than usual, and the vocal cords have lost their normal pearly lustre and are pink or grey; they are usually somewhat thickened at the edges, and enlarged vessels may be visible on their surface; the vocal processes are often prominent and may be reddened or show up white against the hyperæmic cord. Strings of sticky secretion may stretch between the cords, or a little globule of mucus may form on the centre of the cord during phonation; adduction is frequently imperfect. When the epiglottis is reddened, its yellow edge stands out clearly and enlarged vessels are visible; the ventricular bands are often swollen so as to hide the outer part of the cords. The mucous membrane in the inter-arytenoid space, thickened and relaxed, is seen to be thrown into folds on adduction of the cords, and may form a mass large enough to prevent their approximation.

Atrophic rhinitis usually produces a form of inflammation, *laryngitis sicca*, in which small brown scabs adhere to the cords and posterior commissure, but occasionally the disease itself spreads to the larynx, which is covered by large greenish or brownish-black fetid crusts; more rarely still the crusts extend into the trachea and cause severe dyspnœa, which may prove fatal.

Pachydermia laryngis is a somewhat rare variety of chronic laryngitis, occurring principally in middle-aged men. It is frequently ascribed to alcoholism, perhaps on insufficient grounds, to syphilis and to tubercle; the diagnosis between pachydermia and these two diseases is, however, often a matter of difficulty. The characteristic epithelial thickenings are probably of the nature of corns, resulting from frequent cough and continued irritation. There is hoarseness of a rough raucous character, but no particular discomfort. The epithelial thickening is pink or whitish and occupies the posterior or cartilaginous region of the glottis from the vocal processes backwards to the posterior commissure. A circumscribed swelling appears on each vocal process, with a small cup or depression at the apex; the approximation of the cords is better than would be expected, because the prominence on one vocal process fits into the depression at the other. The epithelium of the inter-arytenoid space is thrown into ridges, which fill up the angles between the arytenoid and the posterior commissure, but leave a depression in the middle line. These firm, opaque, symmetrical swellings, without ulceration, are distinguishable from the soft irregular granulations

of a tuberculous lesion, and the cup-shaped swelling on the vocal process, even when more marked on one side, should not be mistaken for an early epithelioma.

Treatment.—The detection and correction of the ætiological factors are the most important part of treatment. Any constitutional disturbance, such as anæmia, rheumatism, gout or dyspepsia, should receive attention. Over-indulgence in tobacco or alcohol, lack of ventilation and exposure to dust must be considered, and with teachers the black-board chalk is a common source of irritation.

Incorrect voice-production is a factor of great importance especially, but by no means exclusively, among those who use the voice largely in their occupations; in such, a course of lessons in voice-production often works wonders. In a large proportion of cases the primary cause of the laryngitis is to be found in the nose, therefore any source of nasal obstruction, catarrh or suppuration must be carefully looked for and treated; any concomitant pharyngitis should also receive attention.

Locally, treatment must begin with rest of the voice, which should be absolute in the case of professional voice-users. Where there is much secretion a saline lotion may be used in a spray—sodium bicarbonate, borax, sodium chloride, 10 grains of each, thymol water, 120 minims, glycerin, 60 minims, water to 1 ounce. Oily solutions are usually preferred, such as menthol, 5 grains, camphor, 2 grains, chlorbutol, 5 grains, or oil of eucalyptus, pine or gaultheria in similar proportions, to an ounce of liquid paraffin. The direct application of pigments is not often called for, and is to be recommended only when pachydermatous changes are present; in such cases the cautious application of a solution of nitrate of silver on a cotton-wool mop once a week may be tried, beginning with 5 grains to the ounce and increasing the strength gradually to 50 or more grains. Dundas Grant advises an alcoholic solution of salicylic acid, beginning with 1 per cent. and increasing to 6 or 8 per cent.

Internally, small doses of potassium iodide, 2 or 3 grains, or the yellow proto-iodide of mercury, $\frac{1}{10}$ grain, three times a day over long periods, is of value.

CONGENITAL LARYNGEAL STRIDOR

In this condition there is an exaggeration of the infantile shape of the upper aperture of the larynx; the epiglottis is sharply folded laterally, the ary-epiglottic folds are almost in contact, and the opening is thus reduced to a narrow vertical slit. As these parts are very flaccid in infancy, they become sucked together during inspiration and, by their vibration, produce the characteristic stridor. This stridor is noticed very soon after birth, it is inspiratory, of a peculiar purring or even musical character, and is most marked during active breathing and crying. The voice is unaffected, and there is remarkably little sign of dyspnœa or distress. These characteristics distinguish the condition from other forms of obstruction found in infants, such as laryngeal webs or papillomata, or "thymic asthma." It tends to disappear during the second year of life, but the prognosis must be guarded in early infancy, for an attack of bronchitis is more than ordinarily dangerous and kills a proportion of these patients.

SYPHILIS

Congenital Syphilis

The early, or secondary, form appears in the first few months of life and is rarely recognised, but it may be suspected when the cry is hoarse in an infant with active syphilitic lesions.

Tertiary lesions are rare, and usually make their appearance about puberty, less often during the second dentition. The disease takes the form of diffuse infiltration with or without ulceration; the swelling may produce obstruction, and rarely cicatricial stenosis may ensue. The symptoms are stridor with hoarseness, and tracheotomy may be required.

Acquired Syphilis

Symptoms.—Secondary lesions are superficial, cause no symptoms but hoarseness, and seldom come under observation. The commonest manifestation is an erythema which differs from that of catarrhal laryngitis by being more uneven and patchy in its distribution, and may affect one cord, leaving the other normal. Mucous patches are occasionally found on the cords or on any part of the larynx, appearing as superficial erosions with a smooth greyish base and a sharply defined hyperæmic margin. The fauces are nearly always affected at the same time.

Of tertiary lesions, the superficial serpiginous ulcer is occasionally seen with the same characters with which it more commonly appears on the fauces. Diffuse infiltration may attack any part of the larynx, but chiefly, in contra-distinction to tuberculosis, the anterior regions, such as the epiglottis and the front parts of the vocal cords. Subglottic infiltration is fairly frequent and abduction of the cords often limited, so that stenosis is much commoner than in tuberculous disease. The typical circumscribed gumma is distinctly rare; it is single, unilateral, and attacks especially the epiglottis and arytenoids, and usually breaks down rapidly to form a deep excavated ulcer, which may result in perichondritis, exfoliation of cartilage, and, ultimately, in severe cicatricial stenosis. The subjective symptoms are hoarseness, of a peculiar rough "raucous" character, and sometimes dyspnœa with stridor; pain is in general not a prominent symptom, but a gumma on the upper aperture may cause severe dysphagia.

Diagnosis.—From tuberculous disease the diagnosis is discussed under that heading (see p. 1107). From epithelioma a gumma is distinguished by its more rapid evolution; the edge of an epithelioma is thick and everted and its base nodular, whereas these characters are less marked in syphilitic ulceration, the margin of which is hyperæmic and frequently sharply cut; while other parts of the larynx or fauces often show syphilitic lesions. The hard infiltration of secondarily involved glands is characteristic of malignant disease.

Treatment.—General treatment is urgently called for to prevent perichondritis and stenosis. Local treatment is not often required. Tracheotomy should be performed when decided dyspnœa is present; it seems to aid the recovery of the larynx, and the tube can often be omitted in a short

time, when anti-syphilitic medication has removed the obstructing lesion. Necrosed pieces of cartilage must be removed by internal or external operation, and insufflations of orthoform are indicated when dysphagia is present.

LUPUS

Lupus in the larynx is comparatively rare, and is probably always secondary to the disease in the nasal passages.

Symptoms.—The lesions begin on the epiglottis and slowly spread along the aryteno-epiglottic folds; the interior of the larynx is less often attacked and the cords usually escape. The infiltration is composed of tiny red nodules, which develop the typical "apple-jelly" centre and break down to form multiple coalescent shallow ulcers, the smooth base covered by a scanty secretion and with indefinite uninflamed margins. Cicatricial contraction goes on during the progress of the affection, and the epiglottis, if not destroyed, is usually much deformed; but the scars are less thick, and the contraction less severe than in syphilis, and marked stenosis is less common.

Treatment.—The disease shows a decided tendency to spontaneous cure, and in many cases of cutaneous lupus the scars of healed disease can be seen in the larynx. Open-air treatment, as carried out in a sanatorium, with good food, moderate exercise, and cod-liver oil suffices to cure most cases. Arsenic, in large doses, appears to have a specific effect, starting with 5 minims of liquor arsenicalis 3 times a day and increasing the dose gradually to 15 or more minims. Local treatment should be reserved for those cases which general measures fail to cure. If the lesions are confined to the epiglottis, this may be removed; for more diffuse infiltration repeated galvanocautery puncture gives the best results, but over-zealous application will promote stenosis. Good results have been reported from the use of radium, applied externally to the neck in the form of plates.

TUBERCULOSIS

Ætiology.—Primary tuberculosis of the larynx is so rare as to be of no practical importance; in the overwhelming majority of cases the disease is secondary to pulmonary tuberculosis, of which it is a common and important complication. It is probably caused by infection from the sputum, is two or three times commoner in men than in women, and is most frequent between the ages of 20 and 40. St Clair Thomson finds that the difference in sex-incidence is occupational, and that women working in office and factory are as susceptible as men.

Symptoms.—The disease attacks, in order of frequency, the vocal cords, arytenoid region, inter-arytenoid space, ventricular bands and epiglottis; in general the lumen is invaded before the upper aperture, and the posterior rather than the anterior parts of the larynx. The typical infiltration is finely nodular, pallid and soft in appearance; ulcers are shallow, with a smooth speckly base and pale ill-defined margin. On the vocal cord the disease chiefly attacks the posterior half and especially the vocal process, where ulceration readily reaches the underlying cartilage and may produce a deep

triangular excavation. Thickening in the inter-arytenoid region is common; infiltration of the arytenoids results in typical pale semi-translucent flask-shaped swellings, while the epiglottis appears as a firmer red sausage-shaped mass.

Of subjective symptoms, the hoarseness is very characteristic, the voice being weak and effortless and very different from the raucous voice of syphilis. Cough and expectoration are mostly due to the pulmonary disease and not in any considerable degree to the larynx. Pain on swallowing is common and often very intense; there may also be actual obstruction to deglutition and, in a late stage, entry of food into the larynx. Dyspnœa is rare.

Diagnosis.—Although signs of pulmonary tuberculosis are helpful in diagnosis, it is obvious that any kind of laryngeal disease may occur in a consumptive patient.

From simple laryngitis.—In the earliest stage of invasion tuberculous laryngitis may exactly resemble catarrh, but redness of one cord only is certainly not due to catarrh, and the latter quickly improves under treatment. The swollen arytenoids of œdematous laryngitis are less pale and more transparent, while the affection is acute and the entire larynx inflamed. Inter-arytenoid infiltration resembles pachydermia, but the latter is opaquely white, firm and symmetrical.

From lupus, typical tuberculosis differs completely. The former is painless, affects first the epiglottis and upper aperture, is never accompanied by œdema, and tends to cicatrisation. But there is a chronic "lupoid" form of tuberculous laryngitis which attacks the epiglottis and is very similar to lupus.

From syphilis.—The tuberculous ulcer has an ill-defined margin without surrounding hyperæmia; the base has a yellow speckled appearance, and on healing there is little scarring or contraction. The superficial syphilitic ulcer has a well-defined hyperæmic margin, with a smooth, flat base; the deep ulcer is "crateriform," with thickened punched-out edge, and, on healing, leaves a dense scar and marked deformity. In general, syphilitic lesions attack the anterior half of the larynx, tuberculous the posterior; the former look firm and dense, the latter soft, translucent and ill-defined.

From neoplasms.—Only the rare tuberculomata resemble innocent tumours. Occasionally tuberculosis attacks one vocal cord in an elderly patient, and may then easily be mistaken for epithelioma (see p. 1111).

Prognosis.—Any tuberculous lesion of the larynx renders the prognosis of a case of pulmonary tuberculosis much more serious. A considerable number of the superficial lesions become healed; but it is doubtful if any cases of extensive infiltration recover, with the exception of a few rare instances where it is confined to the epiglottis and can be entirely removed.

Treatment.—Tuberculous laryngitis is but a complication of pulmonary tuberculosis, and by far the most important part of the treatment is that of the general infection. For the laryngeal lesions the most valuable remedy is complete silence, but it is a severe and depressing measure and should not be insisted on unless there is a prospect of cure; the pain and irritation

in advanced cases are, however, often relieved by vocal rest. Any concomitant catarrh should receive attention; an oily spray containing menthol and chlorbutol (7 grains of each in an ounce of liquid paraffin) is valuable, and irritable cough should be relieved by a simple lozenge, or, if severe, by heroin, $\frac{1}{12}$ gr. or less in a lozenge or linctus. Attempts to cure by active local treatment must only be made when the pulmonary lesions are quiescent or progressing towards arrest, the general health good, and the local lesions not very extensive. Of these methods the galvano-cautery is the most generally useful, and may be employed to the surface of superficial ulcers, or as multiple puncture of infiltrated areas. Chemical caustics may be applied to ulcerated surfaces, especially on the cords and posterior commissure; lactic acid, 50 to 80 per cent., may be used, or Lake's mixture of lactic acid 50 per cent., formalin 7 per cent., and phenol 10 per cent. Ulcers covered with sprouting granulations may be curetted, and occasionally infiltration of the epiglottis or arytenoid may be removed with punch-forceps.

In advanced cases the dysphagia is so distressing that its relief is of great importance. For this purpose the most valuable drug is orthocaine (orthoform), which may be combined in equal proportions with benzocaine (anæsthesine); it is an insoluble non-toxic powder and is used as an insufflation in doses of 3 to 5 grains half an hour before meals; patients readily learn to inhale it into the throat through a glass tube. Cocaine and morphine should be reserved to the last stages. When the dysphagia is due to infiltration of the epiglottis, the greatest relief is afforded by its removal under cocaine with special punch-forceps; and when the pain is caused by a tense swollen arytenoid, the removal of a piece with punch-forceps relieves tension and gives similar relief. Injection of alcohol into the superior laryngeal nerve is a useful method of alleviating pain in cases of extensive disease. Tracheotomy is seldom required, and tuberculous infection of the wound is common after this operation.

TUMOURS

Innocent Tumours

Singer's nodules are inflammatory epithelial thickenings, and may be considered as a form of pachydermia. They are found in teachers and speakers, rather than in singers, and are caused by faulty voice-production and, especially, by forcing the voice when the cords are inflamed. The appearance is that of a minute pink or whitish nodule on the edge or upper surface of the vocal cord, surrounded by a varying amount of injection; there is usually a nodule symmetrically placed on each cord, but it is frequently larger on one side than on the other. The place where the growth occurs, and which is also the "seat of election" for other innocent tumours, is at the junction of the anterior and middle thirds of the glottis, that is, in the centre of the true vocal cord, for the posterior third of the glottis is cartilaginous. It is here that the cord, if swollen, comes into contact with its fellow on phonation.

Fibromata occur usually on the vocal cord on the same site as the singer's nodule, of which they are in some cases probably a development; or at the

anterior commissure. They are pedunculated, smooth and round, white, pink, or brown from extravasation of blood, and vary from the size of a pin's head to that of a bean. These growths not infrequently become œdematous, when they appear translucent like a nasal polypus, and have been incorrectly described as *myxomata*.

Papillomata are reddish, papillary, pedunculated growths, and occur anywhere on the larynx, but, when single, generally occupy the "seat of election" on the vocal cord, and are seldom found on the posterior half of the glottis. Multiple papillomata occur especially in childhood and, as they present special characteristics, will be considered separately later.

Cysts.—A fibroma may degenerate with the formation of a cystic space in its interior. Apart from this, cysts, which may reach a large size, are found as a rarity on the upper aperture of the larynx, especially on the anterior surface of the epiglottis. They are thin-walled and translucent, with ramifying vessels running over the surface.

Angiomata occur, though rarely, on any part of the larynx either as a flat patch or a raised purple mass resembling a blackberry.

All innocent neoplasms are rather uncommon; in addition to those already mentioned, *lipomata, chondromata* and *thyroid-gland tumours* have been observed.

Symptoms.—A tiny growth situated on the vocal cords, or in such a situation as to prevent their approximation, causes hoarseness and a variable amount of aching and discomfort, but even a large tumour elsewhere may cause no symptoms to attract attention. Dyspnœa results in rare cases when a neoplasm is large enough to block the air-way, but it is astonishing how slight a disturbance may be produced by a large tumour if it has grown slowly; inspiration is more difficult than expiration, except when the tumour lies below the glottis. Angiomata cause hæmorrhage, which may be very severe.

Diagnosis.—This is usually easy on inspection, but a growth on the anterior commissure, or one that drops down below the cords, may be readily overlooked. The rare tuberculoma may so exactly imitate an innocent neoplasm as to be only recognisable under the microscope. The important matter of diagnosis from a malignant neoplasm will be referred to under the latter disease.

Treatment.—Tumours situated away from the glottis and causing no symptoms should be left alone. Cysts are treated by making a large hole with punch-forceps or the cautery, for they refill after simple incision. Angiomata, especially if diffuse, are best left untouched, unless bleeding calls for interference, in which case it can usually be checked by the cautery at dull-red heat; diathermy puncture with a fine terminal through a direct laryngeal spatula, or by suspension-laryngoscopy, is a preferable method; if repeated hæmorrhage becomes a danger, the angioma can be excised by an external operation, but is usually more widely spread than appears on laryngoscopic examination. Singer's nodules, if quite small and sessile, frequently disappear under prolonged rest of the voice; the smaller nodules may be lightly touched with the galvano-cautery; larger ones should be removed with forceps. Fibromata and papillomata are removed with forceps; it causes less disturbance to the patient if this be done under cocaine anæsthesia by the "indirect method," *i.e.* under guidance with the laryngeal mirror

provided that the operator has acquired the necessary skill, but since the introduction of the "direct method" they are usually removed through the tube-spatula. After the little operation, absolute rest of the voice should be enjoined for a few days; in cases of singer's nodule a longer rest is necessary, with training in voice-production and avoidance of dust and conditions of vocal strain.

Multiple papillomata.—This rare but serious condition occurs almost exclusively in children and generally attracts attention between the ages of 2 and 4. The warts may be very numerous, fill the lumen with a cauliflower-like mass, and extend to the subglottic region, down the trachea and sometimes on to the pharynx. The first symptom is hoarseness, and long-continued hoarseness in a child should suggest the possibility of papilloma; dyspnœa ensues later and becomes gradually more severe until tracheotomy is necessary. The growths may disappear after tracheotomy, or spontaneously, or after an acute illness, and tend to vanish or cease to recur about puberty. The growths should be removed through the tube-spatula, or by suspension-laryngoscopy, under general anæsthesia; a preliminary tracheotomy is advisable if there is much dyspnœa; several sittings may be required, and the operation must be repeated as often as the growths recur.

Malignant Tumours

Ætiology and Pathology.—Epithelioma is by far the commonest malignant growth in the larynx, but spheroidal-cell carcinoma and sarcoma also occur. Malignant disease of the larynx proper is rare below the age of 40, and is seldom seen in women; but there is a post-cricoid epithelioma, originating on the mucous membrane of the pharynx, which is relatively common in women, and has been known to occur at such an early age as 23. Secondary or metastatic growths are practically unknown in the larynx; on the other hand, owing to the fact that the laryngeal lymphatics do not anastomose freely with other systems, cancers confined to the lumen of the larynx rarely become disseminated and do not readily infect the glands. Therefore, Krishaber's classification into *intrinsic* and *extrinsic* is valuable for treatment and prognosis; the former are those situated within the cavity of the larynx, while the latter affect the upper aperture, epiglottis, arytenoids, and the outer walls.

Symptoms.—Unfortunately, intrinsic malignant tumours do not cause severe symptoms at an early stage and, particularly in hospital practice, frequently do not present themselves for treatment until they have become extrinsic by extension; hence the importance of a laryngeal examination in all patients over 40 with hoarseness which does not rapidly yield to treatment. Hoarseness is the most general, and usually the only, early symptom; owing to the deep infiltration characteristic of malignant disease, it is often more marked than the size of the tumour would appear to warrant. Cough is not a common symptom. Pain is absent in the early stages of intrinsic cancer, but is severe in the later stages and in the extrinsic forms; it radiates to the ear and side of the head, and is made worse by swallowing, speaking and coughing. The later symptoms include involvement of the glands, fetor of the breath, salivation, hæmorrhage, dyspnœa, dysphagia and general cachexia; often the patient dies of septic pneumonia.

On a vocal cord, epithelioma may appear as a definite tumour resembling a papilloma or angioma, or it may begin as a diffuse infiltration, or merely as a localised area of thickening and congestion. On the ventricular band or posterior commissure it usually shows itself as an irregular papillary dusky-red swelling; cancer of the epiglottis ulcerates early and appears as a dirty white or reddish tumefaction. Often the only sign of a post-cricoid growth is a swollen and fixed arytenoid, or merely a pool of saliva in the pyriform fossa; sometimes the upper edge of the growth is visible, but it may be necessary to pass a tube-spatula, or to pull the larynx forward with a probe passed down to the glottis, before it can be seen.

Diagnosis.—In the earliest stage the diagnosis obviously is a matter of extreme importance and sometimes one of great difficulty. The unilateral character of the infiltration is ordinarily sufficient to exclude a simple inflammatory lesion; though pachydermia may be more marked on one side, the lesions are bilateral and the smooth cup-shaped swelling on the vocal process is characteristic. The difficulties of diagnosis are generally between an innocent neoplasm on the one hand, and a tuberculous or syphilitic infiltration on the other. A papilloma or a fibroma on a vocal cord should be regarded with suspicion in a man over 40, and especially if, after removal, the site fails to heal promptly. An innocent neoplasm has a fine pedicle, moves freely in the air-current on phonation, there is no tumefaction at its site of origin, and it is found at or in front of the middle of the vocal cord. A malignant growth may occur in any situation; it is less movable and pedunculated, the cord in the neighbourhood is frequently swollen and may show a leash of tiny vessels running to the tumour; a white spiky appearance of the papillæ is suggestive of malignancy; a sluggish delayed movement of the cord is an important sign, insisted on by Semon, but its absence by no means excludes malignancy, for it only occurs when the growth has infiltrated the muscles, and its presence increases the gravity of the prognosis. Epithelioma beginning as a flat infiltration may resemble a tuberculous or syphilitic lesion, but usually other signs of these diseases are present to aid the diagnosis; in the latter the Wassermann reaction and, still more, the effect of vigorous anti-syphilitic treatment will clear up the doubt. There is a form of senile tuberculosis in which infiltration of one vocal cord may closely imitate epithelioma, more especially as the pulmonary signs are merely those of bronchitis and tubercle bacilli are very scanty in the sputum. Sometimes a piece may be removed for examination, but frequently the growth is too sessile to permit it; the piece removed must not be very small, and a negative finding is of little value, for the tip of a malignant growth cannot always be distinguished microscopically from a papilloma. Biopsy is more important since the adoption of Broders' histological method of estimating the malignancy and radio-sensitivity of tumours, but it should not be performed in cases too advanced for treatment, for it stimulates the growth and does harm.

Extrinsic epithelioma is most likely to be mistaken for tertiary syphilitic ulceration. A gumma grows and ulcerates more quickly, its edge is smoother and sharper, and its base often covered by a yellow slough. Pain has little diagnostic value, for a gumma of the upper aperture may cause severe dysphagia. Palpation with the finger is of great service, for the firm hard feel of an epithelioma is very characteristic.

Treatment.—Malignant disease cannot be removed with certainty by

the natural passages. Thyrotomy, or laryngo-fissure, is the operation of choice for removal of intrinsic cancer; it consists essentially in wide excision of the disease from the interior of the larynx after splitting the thyroid cartilage in the middle line. The results in suitable cases are probably better than those of removal of malignant disease in any other part of the body; there is now practically no immediate mortality in skilled hands, statistics show from 70 to 80 per cent. of permanent cures, and a useful husky voice remains. When, however, the growth has spread at all extensively to the arytenoid or to the subglottic region, laryngo-fissure is no longer possible and a very different picture is presented. By modern methods of laryngectomy the trachea is fixed in the lower part of the neck, aspiration of septic matter is avoided, and the mortality has been much reduced, while the results as regards freedom from recurrence have been greatly improved. The operation leaves the patient in a condition very different from that after thyrotomy; as he breathes through the tracheal opening in the neck he cannot cough or strain and has no natural voice. Nevertheless he can often produce a fairly audible whisper by means of the air in the pharynx, or with the aid of a tube leading from the tracheotomy wound into the mouth or nose, and a number of patients succeed in passing a surprisingly happy and useful existence. Subhyoid pharyngotomy and lateral pharyngotomy are operations designed to obtain access to cancers at the upper aperture of the larynx; the latter operation gives very good results in strictly limited tumours of this region. The technique of therapy by means of X-rays and radium has now been put on a reliable basis by determination of the appropriate dosage and by adequate screening; in many cases of malignant tumours of the larynx, great improvement can be obtained by both these agencies, and a considerable proportion of cures has been effected. A valuable method, in intrinsic cancer, is the insertion of radium tubes through a window cut in the thyroid ala. Great care and judgment are required in the selection of cases for these various operations, and very many come under observation too late. In these much can be done by palliative treatment; careful attention to the hygiene of the mouth and teeth is of great importance, together with mild antiseptic laryngeal sprays containing hydrogen peroxide, listerine, sanitas or phenol. For dysphagia, insufflations of powdered orthocaine, with or without benzocaine, is the most reliable remedy; cocaine is disappointing, for its effect is very transient and the resulting numbness interferes with swallowing; the judicious administration of morphine or heroin is eventually necessary, but the local application of these drugs is useless. Palliative tracheotomy or gastrotomy may be called for, and curettage or partial removal by knife or diathermy gives relief in some cases of cancer at the upper aperture.

PARALYSIS

Paralysis of a vocal cord is a frequent symptom of various diseases of the thorax and of the nervous system, and the laryngoscope is therefore of great value to the physician as an aid to diagnosis; this is more especially the case in that the common early form, abductor paralysis, causes no symptoms, and can only be recognised by laryngoscopic examination.

The original function of the laryngeal muscles is that of a sphincter to

prevent the entrance of fluid into the lungs, and this sphincter, or adductor, is the only muscle present in the larynx of the most primitive air-breathing animals; the abductors are a later addition, to assist the entry of air. Accordingly, in lesions of the nerve path, the abductor muscles are affected first and the primitive adductors are more resistant. But the function of phonation, much more recently acquired, is associated with adduction, and is under direct control of the will. Functional disturbances, therefore, always cause adductor paralysis, while organic lesions first affect the movement of abduction.

Organic Paralysis

The crico-thyroid muscle is supplied by the superior laryngeal nerve, and, when this is injured, the affected cord remains slack on phonation, but, owing to the short course of the nerve, isolated paralysis of this muscle is extremely rare; it results from surgical or suicidal wounds, or by pressure from glands, but most often occurs after diphtheria. In lesions of the vagus above the origin of this branch the signs of this paralysis are obscured by that of the other muscles of the cord. The recurrent laryngeal nerves supply all the other muscles. In any progressive lesion of the nerve-path the muscles become paralysed in a definite order, the enunciation of which is known as Semon's law; the abductors are first affected, then the tensors or thyro-arytenoidei, and finally the adductors.

In *abductor paralysis* the affected cord lies in the middle line; during phonation the sound cord adducts to meet it and the larynx appears normal, but on inspiration it is drawn outwards and backwards and appears longer than its paralysed fellow, which remains unmoved. As would be expected from the course of the recurrent nerves, the left cord is far more often affected than the right. The voice is unaltered, but, although the glottic aperture is reduced by half, there is usually dyspnœa only on exertion, except in children, in whom the narrowing of the naturally small glottis may produce sufficient obstruction to necessitate a tracheotomy.

When the thyro-arytenoid fails, the edge of the cord is concave on phonation, the cord appears narrower than its fellow, and the voice gradually becomes husky. Finally, when *total recurrent paralysis* has occurred, the cord assumes the "cadaveric position" between the middle line and the normal position of rest. On phonation, the healthy arytenoid crosses the middle line and pushes the paralysed cartilage aside; sometimes the latter drops forward and exposes its broad posterior surface, which may be mistaken for a swelling. As the cords are still able to approximate, the voice is not necessarily lost, but is hoarse and easily tired, with a characteristic breathy quality from waste of air, or a diphonic character, due to unequal vibration of the two cords.

In cases of *bilateral abductor paralysis* the cords lie together near the middle line. The voice is good, but the inability to take a full breath gives the speech a peculiar character; dyspnœa is a marked symptom accompanied by inspiratory stridor and severe paroxysmal exacerbations. When the disease progresses to complete *bilateral recurrent paralysis*, both cords remain in the cadaveric position, the dyspnœa becomes less severe but the voice is reduced to a whisper.

Diagnosis. — The diagnosis is almost entirely a matter of accurate

inspection. Obliquity of the laryngoscopic image, due to faulty position of the mirror, may cause confusion. In nervous subjects the cords are sometimes adducted on inspiration, but they will abduct naturally during the involuntary inspiration which follows a prolonged phonation. The only condition which really imitates paralysis is the fixation of the arytenoid cartilage which results from disease in or around the joint; its complete immobility with the presence of swelling or scarring often aids the diagnosis, but in old-standing cases of paralysis secondary fixation frequently occurs.

Ætiology.—The ætiology is of importance, for it is on our knowledge of their causation that the diagnostic value of these lesions depends. The movements of the cords are represented bilaterally in the cortex cerebri, and stimulation of either centre produces movement (adduction) of both cords, from which it follows that no unilateral lesion above the bulbar nuclei can paralyse the larynx, and clinically we find that it is never affected in cases of hemiplegia. The bulbar centres lie in the floor of the fourth ventricle, and here a lesion of one centre causes paralysis of the cord on the same side which, in a gradually progressive lesion, affects first the abductor muscle. Thence the nerve fibres pass in the roots of the bulbar-accessory to the vagus and recurrent laryngeal nerve; the cause of the paralysis may, therefore, be situated (1) in the medulla, (2) at the base of the skull, (3) in the vagus, or (4) in the recurrent laryngeal nerve.

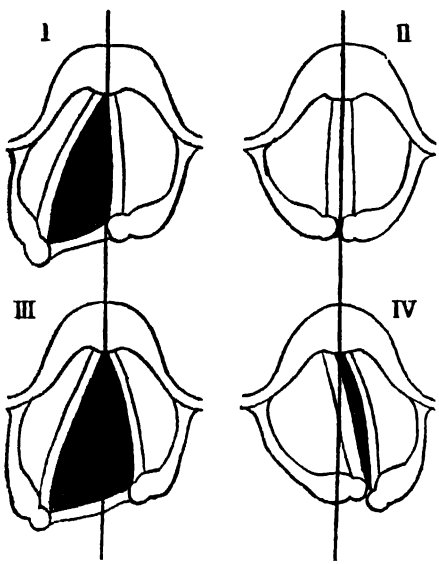


FIG. 97.—Organic Paralysis: I. Abductor paralysis of left cord on inspiration; II. Abductor paralysis of left cord on phonation; III. Total paralysis of left cord on inspiration; IV. Total paralysis of left cord on phonation. (*Lancet.*)

Paralyses of bulbar origin are often, but by no means always, bilateral. In lesions here and at the base of the skull neighbouring nerves are liable to be involved; thus, paralysis of a cord and of the same side of the palate may coexist (syndrome of Avellis), or paralysis of cord, palate, trapezius and sternomastoid from involvement of the spinal accessory roots, or persistent frequency of the pulse due to damage of the cardio-inhibitory centre or nerves. Tabes dorsalis is the most frequent cause of paralysis of central origin; it may affect one or both cords and may be associated with anæsthesia, paræsthesia or the spasmodic attacks called "laryngeal crises." In general paralysis of the insane laryngeal palsy is not uncommon. It is the rule in bulbar paralysis, and is usually bilateral, but appears late in the disease.

Syphilitic nuclear disease, pachymeningitis and gummata at the base of the brain are frequent causes, and here the ocular muscles, especially the external rectus, are often attacked.

Peripheral causes usually act by compression of the recurrent nerve, the most frequent being aneurysm, enlarged glands, tuberculous or malignant, and cancer of the œsophagus. Other causes are thyroid tumours, usually but not necessarily malignant, mediastinal tumours, cancer of the lung, pleurisy, and pulmonary tuberculosis in which the nerve, usually the right, may be involved in a lesion at the apex of the lung or by tuberculous bronchial or tracheal glands. Neuritis is a cause of laryngeal paralysis; it may be produced by the toxins of the infectious fevers, usually diphtheria, or by organic poisons, especially lead, and more rarely arsenic and alcohol. Finally, the condition is sometimes the result of traumatism, more especially surgical operations on the thyroid gland and œsophagus.

Prognosis.—Paralysis of one cord is not in itself dangerous to life; but when the cause is undiscovered the prognosis must be guarded, for this paralysis may be for a long time the only sign of serious disease; on the other hand, the recurrent nerve may be involved in some non-progressive lesion, such as a fibrotic bronchial gland, and such cases have been under observation for 20 or 30 years without change.

Treatment.—This depends on the cause. In most cases it is but a symptom of disease elsewhere and does not call for special treatment. In traumatic cases, however, the nerve may sometimes be found and sutured; afterwards, and in cases due to neuritis, strychnine and the local application of the faradic current by means of an intra-laryngeal electrode are indicated. Tracheotomy is advisable in bilateral abductor paralysis, but a plug may usually be worn in the tube, to be removed at night and whenever dyspnœa threatens.

Functional Paralysis (Functional Aphonia)

Ætiology.—Functional aphonia is a common manifestation of hysteria, and has been a very frequent symptom of war-neurosis or "shell-shock," but it should be clearly stated that the majority of cases are not purely hysterical. Anything which increases the effort of phonation, such as debility or laryngeal catarrh, predisposes to this affection, which is characteristic rather of feeble neuro-muscular tone than of hysteria; this explains how some women lose the voice completely with every slight cold, while other patients can produce a loud if hoarse voice with severe laryngeal disease.

Symptoms.—Paralysis of the adductors presents a totally different clinical picture from the organic paralysis. It is always bilateral; the larynx appears normal while at rest, but, on attempts at phonation, it is seen that the cords do not adduct into the position necessary for the production of the voice. Very commonly the thyro-arytenoidei are the only muscles which fail to act; the cartilaginous glottis is then properly closed, but an elliptical chink is left between the cords. If the crico-arytenoidei laterales are paretic, the entire glottis remains open to a variable extent, and, very rarely, the arytenoideus is affected alone, when a triangular aperture is left behind the vocal processes. The paralysis is

hardly ever complete; indeed a considerable amount of movement is usually seen, though insufficient to produce phonation. In purely hysterical cases the onset and recovery are sudden, the cough is usually not aphonic and the voice when regained is not hoarse. In some hysterical patients there is also inability to whisper.

Treatment.—In patients suffering from debility the cause should be found and treated; chronic phthisis is such a common cause of functional aphonia that it should always be thought of in this connection. There is frequently a slight degree of laryngitis and in some of these cases the failure of adduction is "myopathic," or due to inflammation of the muscles; in these the local condition must receive appropriate treatment. When the larynx is normal the voice can nearly always be temporarily restored by any powerful local stimulation, such as the intralaryngeal application of chloride of zinc, or any similar drug, or of the faradic current; but the aphonia usually recurs again, and succeeding applications are less effective, so that the most difficult cases to cure are those who have had much local treatment. Far better results are obtained by moral suasion, explaining to the patient that there is no serious disease, but that he is not using his muscles correctly, and that he can produce a good voice quite easily when the laryngeal mirror or tongue-depressor is in position. With a little elementary instruction in voice-production this is usually successful, the patient's confidence is restored and the voice does not again fail; in obstinate cases some perseverance in lessons on production is required. These methods have been extraordinarily successful with shell-shocked soldiers, but it must be confessed that such certain and rapid results are not always obtainable in nervous women.

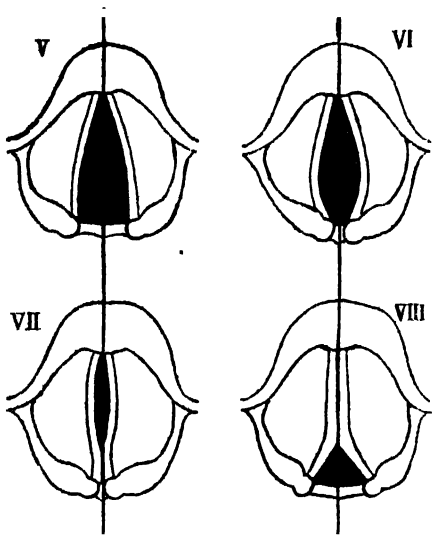


FIG. 98.—Functional Paralysis; all during attempted phonation; V. Paresis of all the adductors; VI. Arytenoideus still active; VII. Paresis of internal tensors; VIII. Paresis of arytenoideus. (*Lancet.*)

SPASMODIC AFFECTIONS

SPASM OF THE GLOTTIS

Spasm of the laryngeal muscles produces adduction of the cords, for, though the abductors are probably affected, they are overpowered by the stronger adductor muscles.

Ætiology.—(1) In the majority of cases the spasm is a reflex set up by local irritation: foreign bodies, including the laryngoscopic mirror, irritating gases; inflammation, ulceration or tumours in or near the larynx, children being much more liable than adults to spasm from local irritation. (2) Spasm is also caused by irritation of the recurrent laryngeal nerves by enlarged glands, mediastinal tumours and, especially, by aneurysm. (3) Central nervous lesions, especially tabes. (4) Functional disturbances, frequently hysterical, often associated with globus hystericus, and sometimes excited by sexual disturbances.

Symptoms.—The attacks vary much in different subjects in severity and duration. The patient is usually aware of its onset, and clutches some support or rushes to the window. The respirations are rapid and shallow, with loud inspiratory stridor, and, in the height of a severe attack, are completely arrested with all the signs of asphyxia. The subjective sensations include a horrible feeling of anxiety, but consciousness is not lost. Many cases are less acute but persist longer, even for several hours.

Prognosis.—The attacks are practically never fatal, unless a foreign body or tumour be present.

Treatment.—During the attack amyl nitrite or chloroform may be inhaled, and ampoules of these drugs should be kept on hand. Between the attacks sources of irritation should be sought for and removed, the upper air-passages brought to a healthy condition, and the general health and mode of life should receive attention. Administration of bromides may be required when the attacks recur frequently.

Laryngismus Stridulus

Ætiology.—This is a condition, clinically similar to glottic spasm, occurring in children. It is far commoner than the spasm of adults, and it has been suggested that the asphyxial attacks of laryngismus are caused by collapse of the soft and yielding cartilaginous framework of the larynx, and not solely by spasm of the muscles. It is commonest between the ages of 6 months and 2 years, but may persist later; it occurs in ill-nourished, unhealthy children, usually in association with rickets, and practically always in association with adenoids.

Symptoms.—The onset is sudden and usually at night. The child wakes gasping for breath, and a series of short noisy inspirations is followed by complete cessation of breathing and terminated by a long, crowing inspiration. There are retraction of the lower ribs and epigastrium, cyanosis and great terror and distress and, in severe cases, carpo-pedal contractions, convulsions and evacuation of urine and fæces. When the attack is over the child is perfectly normal and there is no hoarseness. Slighter and less typical attacks often occur.

Diagnosis.—This is easy if the symptoms are carefully noted; the sudden attack of dyspnœa, with complete absence of symptoms in the intervals, is quite distinctive.

Prognosis.—The prognosis is somewhat grave in severe cases; an infant rarely dies in an attack, but is often worn out and succumbs to collapse of the lungs.

Treatment.—During the attacks the face and chest may be freely

sponged with cold water, and the inhalation of amyl nitrite from a capsule broken in a handkerchief may be tried. The quickest relief can usually be obtained by drawing the tongue forward with a finger passed into the mouth to its base, a manœuvre easily performed by the mother or nurse. The attacks are so short and sharp that there is no time for the hot bath or administration of bromides frequently recommended.

Prevention involves general tonic treatment, fresh air, wholesome food and correction of digestive disturbances. The removal of adenoids is of great importance, even if not large enough to be definitely obstructive, as is the treatment of naso-pharyngeal catarrh with the usual saline lotion which, in small children, may be dropped into the nostrils from a pipette. Bromides are to be avoided if possible as depressing, but 10 to 30 drops of liquid extract of grindelia may be given 3 or 4 times a day in milk or sweetened water as recommended by Eustace Smith.

CICATRICIAL STENOSIS

Ætiology.—Suicidal and other wounds, gunshot injuries and scalds may produce cicatricial narrowing of the lumen of the glottis. After thyrotomy a web may form across the anterior commissure. In the haste of an emergency tracheotomy, the wound has often been made too high and the cricoid cartilage cut through; in these cases it generally happens that, after the subsidence of the acute condition, dyspnœa follows every attempt to remove the tube, and a stenosis is found to have resulted from swelling and narrowing in the subglottic region. Similarly, a proportion of cases intubated for diphtheria are unable to breathe without the tube, by reason of a subglottic stenosis. Lupus and tuberculosis of the larynx can produce cicatricial stenosis, and especially when the cautery has been extensively employed in treatment. Syphilis is the most fruitful cause of this condition, and the great difficulty of obtaining a cure at this stage is a powerful reason for early and thorough treatment of syphilis of the larynx. Leprosy and scleroma cause stenosis, but are rarely seen in this country. The perichondritis which is an occasional complication of enteric fever, small-pox and diphtheria commonly ends in severe stenosis.

Symptoms and Diagnosis.—The principal symptom is naturally dyspnœa, but in chronic cases it is remarkable how great may be the narrowing before dyspnœa becomes severe. The obstruction and the stridor are most marked on inspiration, in contra-distinction to tracheal stenosis where the stridor is both inspiratory and expiratory. The larynx moves downwards with each inspiration; this "respiratory excursion" of the larynx is a further diagnostic sign of laryngeal obstruction, but is not always present. The patient sits upright, with the head thrown back; whereas in tracheal obstruction he bends the neck forward to relax the trachea.

Treatment.—In all cases with decided dyspnœa tracheotomy should be first performed, and in syphilitic cases it is important that all active disease should be arrested by thorough treatment before any attempt at dilatation be begun, and the stenosis itself will often be greatly improved by such treatment. The administration of iodides is dangerous in these cases, for the increased secretion is pent up behind the stenosis and may overwhelm

the lungs. Difficulty in dispensing with the tube after tracheotomy is sometimes due to nervousness on the part of the child, and can then be surmounted by using a fenestrated tube which is plugged occasionally and by encouraging the patient to breathe through the mouth by blowing soap-bubbles or sounding a whistle. When the tracheotomy wound is too high, a low tracheotomy should be performed and the original wound allowed to close; this is often sufficient to overcome the difficulty.

The successful treatment of severe cicatricial stenosis demands the greatest skill and perseverance on the part of the surgeon as well as the patient co-operation of the sufferer. The whole circumstances of the case should be carefully considered before advising difficult and prolonged treatment. Adult patients can live active lives with a permanent tracheotomy opening, which is not so serious a disability as it is generally considered to be. If the stenosis be not too extreme, a fenestrated tube may be worn which can be kept plugged during the day, so that the patient may have the use of speech and respiration by the natural passages. In children and young people a permanent tracheotomy is more harmful, but the prospect of cure by dilatation is better; the best method of dilatation is by the use of intubation tubes.

HAROLD S. BARWELL.

DISEASES OF THE TRACHEA

INFLAMMATION OR TRACHEITIS

ACUTE TRACHEITIS

Acute tracheitis may occur from any condition leading to irritation of the mucous membrane of the trachea. When it occurs as a result of bacterial or chemical agency, the whole of the upper air-passages are usually involved in greater or less degree, and the clinical manifestations are not confined to the trachea. In some cases, however, the stress of the resultant reaction falls upon this tube, and the condition therefore requires separate consideration.

Ætiology.—1. *Microbic invasion.*—This is the commonest cause. The bacteria usually found associated with tracheitis are the so-called catarrhal organisms, such as the *Micrococcus catarrhalis*, the pneumococcus, the Freid länder pneumo-bacillus and Pfeiffer's *H. influenzæ*. It is probable that the primary organism in many cases is of filter-passing type. Frequently a member of the streptococcus group may be found, either alone or in association with one or more of those just mentioned. As with catarrhal inflammation of other parts of the upper air-passages, damp, cold or foggy climatic conditions predispose to tracheitis. It is more common in young and middle-aged adults than in infancy or in old age. Mouth-breathers are more liable to this condition. Exposure to sudden changes of temperature may be a factor in its onset.

Tracheitis may also occur as part of the clinical picture in some of the acute specific diseases, such as enteric fever, diphtheria, whooping-cough

and measles. It is often a troublesome and distressing association or sequel of true influenza.

2. *Chemical agencies.*—Irritating or poisonous fumes and vapours may lead to a very acute form of tracheitis. It may, therefore, occur in certain occupations, unless adequate precautions are taken. The use of "poison gases" in warfare has drawn widespread attention to this form of the condition, since tracheitis was an almost constant result of certain forms of "gassing." The chief chemical irritants used in the War of 1914–1918 were chlorine, phosgene and yperite, or dichlordiethyl sulphide, commonly known as yellow cross or mustard gas. Of these the last was perhaps the most irritant to the trachea, and fatal cases invariably showed tracheal lesions. Direct inhalation of steam may also induce an acute tracheitis.

3. *Mechanical causes.*—The presence of a foreign body, or the invasion of the trachea by extension from malignant growth in adjacent structures may lead to a local or even to a general tracheitis. It is noteworthy, however, that the trachea is frequently spared in occupations involving the respiration of dusty air, which leads to deposits in the lungs and bronchial glands with resulting pneumonokonioses. Although a coal miner's lungs are black, yet his trachea may be practically normal.

Pathology.—The changes found in the trachea vary from simple catarrhal inflammation to intense destructive changes with ulceration, and in some cases croupous or membranous exudate. In the catarrhal forms, the mucous membrane shows changes similar to those in bronchitis. It is at first swollen, red and dry, the vessels running across the trachea being engorged and clearly visible. Then, owing to increased activity of the mucous glands, excessive mucoid secretion occurs and the mucous membrane becomes moist, after which resolution may take place, or the process may proceed to a muco-purulent stage, when the fluid on the membrane coheres to form yellowish or green tenacious pellets. Occasionally numerous red blood cells are extruded and the tracheal exudate becomes streaked, tinged or uniformly pinkish.

In some inflammations, such as those induced by poison gases or inhaled steam, the mucous membrane may be intensely engorged and actual destruction may occur, involving even the deeper structures and the cartilages, so that greyish yellow sloughs result, which on separation leave ulcers. In diphtheria the characteristic false membrane composed of necrosing fibrin, leucocytes and bacilli may be found loosely attached to the mucous membrane, as in other localisations of this process. It may be primary or secondary to faucial or laryngeal diphtheria, either by direct extension or through diphtheritic infection of a tracheotomy wound.

In influenza the pink appearance of the trachea is of such constancy in fatal cases that it has come to be regarded as one of the most characteristic post-mortem changes found in this disease. The bright injection generally involves the lower half of the trachea, but it may occur along the whole length of this tube.

In whooping-cough the inflammatory reaction is usually less acute.

In typhoid fever small ulcers may occasionally be found in the trachea similar to those occurring more commonly in the larynx.

Symptoms.—Acute catarrhal tracheitis usually begins more or less acutely, like the common "cold," of which it is to be regarded as one form, with malaise, slight headache, and a mild degree of fever, the temperature

being usually between 99° and 100° F., rarely 101° F. The patient soon experiences a sensation of irritation behind the sternum, rapidly leading to a harsh, dry cough of noisy character. The cough aggravates the retrosternal discomfort, which develops into a sensation of rawness or soreness, making the cough very painful and distressing. If the larynx is involved at the same time, the voice becomes hoarse and sometimes lost, or reduced to a raucous whisper. In tracheitis alone the voice is usually unaffected. After from 12 to 24 hours the condition passes into the mucoid stage. The cough becomes looser and less painful, and small pellets of tenacious mucus are coughed up, usually greyish or black in town-dwellers, whitish in those in rural conditions; in either case, the mucus may be streaked with blood or even tinged a uniform pink colour; in the more acute forms it sometimes becomes yellow and more purulent. In the mucoid stage, the retrosternal soreness becomes less, the constitutional symptoms abate, while the temperature subsides and becomes subnormal. The patient often feels weak and out of health for some days, and is sometimes left with a noisy morning cough and tracheal irritation which may last for days or weeks. The aspect of the patient shows nothing characteristic. There is the general appearance of fever, malaise and discomfort. The rise of temperature and increase in pulse-rate are usually moderate. In the early stages physical examination of the chest shows no abnormality, but when exudation occurs a coarse wheeze may be audible over the trachea, particularly when the patient takes a deep breath or just before a cough occurs.

Diagnosis.—The association of catarrhal symptoms with a dry, harsh cough and retrosternal soreness, without signs of bronchitis, is almost pathognomonic. In some cases the diagnosis can be established with the laryngoscope or by endoscopy, but in most the discomfort which these examinations entail is unnecessary.

Prognosis.—This is almost invariably good, except in debilitated subjects or in those with cardiac or renal disease, in whom the process may spread to the larynx, bronchi or lungs. The usual course is from 2 days to a week, though cough and expectoration may persist for days or weeks. The condition may become chronic. To some extent the prognosis depends upon the care and treatment in the initial stage. Cases that are neglected are liable to become chronic.

Treatment.—The prophylactic and remedial treatment of acute tracheitis is practically identical with that of acute bronchitis of the larger tubes. Even in mild cases the patient should go to bed, though this may be necessary only for 1 or 2 days; but he should keep to his room till his temperature has become normal. There may be less need for expectorants than in bronchitis, and a simple saline diaphoretic mixture, with the addition later of tinct. ipecac. and tinct. opii camphorata, may be all that is necessary. Sedative inhalations, such as vapor benzoini, are useful, and counter-irritation to the sternal region is comforting and grateful to the patient. When a chronic noisy cough develops, a mixture containing small doses of apomorphine and tinct. chloroform. et morphin. co. often gives relief, or codeine linctus B.P.C.

When tracheitis occurs as part of some specific disease, such as diphtheria or influenza, the treatment should be that appropriate to the primary disease.

In "gassing," every effort should be made to relieve the distressing and

painful symptoms, and for this purpose morphine, either alone or in combination with atropine and strychnine, may be required. Various inhalations may be tried, and useless cough should be checked by sedative mixtures or by a linctus of heroin, morphine or codeine.

Chronic Tracheitis

Ætiology.—Chronic tracheitis may follow an acute attack, or it may develop insidiously in patients suffering from chronic laryngitis or bronchitis. Inhalation of cigarette smoke is a not infrequent cause. It is also sometimes a sequel of chronic rhinitis, especially of the atrophic form or ozæna. A certain degree of chronic tracheitis accompanies the specific lesions of syphilis and tuberculosis, which are described below.

Pathology.—Various degrees of chronic inflammatory lesions may be found. In chronic catarrhal tracheitis, the vessels are distended or engorged, and the mucous membrane of the trachea becomes thickened and more or less covered with mucoid or muco-purulent secretion, the histological changes being those of chronic catarrhal inflammation, namely, shedding of the ciliated epithelial cells, overactivity of the mucous glands, and sometimes thickening and induration of the submucous tissues from proliferative changes. A condition of perichondritis of the tracheal cartilages may, in this case, be observed, and this may result in a mammillated appearance in the internal aspect of the trachea. In ozæna, crusts similar to those in the nose and pharynx may form on the tracheal mucosa.

Symptoms.—The symptoms of chronic tracheitis are similar to those of the acute form. There is a sense of discomfort and irritation about the trachea and a chronic, almost dry cough, often worse in the morning. There is generally some scanty, sticky expectoration, mucoid or muco-purulent, darkened by carbon particles and occasionally blood-tinged.

There are practically no physical signs of this condition, except that the tracheal changes can be observed by the laryngoscope or by endoscopy of the trachea.

Diagnosis.—This is concerned chiefly with its differentiation from chronic changes in the trachea due to syphilis, tuberculosis or leprosy and to the effects of new growths. It must largely be made by endoscopic examination.

Prognosis.—The prognosis depends upon the cause. When this can be removed, as by treatment of predisposing conditions in the nose and throat, the outlook is good. When the tracheitis is due to other conditions, such as syphilis and tuberculosis, it depends upon the situation and extent of the other lesions and upon the treatment adopted.

Treatment.—This is, in its main features, similar to that of acute tracheitis, but climatic treatment may be of great importance. The patient may perhaps spend the winter months in a warm or equable and clear climate with great advantage. Vaccine treatment may also yield good results. When other conditions are concerned, such as ozæna, syphilis or tuberculosis, the treatment appropriate to them should be employed as well.

CYSTS AND TUMOURS

These are rare conditions, but require careful consideration.

Cysts

Owing to weakening of the wall of the trachea, local bulging may occur, giving rise to a cystic, air-containing swelling in the neck, in direct communication with the lumen of the trachea. Such cysts are known as "tracheoceles" or "aeroceles." They are resonant to percussion and can often be temporarily reduced by pressure.

Small retention cysts may occur in the posterior wall of the trachea, from obstruction of the ducts of the mucous glands as they pass through the trachealis muscle. They are of pathological interest only, and do not give rise to symptoms.

Simple Tumours

The most important is papilloma. It occurs chiefly in children and is usually pedunculated. When it grows in polypoid form it may lead to obstruction of the trachea low down, in which case tracheotomy may fail to give relief, and death results unless the tumour can be removed by endoscopic methods.

Other innocent tumours occur, but are rare. They include enchondrosis from localised overgrowth of cartilage, multiple enchondromata, and osteoma from ossification of a pre-existing enchondroma. Lipoma and aberrant thyroid tumours may occur, but are very rare.

Symptoms.—These tumours produce varying degrees of tracheal obstruction, and can usually only be recognised by endoscopy. Treatment is considered under that of tracheal obstruction.

Malignant Tumours

A few cases of primary carcinoma of the trachea have been recorded. Secondary growths are not common, but the trachea is often involved and infiltrated by primary carcinoma in adjacent structures, such as the œsophagus, the thyroid, the larynx, or by the extension of secondary deposits in the cervical or mediastinal glands.

Primary sarcoma of the trachea is also very rare. The growth is usually smooth and not pedunculated. Secondary deposits of sarcoma in the trachea may occur from sarcoma of distant organs, such as the kidney; or it may be invaded directly by sarcoma originating in the thymus or other mediastinal structures, and especially by lympho-sarcoma of the mediastinal glands.

Symptoms.—The tracheal symptoms and signs are usually those of obstruction, accompanied by pain. When the primary growth is in the œsophagus, antecedent dysphagia and sometimes laryngeal paralysis reveal the origin of the tracheal symptoms when they occur. In this case copious frothy mucoid expectoration is frequent, and when ulceration develops with perforation, food particles may enter the trachea, excite cough and soon lead to inhalation broncho-pneumonia or gangrene. When the growth is near the bifurcation, urgent dyspnœa is the rule, and spasmodic attacks may

occur, causing extreme distress. In most cases of tracheal growth the characteristic clanging brassy cough (gander cough) of tracheal obstruction can be heard. The trachea may be pushed to one side and its lumen distorted and obstructed by growth in the cervical glands. In mediastinal new-growth invading the trachea, the pressure signs and symptoms characteristic of that disease usually render the explanation of the tracheal symptoms apparent.

Course.—This is generally rapidly progressive.

Diagnosis.—Intratracheal growths have to be differentiated from other causes of tracheal obstruction, and the diagnosis is considered in detail under that condition. Endoscopy affords valuable confirmation if it is practicable or desirable. In œsophageal and mediastinal new-growths invading the trachea, X-ray examination may assist in diagnosis.

Prognosis.—This is hopeless, death occurring from asphyxia or from some complication or by asthenia.

Treatment.—Treatment can be palliative and symptomatic only. In obstruction, it may be possible in rare cases to give temporary relief by a low tracheotomy, but as a rule this is impossible, owing to the presence of obstruction below any point where the trachea is accessible.

THE INFECTIVE GRANULOMATA

Syphilis

The trachea may be affected in both the congenital and acquired forms.

In congenital syphilis, a progressive cicatrisation may occur, leading to stenosis. In acquired syphilis, during the secondary stage, the mucous membrane of the trachea may become generally hyperæmic, or small raised mucous patches may develop locally. In the tertiary period, gummata may occur in the trachea, the commonest site being towards the lower end. Degenerative processes, leading to necrosis and softening, eventually result in ulceration, sometimes with local sloughing of parts of the tracheal rings. In the process of cicatrisation a progressive stenosis may develop.

Symptoms.—Symptoms are those of chronic tracheitis and tracheal irritation in both the secondary and tertiary manifestations, but in the latter, signs of tracheal stenosis may develop when scarring and healing are in progress. Laryngeal involvement occurring at the same time tends to distract attention from the tracheal lesions or to obscure them.

Diagnosis.—The diagnosis of syphilis of the trachea depends upon a careful study of the history of the case, indications of tracheal irritation, laryngoscopic or endoscopic examination, the coexistence of other manifestations of syphilis, and in their absence, a positive Wassermann reaction.

Prognosis.—If the condition is recognised early, excellent results may be obtained by treatment, but it is obvious that where deep destructive changes have resulted, medicinal measures can only palliate.

Treatment.—Anti-syphilitic treatment should be administered vigorously, and after a course of neoarsphenamine, mercury or bismuth preparations should be given. Inunction seems sometimes of special value in such cases. In cases of stenosis of the trachea from cicatrisation, dilatation of the stricture by means of bougies introduced through an endoscope may be practicable and afford useful help.

Tuberculosis

Tuberculosis of the trachea is occasionally found post mortem in advanced cases of pulmonary tuberculosis, usually in those with extensive laryngeal involvement. Primary tracheal tuberculosis is unknown. The rarity even of secondary lesions in this tube is probably to be explained by the ciliated epithelium preventing lodgment of the bacilli.

Pathology.—Tuberculous lesions may occur at any part of the trachea, but they are more frequent in the lower part and on the posterior wall. When they occur they are usually numerous. There may be some general hyperæmia, or small tubercles, varying in size from a pin's head to a split pea, may be visible. Later, superficial ulceration occurs, forming irregular punched-out ulcers. Occasionally, the process may extend deeper, and erosion of the cartilages may occur, with the formation of sinuses and even fistulous communication with the œsophagus.

Symptoms.—Since tracheal tuberculosis is usually a late manifestation of advanced disease, its clinical indications are slight and are usually obscured by the more obvious laryngeal and pulmonary symptoms and signs, though if the process extends deeply and produces sinuses and fistulous tracks, it may become apparent. The actual tracheal symptoms are those of cough and retrosternal soreness.

Diagnosis.—This condition has to be distinguished from other chronic tracheal lesions, and a diagnosis can only be made from a careful review of the history, the general evidence of tuberculous disease and by the tracheal involvement which may be visible by endoscopy.

Treatment.—This must, from the nature of things, be largely palliative, and is in effect practically identical with that of laryngeal tuberculosis, notably intratracheal insufflation with orthoform and benzocaine (anæsthesine).

Leprosy

In some cases of this disease, granulomatous lesions occur in the trachea, and these may eventually give rise to tracheal stenosis, owing to the contraction of new-formed fibrous tissue. The diagnosis can only be made from the occurrence of tracheal symptoms in a case with established lesions of leprosy in other parts.

The treatment is symptomatic.

Scleroma

Although in most cases this condition affects the nose only, scleromatous lesions may be found in the trachea as a pathological curiosity. The disease in any form is rare in England, and occurs chiefly in Poland and Austria. The nodules of granulomatous tissue in the trachea may cause partial obstruction mechanically, or, on contraction, lead to actual stenosis.

TRACHEAL OBSTRUCTION

Obstruction to the lumen of the trachea may be produced by foreign bodies, by conditions originating in the trachea, and by pressure from without.

Foreign Bodies in the Trachea

The commonest route by which foreign bodies enter the trachea is through the mouth and larynx, in the acts of breathing, laughing, yawning, sighing, or before and after coughing, when food or some foreign substance is in the mouth. A piece of bone, a stud, button, false teeth, chewing gum, peas, articles of food, nuts, grains of wheat, beads or blades of grass are among the substances which may gain entrance to the trachea in this manner. Surgical operations in the mouth and throat may lead to the inhalation of a tooth, a piece of tonsil or a mass of adenoid tissue. Material vomited from the stomach, such as food, blood clot or intestinal worms, may be inhaled into the trachea. A large blood clot in hæmoptysis may temporarily obstruct it. Foreign bodies may also gain access through the tracheal wall, such as small projectiles in wounds of the neck, a piece of new growth, or tuberculous glands by ulceration through the wall.

Unless it becomes impacted, or is too large to enter one of the two main bronchi, a foreign body rarely remains long in the trachea. It either causes death with dramatic rapidity, is coughed out again, or passes down into one or other of the large bronchi or their secondary divisions, where it produces results which are described in the section on diseases of the bronchi.

Symptoms.—These depend upon the mode of entry, the size of the foreign body, and the degree of obstruction to the air current which it induces, but in general the tracheal symptoms are less urgent than those of laryngeal obstruction, and less serious than those of obstruction of one or other main bronchus. There may be intense dyspnœa, with great discomfort and alarm during the actual passage through the larynx of a small foreign body, especially if it is temporarily arrested there; but when it enters the trachea there is an almost instantaneous cessation of the acute distress, though some degree of dyspnœa may persist. The type of dyspnœa is inspiratory in the main, though a minor degree of expiratory difficulty may be apparent if the foreign body is of considerable size. There may be a definite stridor with both phases of respiration, but it is more pronounced in inspiration. If the foreign body remains loose in the trachea, which may occur if it is rounded and too large to engage in one of the main bronchial divisions, a sound of vibratory character may be heard on auscultation of the trachea, sometimes described as the *bruit de grelottement*. This may be produced by friction of the foreign body against the tracheal wall, or more commonly by the air passing over it during respiration. A paroxysmal cough may occur, caused by the foreign body irritating the sensitive posterior wall of the trachea, and during such an attack the foreign body may be forced up to the larynx, obstruct it, or cause reflex spasm with intense dyspnœa and cyanosis and a risk of suffocation, unless it drops back, is coughed out, or removed. When sudden rupture of caseous material into the trachea occurs, the lumen may be blocked and death take place rapidly.

Course.—A foreign body impacted in the trachea may give rise to septic inflammation of its walls, with subsequent cicatrisation after removal, or it may lead to secondary infective processes in the lungs, such as purulent bronchitis and broncho-pneumonia.

Diagnosis.—The history of disappearance of some object from the mouth during coughing, breathing or laughing should give rise to suspicion of an

inhaled foreign body, and this may be confirmed by seeing the object directly by endoscopy, or indirectly by means of the X-rays.

Prognosis.—This depends in the main on the nature of the foreign body, and the time elapsing before its removal. An irregular, rough or soft foreign body is more likely to induce septic complications than a smooth, hard substance. Apart from rapidly fatal results, the prognosis is better with intratracheal foreign bodies than with those reaching the bronchi. If removal is effected within 24 to 36 hours, recovery is usually rapid and complete.

Treatment.—Treatment consists in rapid removal with as little damage to the trachea and larynx as possible. This may be effected by means of forceps passed through a bronchoscope, or rarely by tracheotomy alone, when the foreign body may be coughed out through the opening or be easily removed by forceps. Inversion of the patient in the hope that gravity may assist the expiratory efforts of cough is dangerous and should only be attempted after tracheotomy has been performed. Where rupture of a caseous gland or softening new-growth occurs into the trachea, an immediate tracheotomy may be necessary.

Obstruction from Cicatrisation of the Tracheal Walls

Ætiology.—This may result from any condition leading to ulceration of the tracheal walls, with subsequent healing, such as a syphilitic gumma, or less commonly other granulomata, such as tubercle, leprosy or scleroma. Another cause is cicatrisation from wounds of the trachea, accidental, suicidal or after tracheotomy, when the incision has been made too near the cricoid, or when the wound has become infected or the tube left in too long. Scarring from damage to the trachea by the inhalation of boiling or caustic liquids or even by inhaled gases may lead to stenosis.

Pathology.—The deformity of the trachea and the obstruction of its lumen depend upon the situation and the extent of the cicatricial contraction of its walls. It may be local, producing an hour-glass constriction, or involve a long extent of the tube. Occasionally, especially in syphilitic lesions, stenosis may occur at two different levels.

Symptoms.—These depend upon the degree of stenosis, the rapidity with which it develops, and the condition of the larynx, bronchi and lungs. When the stenosis is produced gradually, as in cicatrisation, a degree of obstruction may result, greater than would be compatible with life if suddenly induced. In the early stages of a progressive stenosis, slight dyspnœa may be present on exertion, and during sleep a faint stridor may be audible, disappearing when the patient is awake. As the contraction progresses, the dyspnœa becomes more marked, and a definite and persistent stridor develops, at first inspiratory only, though expiration may become both noisy and obstructed. The patient may experience a sensation of obstruction referred to the neck or under the sternum, accompanied by pain and irritation, leading to cough, which may be dry, noisy and metallic, or accompanied by more or less frothy sputum, if the primary condition is associated with widespread tracheitis. The voice may lose tone and volume, and the patient talk more quietly than normal and with some evident effort. In advancing stenosis, sudden and alarming attacks of dyspnœa may occur,

leading to cyanosis and threatening suffocation. These attacks are usually due to an accumulation of mucus at the site of the stenosis. The patient in advancing degrees of obstruction cannot lie down, and generally sits leaning forward with chin depressed. It may be noted that the extraordinary muscles of respiration contract forcibly, and yet the laryngeal excursions may be small or hardly noticeable, in contrast with those of laryngeal obstruction in which they are maximal. This distinguishing sign was first pointed out by Gerhardt, and is of value, but unfortunately it is not absolute and cannot, therefore, be regarded as pathognomonic. On auscultation over the trachea, a noisy roar may be audible, of maximum intensity near to the obstruction, whereas the breath-sounds over both lungs may be deficient, although the stridor may be conducted bilaterally.

Course.—The course of cicatricial stenosis is usually progressive, unless arrested by treatment, and the dyspnœic attacks become more frequent and alarming.

Diagnosis.—Tracheal obstruction from cicatrisation has to be distinguished from laryngeal obstruction, in which the symptoms are usually more acute and more urgent. Gerhardt's sign described above may also be suggestive. It has also to be differentiated from obstruction due to pressure from without (*vide infra*). The only reliable method of distinction is by direct inspection with the bronchoscope.

Prognosis.—Early syphilitic stenosis may be arrested by appropriate anti-syphilitic treatment. Obstruction due to other granulomatous conditions varies with the severity and extent of the primary lesions. Caseous material or degenerated growth ulcerating into the trachea is usually immediately fatal, or leads to death within a few days from pulmonary complications.

Treatment.—Rest, avoidance of exertion, smoking and alcohol should be advised. The patient's fears should be allayed and symptomatic treatment ordered, such as sedative inhalations or a linctus to check useless cough. In syphilitic stenosis vigorous anti-syphilitic treatment with neoarsphenamine,[1] mercury or bismuth preparations should be given. A low tracheotomy may be necessary for an intractable stricture high up in the trachea. In some cases where an ordinary tracheotomy cannot be performed below the stricture, it may be possible to insert Koenig's long tracheotomy tube through an opening in the trachea made above it. In other cases, dilatation of a fibrous stricture by bougies passed through an endoscope may be feasible.

Obstruction from External Pressure

Pressure on the trachea may occur in the neck or in the mediastinum.

Causes of pressure in the neck.—Strangulation, throttling or garotting leads to death by occlusion of the trachea and suffocation. Enlargement of both lobes of the thyroid body may cause lateral compression of the trachea, until eventually its lumen is reduced to a narrow slit—the so-called "scabbard trachea." Irregular or unilateral enlargements on the other hand cause deviation of the trachea, with kinking of its lumen. Other less common

[1] According to Mr. Harold Barwell, administration of potassium iodide is very dangerous, as it increases the secretion which is pent up behind the stenosis. It may be given in combination with belladonna, but it is better withheld until the severity of the condition has been relieved by neoarsphenamine.

causes of compression of the trachea are enlargement of the cervical glands from tuberculosis, malignant disease, Hodgkin's disease or leukæmia. The trachea may be pressed on from behind by a foreign body impacted in the œsophagus, or by a bony tumour arising from the vertebræ.

Causes of pressure in the mediastinum.—An aneurysm of the aortic arch may press directly upon the trachea at, or near, the bifurcation and cause obstruction. Similarly deep pressure may be caused by a retrosternal goitre, a persistent and enlarged thymus, or a thymic abscess, mediastinal glands enlarged from any cause, usually malignant disease, a dermoid cyst or a bony tumour originating in the sternum.

Symptoms.—The symptoms are in the main identical with those of stenosis of the trachea from intrinsic causes, with the special symptoms due to the primary external condition superadded.

Diagnosis.—This may be simple and obvious, as in those cases due to pressure from tumours in the neck, whereas, in those due to mediastinal pressure, it is usually only possible after a careful survey of all the symptoms, and is in brief identical with that of aneurysm or mediastinal new-growth, to which reference should be made. In some cases X-ray examination may give valuable information.

Prognosis.—This is good in obstruction due to causes in the neck other than malignant disease, but it is almost uniformly bad, indeed hopeless, in obstruction due to mediastinal causes, with the exception of abscess and some thymic conditions.

Treatment.—The treatment is that of the primary condition. In goitre and tuberculous glands, in simple tumours, cysts and some thymic conditions, operation may be possible and may effect complete cure. In those due to mediastinal pressure, especially from aneurysm or new-growth, treatment, in most cases, can be only palliative or symptomatic, and directed to the relief of pain, dyspnœa, cough and distress.

INJURY

Direct violence to the trachea has been known to cause rupture when the chin is raised upwards and the trachea is, therefore, extended.

R. A. Young.
G. E. Beaumont.

DISEASES OF THE BRONCHI

BRONCHITIS

Inflammation of the bronchi, or bronchitis, is one of the commonest maladies and may be induced by a variety of causes. These, in the main, fall into three groups: bacterial, chemical and mechanical, similar to the causes of tracheitis, which is, indeed, in many cases, a concomitant or antecedent of bronchitis, so that tracheo-bronchitis would be a more accurate designation of the majority of cases. At the same time it should be recognised

that the trachea may be alone or predominantly affected, while, on the other hand, in many cases of bronchitis of the smaller tubes, the trachea may escape, or be only slightly involved.

Bronchitis is so varied in its extent and in the form and severity of its manifestations that a satisfactory classification is somewhat difficult to formulate. We propose to consider the clinical manifestations of bronchitis according to the following classification:

1. ACUTE FORMS—(*a*) Catarrhal bronchitis, (1) of the larger tubes, (2) of the smaller tubes; (*b*) suppurative; (*c*) secondary bronchitis; (*d*) bronchitis due to mechanical and chemical agencies; (*e*) fibrinous.

2. CHRONIC FORMS—(*a*) Catarrhal, (*b*) suppurative, (*c*) secondary, (*d*) due to mechanical agencies, and (*e*) fibrinous.

1. ACUTE BRONCHITIS

ACUTE CATARRHAL BRONCHITIS OF THE LARGER TUBES

Synonyms.—This condition is often called Bronchial Catarrh, or Acute Tracheo-bronchitis.

Ætiology.—*Predisposing causes.*—Climate and latitude undoubtedly play an important part. Catarrhal bronchitis is rare in polar and arctic regions and near the equator, but is very prevalent in damp and foggy climates. In England, attacks are common in late autumn, winter and early spring. It is probable that some degree of hereditary predisposition occurs, since "weakness of the chest" is common in some families. Owing chiefly to greater exposure, the disease occurs more frequently in men than in women. It is most common at the extremes of life, infancy and old age, but it is not infrequent at any age. Fatigue and privation play their part, and exposure to cold, wet or fog so frequently seems to initiate the attack that it is often regarded as the exciting cause. Scoliosis, kypho-scoliosis and other malformations or deformities of the chest predispose to bronchitis, and some of them are induced or aggravated by bronchitis early in life. Chronic cardiac and renal disease both render their subjects more liable to bronchitis, as do also conditions of the nose and pharynx which lead to mouth-breathing, in consequence of the inhalation of air which is unwarmed and unfiltered by the nose. In childhood, dentition seems to be a frequent predisposing condition.

The exciting cause is usually one of the catarrh-producing organisms, and one or more of the following may be found in the sputum: the pneumococcus, Friedländer's pneumo-bacillus, streptococci, *Micrococcus catarrhalis*, staphylococci, *M. tetragenus*, and filter-passing organisms. It may also be caused by the *Spirochæta bronchialis*.

Pathology.—The changes induced in the bronchi are similar to those in the nasal mucosa in coryza and in the trachea in tracheitis. Three stages may be described: An initial dry stage, when there is active hyperæmia of the bronchial mucosa, with exudation into the submucous layer, causing temporary diminution of the bronchial secretion from occlusion of the mucous ducts. The second or mucoid stage is associated with copious discharge of mucoid secretion, owing to increased activity of the mucous

glands, this secretion being mixed with shed ciliated epithelial cells and scanty leucocytes. Sometimes in acute cases a few red blood corpuscles are present. The third stage is that of resolution, though not infrequently a muco-purulent stage occurs, when the sputum becomes less copious and greenish in colour from large numbers of pus cells.

In fatal cases the lung tissue may appear slightly distended and red, while the bases may be sodden from œdema. On section, the bronchi appear injected and the mucosa is swollen. On squeezing the lung, beads of mucoid fluid or muco-pus exude from the cut ends of the bronchi. There is no consolidation and the lung tissue floats in water.

Symptoms.—An attack of acute bronchitis generally begins suddenly, with malaise, aching in the limbs, and a sense of oppression in the chest. If the trachea is also involved, there is the characteristic feeling of rawness under the sternum. The temperature rises, varying from 99° to 100° F. in mild cases to 103° F. in more severe ones. The cough is at first dry, irritating and ineffective, but in a few hours it becomes looser. The sputum in the early stage is scanty, tenacious and sometimes streaked with blood; it then becomes copious, mucoid and frothy in character, and is found to contain mucus, shed epithelial cells, leucocytes and red blood corpuscles. Later it lessens in quantity and may become thick, yellow and muco-purulent. With the onset of expectoration there is generally an abatement in the symptoms, the rawness under the sternum disappears, and the feeling of pain or soreness about the pectoral muscles and the costal attachments of the diaphragm lessens. The febrile reaction may last only 3 or 4 days, but the cough and expectoration may go on for 10 days or longer, gradually diminishing, until they are present only night and morning, and then cease completely. SIGNS

In the early stage the patient is flushed and the breathing may be slightly increased in rate, but it is rarely or never laboured, unless emphysema co-exists. Vocal fremitus is unaltered, but rhonchal fremitus may sometimes be felt over one lung or both. The chief physical signs are discovered only on auscultation. The breath-sounds may be harsher and higher-pitched, particularly in infants and children, but they remain vesicular, and expiration may be prolonged. The voice conduction is unaltered. As a rule rhonchi, either sonorous or sibilant, according to the size of the bronchus in which they are produced, are audible over both lungs, and during the mucoid stage bubbling râles may be heard, especially at the bases.

Complications and Sequelæ.—Bronchitis may go on to broncho-pneumonia or may be followed by lobar pneumonia, fibroid induration or bronchiectasis. It may lead to chronic bronchitis, or be followed by active tuberculosis. Occasionally acute interstitial emphysema may result from violent coughing.

Course.—This is variable. The patient may be convalescent in from 7 to 14 days, but cough, expectoration and a condition of debility may continue for several weeks, though, in this case, the possibility of pulmonary tuberculosis should always be considered.

Diagnosis.—The diagnosis of bronchitis is usually easy, owing to the characteristic rhonchi, but it is important to differentiate primary bronchitis from bronchitis occurring as a secondary condition in acute specific fevers and other diseases.

Prognosis.—Bronchitis of the larger tubes is rarely fatal, except when it occurs in infants or the aged, or as a complication of advanced cardiac or renal disease.

Treatment.—PROPHYLACTIC.—This consists in the avoidance of stuffy, ill-ventilated rooms and places of entertainment when catarrhal infections are rife. In mouth-breathers, steps should be taken to deal with the conditions of the naso-pharynx inducing this habit, and instruction in normal breathing given. In dusty occupations, suitable measures should be taken to minimise the irritant particles in the air, as is now done in most factories and workshops. Where poisonous gases have to be encountered, some form of efficient gas-mask should be utilised.

Prophylactic inoculation by vaccines, either from stock mixtures such as are now available, or from autogenous cultures, is now being extensively used, and with some success. An autogenous vaccine is usually to be preferred, if possible. The dose given depends upon the organism and varies from 1 to 50 or 100 millions. Two or three doses at intervals of 7 to 10 to 14 days are usually given in the case of the stock vaccines, whereas with the autogenous a course of 6 to 12 gradually increasing doses is given at intervals of about a week.

CURATIVE.—No matter how mild the attack may be at the onset, the patient should be kept in bed. This may only be necessary for 1 or 2 days, but he should keep to his room till his temperature has returned to normal. The Turkish bath taken by some patients at the first onset is unwise and should be discouraged. The room temperature should be kept at 60° to 65° F. While the temperature is raised the diet should be the ordinary, simple, liquid diet suitable to febrile conditions, namely, milk, weak tea, cocoa and simple gruels, broths or one of the many invalid foods. The patient is often thirsty, and warm or hot demulcent drinks, such as toast water, fruit juices in hot water, and linseed tea sometimes afford great comfort. The air of the bedroom may be moistened by means of a steam kettle in the dry stage, but the use of a steam tent is to be avoided. Local applications over the sternum, acting as counter-irritants, seem to give some relief to the distressing soreness so often complained of. A mustard leaf or one of the medicated wools is the most easy to apply, but a linseed poultice, kaolin poultice or a liniment, such as camphorated oil or the acetic turpentine liniment, may be ordered. Some patients find a cold or hot compress to the neck comforting. Medicated inhalations may be used, either in a special inhaler or in a domestic substitute, such as a jug. At first vapor benzoini —60 minims to the pint of water at 160° F.—is the most comforting, but in later stages vapor pini (olei pini, min. 10; mag. carb. levis, gr. 10; aquam ad min. 120)—120 minims to the pint—or a dry inhalation of creosote, terebene and spirits of chloroform may be useful. It is often wise to start treatment with an aperient, unless this is contra-indicated. In the dry stage a simple saline diaphoretic mixture may be given, with tinct. ipecacuanhæ or vin. antimoniale in small doses. One-drop doses of tincture of aconite are also sometimes given. When expectoration starts it may be encouraged by saline and stimulating expectorants, such as ammonium chloride or carbonate, combined with squills and flavoured with syrup of tolu or of Virginian prune. For the first night it may be well to give 10 grains of Dover's powder to relieve discomfort and secure sleep.

During convalescence the patient should take care to avoid chill and should be given a more liberal diet. A mixture of strychnine and phosphoric acid may be given for a few days, and a linctus or lozenge containing small doses of diamorphine (heroin) or other sedative, to lessen the ineffective cough, which not infrequently occurs, especially at night. Convalescence is usually shortened by a few days' stay at the coast, especially the south.

When bronchitis occurs as a part of some specific disease, such as diphtheria or influenza, the treatment should be that appropriate to the particular disease.

Acute Catarrhal Bronchitis of the Smaller Tubes

Synonym.—Capillary Bronchitis.

It is open to question whether this condition exists as a separate entity. When the finer bronchi and bronchioles are inflamed the alveoli invariably become involved, since very little swelling of the bronchiolar walls is sufficient to occlude the lumen of the tube, with the inevitable production of an area of lobular collapse. The transition from this condition to actual lobular pneumonia is a very small one. In any case, the causes, the symptoms and the treatment of capillary bronchitis and broncho-pneumonia are identical. (See Secondary Broncho-pneumonia.)

Acute Suppurative Bronchitis

Synonyms.—Sometimes called Acute Purulent Bronchitis, or Suffocative Catarrh.

This condition was brought into prominence during the Great War. In 1916 and 1917 it appeared in epidemic form amongst the British troops in England and France. Although it was then regarded by some observers as a new disease, it is more probable that it was, in reality, an epidemic form of a condition usually rare and sporadic and previously termed "suffocative catarrh." That name has unfortunately been applied loosely to a number of conditions associated with acute dyspnœa.

Ætiology.—*Predisposing causes.*—The exceptionally severe winter of 1916–17, together with conditions of overcrowding in huts and billets, were undoubtedly concerned in the epidemic just mentioned. The condition affects young adults chiefly, and is much more common in men. Over-exertion, fatigue and debility predispose to it, but the disease may occur in robust and healthy persons. A history of chill may be given, but often no obvious cause can be discovered.

Exciting cause.—The organisms usually found are the pneumococcus and Pfeiffer's *H. influenzæ*, the latter being reported in 90 per cent. in some series of cases. The *Micrococcus catarrhalis* is also sometimes present.

Pathology.—A very intense inflammation occurs in the medium-sized and small bronchi, leading to an exudate rich in leucocytes. The inflammatory process may extend to the alveoli, which then contain a fibrinous fluid, with entangled red cells. The condition occurs in both lungs and is usually almost universal, no portion being spared. Post mortem the lungs are heavy and red in colour. On section the bronchi are found to contain a thick yellow purulent fluid. Small areas of collapse and sometimes of broncho-pneumonic consolidation are seen, and there is usually œdema of the

bases. Plastic pleurisy is not infrequent, and the glands at the root of the lung are enlarged.

Symptoms.—The onset is usually abrupt, often in young people apparently in robust health. A definite chill may occur, or only coryza and general malaise, with aching of the muscles. The temperature rises quickly and may reach 104° F. early in the disease. A cough soon develops and extreme dyspnœa is a characteristic feature. Expectoration starts early, often on the second or third day. At first it may be streaked with blood, but it soon becomes yellowish green and nummular; it consists of almost pure pus; there is often as much as 5 or 6 ounces in 24 hours. In most instances there is great prostration. In grave cases the patient becomes unconscious and loses control of the sphincters.

There is intense cyanosis, the face, lips and ears being purple. Respiration is rapid, 30 or 40 per minute, and the accessory muscles are often in full action. Palpation and percussion may not show any abnormality though slight dullness is sometimes present at the bases. At first no signs may be discovered on auscultation, but soon the breath-sounds become largely obscured by medium-sized bubbling râles, often audible from apex to base, both front and back. The pulse is frequent, the right heart may dilate and the heart-sounds become weak.

Complications and Sequelæ.—In severe cases recurrent bronchitis, broncho-pneumonia, fibroid disease or emphysema may follow.

Course.—In favourable cases complete restoration to health results. In severe cases the course is rapid, the patient becomes comatose from toxæmia, expectoration ceases and death occurs from exhaustion in 2 or 3 days from the onset. In other cases the disease may last for weeks and proceed to recovery or death.

Diagnosis.—The early occurrence of marked dyspnœa and cyanosis, the expectoration of copious pus, and the widespread râles without dullness are very suggestive of acute suppurative bronchitis. The disease must be differentiated from other conditions described as acute suffocative catarrh that are associated with extreme dyspnœa and cyanosis.

Acute pulmonary œdema is usually afebrile, and the sputum is albuminous, frothy and copious. The condition leading to it, such as cardiac or renal disease, may be apparent.

Capillary bronchitis or broncho-pneumonia may give rise to difficulty, but in these conditions the sputum is scanty, tenacious, sometimes rusty, and but rarely purulent; moreover, cyanosis and dyspnœa develop late and depend upon the extent of the disease and the condition of the right side of the heart.

Pneumonia of the wandering type may simulate this condition, but the character of the signs, with dullness and tubular breathing, and the rusty sputum, usually render diagnosis easy.

Prognosis.—This is very grave. The mortality is high, often as much as 50 per cent. Cases extending to 3 weeks or more with swinging temperatures usually recover.

Treatment.—Cases of this disease should be isolated. If there are indications of an epidemic spread, prophylactic inoculations with a vaccine made from the special strain of pneumococci concerned may be useful in limiting it. In any future epidemic, a trial should be made of sulphapyridine

(M. & B. 693). The steam tent and the inhalation of medicated vapours, such as vapor benzoini, may give a little relief to the dyspnœa. Oxygen should be administered either by means of an oxygen tent, the double nasal catheter or the B.L.B. mask. Venesection may give temporary relief, but produces no lasting effect. Ammonium carbonate and potassium iodide are generally recommended. Stimulants, such as brandy and strychnine, should be given freely, and hypodermic injections of nikethamide (coramine) or leptazol (cardiazol) may be given.

Secondary Bronchitis

Ætiology.—Bronchitis, usually of catarrhal type—indistinguishable as regards symptoms and signs from primary acute catarrhal bronchitis—occurs as a definite part of many acute infectious diseases and as a complication in others. Among these may be mentioned measles, whooping-cough, influenza, the enteric group, small-pox, diphtheria, malaria and plague. Acute nephritis of infective origin is often accompanied by acute bronchitis. Other conditions associated with bronchitis are pulmonary tuberculosis, glanders, secondary syphilis, pleurisy and gunshot wounds of the chest.

Diagnosis.—Bronchitis is easy to recognise, but it is important not to overlook the fact that it may not be the primary condition. In all cases of bronchitis in the early stages, the possibility of a primary acute specific infection should be borne in mind. The diagnosis is also of importance in regard to treatment—for example, in malaria, nephritis and syphilis, in which treatment directed to the primary condition may be more helpful than the ordinary treatment of catarrhal bronchitis.

Bronchitis due to Mechanical and Chemical Agencies

Ætiology.—*Mechanical.*—Attacks of acute bronchitis may be caused by the inhalation of dust-laden air. In occupations where the worker is liable to inspire fine particles of carbon, silica, steel, iron, asbestos or kaolin, acute bronchitis may result, but more often these conditions lead to chronic bronchitis and pneumokoniosis. Pressure on a bronchus by aneurysm or new-growth, or irritation by the presence of a foreign body, may induce local acute bronchitis. The symptoms and signs are practically identical with those of the catarrhal form and need no special description.

Chemical.—Acute bronchitis may follow the inhalation of chemical irritants, either as a result of occupation, accidents, attempts at suicide, or the use of poison gases in warfare. Special attention has been drawn to this subject by the large number of cases of " gassing " dealt with in the War of 1914–1918. Death not infrequently occurred, much acute suffering was caused, and some permanent damage has resulted in many cases which recovered. " Mustard gas " produces its chief effects upon the skin, the eyes and the bronchi. A fibrinous exudate forms on the mucosa as a false membrane, which separates as a slough. The suffocative gases chlorine and phosgene affect the alveoli primarily and more intensely. Chlorine inhaled in a concentration of 1 in 10,000 causes a rapid alveolar flooding with a serous and highly albuminous fluid, and if the victim does not die at once he is liable to suffer from an acute bronchitis. A condition called bronchiolitis fibrosa

obliterans may occur as a sequel. It is often associated with asthmatic dyspnœa.

Symptoms.—These are similar to those of acute catarrhal bronchitis, but there is great pain, distress and almost constant cough, often with copious expectoration.

The treatment is referred to under the heading of Tracheitis, and is, in the main, symptomatic and directed to the relief of pain, useless cough and distress. If there is cyanosis, oxygen should be given continuously if necessary by double nasal catheter or B.L.B. mask.

Acute Fibrinous Bronchitis

Synonym.—Acute Plastic Bronchitis.

Definition.—A comparatively rare acute disease in which there is inflammation of the bronchi, with the formation of casts. These may be hollow or solid, and are coughed up in the expectoration.

Ætiology.—The cause of the disease is unknown. It is more common in males, and is met with both in children and in adults. It may begin as a primary catarrhal bronchitis, or develop as a complication of enteric fever, measles or pulmonary tuberculosis. Such organisms as the pneumococcus or a streptococcus may be found in the casts.

Pathology.—The casts may involve the main bronchi only, or more frequently the smaller ones and the bronchioles. They are greyish white, solid or tubular, and when large, bear the impress upon their exterior of the bronchial walls in which they have been enclosed. Thus, when a cast extends up to the lower portion of the trachea, the indentations made by the tracheal rings may be seen impressed upon it. The fine terminations generally show a spiral moulding. Chemically, they consist of fibrin or of fibrin and mucin. Post mortem the casts may be seen in some places *in situ*; in other areas the bronchi from which they have been expelled may be recognised. The bronchial mucous membrane is at times acutely inflamed, red in colour, with the lining epithelial cells desquamating, or it may appear pale and unaffected. There is usually a certain degree of emphysema, and there may be collapse of lung tissue beyond the site of obstruction.

Symptoms.—The disease generally begins somewhat abruptly with a cough and malaise. In the course of a few days the patient becomes considerably worse, dyspnœa develops and a certain degree of pyrexia, but the temperature is often not more than 99° or 100° F. The dyspnœa becomes more intense, and is the prominent and all-important symptom. The face is seen to be cyanosed, the alæ nasi and the accessory respiratory muscles are in violent action, sometimes with retraction of the intercostal spaces. There may be diminished movement of the chest, either bilateral or unilateral. If there is unilateral pulmonary collapse the heart may be slightly displaced towards the same side. Vocal fremitus may be normal or locally diminished. The percussion note is somewhat hyper-resonant over the anterior chest-wall, but behind there may be some degree of dullness over one or other lobes. If the bronchi are unilaterally affected there may be dullness limited to one lower lobe, with diminution of air entry and no adventitious sounds. Vocal resonance over the affected area is lessened. There is usually some diffuse bronchitis, as indicated by the presence of rhonchi or râles. Marked stridor

is sometimes heard with respiration. A special sign, the "bruit de drapeau," has been described when the cast lies free in the bronchial lumen. It is a dry clicking sound, caused by the flapping of the cast against the wall of the bronchus as the air passes over it. The ordinary sputum does not show any peculiarities. It may, however, show Curschmann's spirals, Charcot-Leyden crystals and eosinophile cells, and it may be absent until the crisis occurs. This consists in the expectoration of the cast after a violent fit of coughing. The cast may be stained with blood, or there is sometimes actual hæmoptysis. The peculiar nature of the expectoration often escapes notice, unless it is examined by floating in water, when a large intact cast is revealed. The dyspnœa ceases immediately after the cast has been expelled.

Complications and Sequelæ.—Emphysema may occur as the result of the violent coughing, or the disease may become chronic, recurring at intervals of varying duration. The most serious complication is laryngeal obstruction, caused by the cast becoming impacted between the vocal cords.

Course.—The disease is generally self-limited, terminating with the separation and expectoration of the cast. The acute stage does not, as a rule, continue for more than 12 to 24 hours.

Diagnosis.—The stridor and respiratory obstruction are suggestive of œdema of the glottis, but auscultation will show that the site of the lesion is lower down the respiratory tract. Asthma, and all causes of laryngeal and tracheal obstruction, must be excluded. The dyspnœa and the presence of signs localised to one lobe may suggest an active lobar collapse, or a lobar pneumonia, but the dyspnœa is more intense than is met with in either of these conditions. Casts are expectorated in diphtheria, pneumonia, chronic disease of the heart, pulmonary tuberculosis and hæmoptysis. The casts of acute fibrinous bronchitis are firmer than those found in these affections, and are expectorated in long pieces, showing the many branches and bifurcations of the bronchial tree.

Prognosis.—The immediate outlook is fair. Death may occur in the first attack, or recurrences may take place, which lead to an increasing degree of emphysema, with its usual results. The ultimate prognosis is, therefore, not good.

Treatment.—The patient should be kept in bed and treated as a case of acute bronchitis. Inhalations of medicated vapours often afford relief. Potassium iodide is believed to expedite the separation of the cast. Intratracheal injections of olive oil or lime water have been recommended, as the casts tend to dissolve in the latter. Tracheotomy instruments should always be at hand in case of laryngeal impaction.

2. CHRONIC BRONCHITIS

Chronic bronchitis is perhaps even more difficult to classify than the acute varieties, each one of which may have its counterpart in chronic form, so that the same classification may be followed. At the same time it must be admitted that, especially in the catarrhal forms, the clinical manifestations are somewhat varied

Chronic Catarrhal Bronchitis

Ætiology.—The causes are practically identical with those of the acute form, of which it is in most cases a sequel.

This affection may commence at any age, although it is more common in middle life and with advancing years. Men are more frequently affected than women. It seems also to have a special incidence in some families. It is more common in damp and foggy climates, and is favoured by urban conditions and by dusty occupations. It starts each winter with a more or less acute catarrhal attack, but each year the summer intermission becomes shorter, until the bronchitis persists throughout the year. It tends to produce emphysema and is aggravated in turn by this condition. It is especially favoured by cardiovascular lesions, such as valvular defects and arterial disease; also by gout, chronic nephritis, syphilis and alcoholism. Conditions associated with chronic cough predispose to it, notably emphysema, asthma, arrested pulmonary tuberculosis, mouth-breathing and cigarette-

The bacteria found are practically identical with those in acute bronchitis, the commonest being the pneumococcus, Friedländer's pneumobacillus, *Micrococcus catarrhalis*, streptococci and staphylococci. Mixtures of two or more of these may be present. A rarer cause is bronchial spirochætosis, from infection with the *S. bronchialis*.

Pathology.—The bronchi show chronic inflammatory changes of a catarrhal nature. The walls are thickened from chronic hyperæmia and also from productive changes in the connective tissues. The mucous glands may be hypertrophied or atrophied, and there may be widespread desquamation of the ciliated epithelial lining of the bronchi. In long-standing cases there is usually some peribronchitis, leading to cylindrical bronchiectasis and distortion of the bronchi by fibrosis. There is almost invariably a greater or less degree of emphysema, which may be generalised or only marginal. Post mortem, the lungs are generally red and somewhat engorged, but if much emphysema has resulted they may be paler than normal. On squeezing the lung after section, pus or muco-pus exudes from the cut bronchi, and there is usually some evidence of œdema at the bases.

Symptoms.—A patient with chronic bronchitis complains of his "chest." By this he means that he suffers from cough, expectoration and shortness of breath on exertion. The cough varies greatly in its severity. During the warm weather the patient may be completely free, and yet suffer for years from a winter cough. It may occur frequently throughout the day and in attacks at night, or only in the mornings and evenings.

The expectoration varies considerably in quality and quantity, so much so that the old classifications of chronic bronchitis were based on this factor. Thus, there may be practically no sputum or only small tenacious pellets, the "crachats perlés" of Laennec; on the other hand, there may be a profuse expectoration resembling unboiled white of egg diluted with water, constituting the form described as "pituitous catarrh" or "bronchorrhœa serosa." Usually the sputum is mucous or muco-purulent and contains greyish-black particles mixed with a frothy fluid. The dyspnœa is largely due to the accompanying emphysema, and so indicates the degree of chronicity of the disease. At first the patient may only notice that he gets out of breath on going upstairs or on mounting slopes, but later even walking on the level causes dyspnœa.

Slight rises of temperature occur in the acute exacerbations of the catarrhal process. Slight cyanosis is frequently observed, especially after

exercise, when the accessory respiratory muscles are called into play. Sometimes rhonchal fremitus is felt. Movement of the chest is restricted by emphysema, and the percussion note then becomes hyper-resonant. On auscultation, expiration is prolonged and sonorous or sibilant rhonchi are heard all over the lungs, with bubbling râles if there is thin secretion in the smaller bronchi. On the other hand, rhonchi may be scanty or only occasionally heard. Voice conduction is unaffected. The fingers may be slightly clubbed, and further evidence of venous obstruction apparent in the dilated venules on the cheeks or along the costal attachments of the diaphragm.

Complications and Sequelæ.—The following changes may occur in the lungs—peribronchial fibrosis, bronchiectasis and emphysema. Asthma or attacks of bronchial spasm sometimes form a complicating factor in chronic bronchitis, especially in the cases of so-called bronchorrhœa. The increased cardiac strain may lead to right-sided dilatation, with basal pulmonary congestion, ascites and œdema of the legs. Late in the disease, as the result of the cyanosis, a peculiar form of confusional delirium is met with, which is worse at night.

Course.—The disease once firmly established, unless relieved by suitable climatic treatment, remains chronic and becomes progressively more severe as further damage is wrought in the lungs with each hibernal exacerbation. As the emphysema develops, a vicious circle is initiated, the aerating power of the lungs diminishes, and finally cardiac failure ensues.

Diagnosis.—Chronic bronchitis must be distinguished from pulmonary tuberculosis, bronchitis secondary to heart failure, and from bronchiectasis. In tuberculosis with bronchitis there is generally wasting, and often flattening 1
of the chest-wall, owing to fibrosis of the lungs. In all cases where the summer intermission of the symptoms fails suddenly rather than lessens gradually, tuberculosis should be suspected. The diagnosis is clinched by the presence of tubercle bacilli in the sputum. In bronchitis secondary to 2
heart failure, in addition to the cardiac signs, the râles in the lungs are chiefly basal and the rhonchi are not so universally distributed. In bronchiectasis 3
the signs are usually characteristic and often limited to one lobe. The X-rays may afford useful aid in diagnosis.

Prognosis.—The immediate prognosis is good, the ultimate is bad. Much depends upon the patient's social condition and opportunities for treatment, especially in respect to climate. The expectation of life of a patient suffering from chronic bronchitis is considerably shortened.

Treatment.—Those subject to chronic bronchitis should live in a warm, equable and dry climate. In England the south-western districts are best, but it is advisable to winter farther afield if possible, either on the Riviera, the north coast of Africa, or in Madeira. High altitudes should be avoided if emphysema is present or if there are cardiac complications. Exposure to wet and chill is dangerous. The question of occupation is often difficult. Much time should be spent out of doors, provided that the patient is not exposed to the inclemencies of the elements; and, further, the work undertaken must not involve severe muscular efforts, or the inhalation of dusty or irritant particles.

In England it is difficult to find an outdoor occupation conforming with these desiderata, consequently light indoor work in a good atmosphere should be advised. Clothing should be warm but light, and afford special

protection to the chest without overloading, as some patients are liable to do. Excesses in diet are to be avoided, also alcohol and heavy smoking. The general nutrition should be well maintained, and many patients, especially those of spare habit, seem to derive great benefit from cod-liver oil during the winter months.

If cough is troublesome and expectoration tenacious or scanty, various combinations of expectorant remedies are useful, such as ammonium carbonate or chloride, tinct. ipecacuanhæ, preparations of squills or senega, with tolu, liquorice or Virginian prune as flavouring agents. A simple saline mixture such as ℞. Sodii bicarb., grs. 10 ; sodii chlorid., grs. 3 ; sp. chlorof., min. 5 ; aquam anisi ad fl. oz. 1, taken with an equal quantity of hot water in the morning or at night, may help to "clear the tubes" and give the patient a spell of freedom from cough. In older patients the ether and ammonia mixture may be given, and in cases with bronchial spasm potassium iodide with anti-spasmodics, such as stramonium, lobelia, belladonna or grindelia, may be of great value. Various antiseptic drugs, such as turpentine min. 10, terebene min. 5–10, creosote min. 3 in capsules or perles, have been recommended, and the elixir thymi et diamorphin. B.P.C. min. 60. Sedative lozenges, such as compound liquorice, heroin or codeine, are often useful in checking useless cough. Intercurrent attacks of acute bronchitis must be treated on the principles described under that condition and the patient kept indoors or in bed, as may be necessary. When an advanced degree of emphysema coexists the treatment appropriate to that condition should be applied. Sometimes benefit may follow the use of the compressed air chamber. When failure of the right heart ensues, with visceral engorgement, the treatment must be modified suitably as described under emphysema. Liniments applied to the chest-wall, especially those containing camphor, turpentine or belladonna, are soothing and afford relief. Care should be taken that any tendency to constipation is checked. In some cases, especially when the predominant organism is the *Micrococcus catarrhalis* or Friedländer's pneumo-bacillus, an autogenous vaccine prepared from the sputum ameliorates the symptoms when given in small doses. This should be considered especially in cases unable to undergo suitable climatic treatment.

Chronic Suppurative Bronchitis

Synonym.—Fetid Bronchitis.

Ætiology.—This condition is not sharply defined and is not a specific and separate nosological entity, but it is a convenient group to include cases with fetid purulent sputum. In some forms of chronic bronchitis the secretion may from time to time accumulate in the bronchi and prove offensive on expectoration. In some instances this condition becomes chronic and the expectoration is fetid up to the time of death.

Pathology.—There is chronic inflammation of the bronchi, with marked peribronchial thickening. The bronchial secretion becomes purulent, and ulceration of the bronchial wall or dilatation of the lumen may occur. Post mortem, the lungs are soft, and on section some broncho-pneumonic areas, with œdema of the bases, may be seen. Pus of an offensive nature exudes from the cut ends of the bronchi.

Symptoms.—These resemble those found in chronic bronchitis, with,

in addition, the unpleasant characteristics of the sputum, in which Dittrich's plugs may be found. These are small, yellowish bodies, with an intensely offensive odour, composed of compact secretion.

Complications and Sequelæ.—Ulceration of the bronchial walls, abscess or gangrene of the lung, and areas of broncho-pneumonia may develop. As with bronchiectasis, pyæmia sometimes ensues, with the formation of secondary abscesses in the brain.

Course.—The disease is progressive, but in the early stages there may be long remissions in which the sputum is not offensive although the bronchitis persists.

Diagnosis.—The sputum is offensive in abscess and gangrene of the lung, bronchiectasis and interlobar empyema. X-ray examination of the chest is of great value in revealing these conditions, and lipiodol or neo-hydriol investigation will usually serve to distinguish between them.

Prognosis.—As the disease becomes firmly established the patient's strength is gradually undermined from the absorption of toxins, and death ensues in the course of a few years, either from exhaustion, toxæmia or pyæmia.

Treatment.—An endeavour should be made to lessen or prevent the offensive character of the sputum. For this purpose creosote or garlic may be administered, as in bronchiectasis. If sputum is copious, postural drainage by means of a Nelson bed may be useful. Creosote vapour baths are also of great value. Apart from this, the treatment is as for chronic bronchitis.

Chronic Secondary Bronchitis

Chronic bronchitis is a common association of chronic cardiac and renal disease, and possibly also of gout. Its clinical characters do not need special description. It is only necessary to emphasise, as in the acute forms, the importance of recognising that the bronchitis is not the essential condition, and that treatment must be directed especially to the primary disease.

Chronic Bronchitis from Mechanical and Chemical Agencies

This usually proceeds to interstitial changes in the lung, and these results may be studied more conveniently under the heading of the pneumokonioses.

Chronic Fibrinous Bronchitis

Acute fibrinous bronchitis has been described above. In certain cases of chronic catarrhal bronchitis a fibrinous exudate may occur from time to time, with the formation of intrabronchial casts. There is then cough and dyspnœa, which abate with the expectoration of the cast. It therefore very closely resembles acute fibrinous bronchitis, and the treatment indicated is that described above.

TUMOURS OF THE BRONCHI

Tumours arising in the bronchi may be (*a*) simple or (*b*) malignant.

(*a*) *Simple tumours.*—The following varieties occur: Adenoma, lipoma, myxoma, papilloma and chondroma. Any of these may lead to bronchial

obstruction and, in consequence, to either collapse or bronchiectasis. Adenoma is of sufficient frequency and importance to require separate description.

(*b*) *Malignant tumours.*—Primary carcinoma or sarcoma may originate in the bronchi. In carcinoma the growth is usually of the columnar type, and arises from the lining epithelium of the bronchi or from that in the mucous glands. Oat-celled tumours also occur, and occasionally squamous-celled carcinoma. In some instances secondary deposits of carcinoma may follow very closely the paths of the main bronchi. Sarcoma may originate in the connective tissue of the bronchial walls.

Although the majority of primary malignant tumours within the lung originate in the bronchi, either from the lining epithelium or from the cells of the mucous glands, their pathological effects and clinical manifestations are in the main pulmonary, and it is therefore more convenient to describe them as tumours in the lung (see pp. 1219–1222).

Adenoma of Bronchus

Ætiology.—Adenoma of the bronchus occurs about equally in the two sexes, and usually in adults below the age of 40.

Pathology.—The tumour is at first small and of polypoid form, as a rule arising in a main bronchus, but not infrequently in the branch to the lower lobe. It is about twice as common on the right side as on the left. The bulbous end is generally directed towards the trachea. The surface is usually smooth and shiny, but may be nodular. An erroneous diagnosis of carcinoma was not uncommon in the past owing to differences of staining of certain of the constituent cells and their irregular distribution in the connective tissues. Metastases, however, are unknown. An adenoma often projects through the bronchial wall, giving it a dumb-bell or cottage-loaf conformation.

Clinical Features.—Often the earliest symptom is hæmoptysis, and this may be slight or profuse, since adenomata are very vascular and bleed easily. In other cases the tumour causes bronchial obstruction with resultant cough and wheezing, proceeding later to pulmonary collapse or bronchiectasis. Dry pleurisy may be an early result of infection, and at times pleural effusion or empyema may conceal the underlying cause.

Diagnosis.—Other causes of hæmoptysis must be considered, such as pulmonary tuberculosis, mitral stenosis, dry bronchiectasis or bronchial carcinoma. Pulmonary collapse may suggest an unresolved pneumonia. In cases of pleural effusion or empyema the diagnosis is liable to be overlooked. The injection of lipiodol or neo-hydriol, or tomography, will often reveal a blocked or deformed bronchus, but the diagnosis can only be established by microscopical examination of a portion of the tumour removed through a bronchoscope.

Prognosis.—This varies with the stage at which the diagnosis is established. If the condition is recognised early, and treated before the growth has extended outwards through the bronchial wall and before bronchial obstruction and septic infection have occurred, the outlook is favourable.

Treatment.—When the adenoma is recognised before secondary effects have developed, piecemeal removal through a bronchoscope, followed by radon application is often completely successful. There are, however, the

risks of hæmorrhage, primary and secondary, and of local recurrence, especially when the growth has extended outside the bronchus. Deep X-ray therapy has been recommended. If secondary bronchiectasis and fibrosis have occurred, lobectomy, or in rare cases pneumonectomy, may be necessary.

THE INFECTIVE GRANULOMATA

Syphilis.—During the secondary stage, a generalised hyperæmia of the bronchial mucous membrane may occur, giving rise to slight bronchial catarrh with the usual symptoms and signs, a condition that has been called syphilitic bronchitis. It is frequently beneficially influenced by anti-syphilitic treatment. In the tertiary stage, gummata may form in or near the large bronchi. They tend rather to fibrosis and contraction than to softening and ulceration, although the latter processes may occur. Contraction may lead to bronchial stenosis, with the symptoms and signs described below, or to extensive peribronchial inflammation and bronchiectasis. If the gummata extend into the lung, as may happen in rare instances, destructive lesions with cough, expectoration and hæmorrhage may result. This condition is more fully described in the section on pulmonary syphilis (see p. 1218).

Tuberculosis of the bronchi occurs as part of pulmonary tuberculosis and does not require separate description.

Leprosy.—The bronchi may be involved in this disease, with the production of cellular infiltration and even nodule formation. At first, these lesions may produce bronchitis, and they are progressive, leading to cough, expectoration, wasting and asthenia. The general clinical picture may simulate chronic pulmonary tuberculosis, from which it is distinguished by the presence of leprous lesions elsewhere, and the absence of tubercle bacilli from the sputum.

BRONCHIAL STENOSIS AND OBSTRUCTION

Obstruction of the main bronchi or of their subdivisions within the lungs may arise from causes within the bronchi or from conditions outside them, and these require separate consideration. It is important to emphasise the fact that in both conditions the symptoms differ according to whether the obstruction is sudden and complete, in which case collapse of the corresponding lung is the rule, or whether it is partial and more gradual, when bronchiectasis usually results. Obstruction of the smaller bronchi may result from spasm as in asthma (see p. 1148) or from disease as in small-tube and capillary bronchitis (see p. 1133).

(*a*) Internal Causes

These are most conveniently considered in two groups—(1) Foreign bodies; (2) those due to disease or cicatrisation of the bronchial walls.

(1) Foreign Bodies in the Bronchi

These usually gain access through the larynx and trachea by inhalation. Any inhaled foreign body that is small enough to pass down the trachea may

reach a main bronchus, more commonly the right, or if it is small it may pass into one of the secondary bronchi. It may at once become impacted, or be moved by cough, but unless it is expelled in this way, it is sooner or later drawn into the smallest bronchus that will receive it, and there becomes impacted.

The recorded varieties of foreign body thus reaching the bronchi are very numerous, but among the more common are pieces of bone, beads, pins, coins, ear-rings, studs, pencils, fruit stones, grains, grasses, beans, nuts, teeth and pieces of tonsil or adenoid growths after tonsillectomy. Even a living fish has been inhaled into a bronchus. Foreign bodies may reach the bronchi through a tracheotomy wound, or a gland may ulcerate into the lumen of a bronchus. Broncholiths and pneumoliths, calcareous particles originating in the bronchi and lungs respectively, may be inhaled into a bronchus instead of being expectorated.

Pathology.—The pathological changes resulting from a foreign body in a bronchus depend upon the nature of the foreign body, the duration of its stay, the size of the bronchus obstructed by it, and the degree of obstruction induced. If the foreign body is smooth and comparatively little septic, and if it be removed within 24 hours or so, complete recovery after a very mild local inflammatory reaction may be expected. If, on the other hand, the foreign body is rough, or soft and laden with septic organisms, acute pneumonic processes, often septic in character, may develop very rapidly. A soft type of foreign body may swell and completely obstruct the bronchus it reaches, leading to complete collapse of the corresponding lung area, often the whole or half of the lower lobe. If the stay of any foreign body is prolonged to days, weeks, months or longer, irreparable damage almost invariably results. The forms this may take are numerous. Collapse and septic pneumonia have already been mentioned. If the obstruction is partial, septic bronchitis, with stagnation of the bronchial exudate and pus behind the obstruction, leads in turn to peribronchitis, bronchiectasis and fibroid induration of the corresponding lung area. In other cases gangrene of the lung results. Not infrequently an empyema may occur and the foreign body may be found in the empyema cavity. Suppuration round a foreign body may lead to localised intrapulmonary suppuration or abscess. Simple bronchial obstruction, uncomplicated by sepsis, may lead to bronchiectasis, owing to the resultant lowering of intrapleural pressure.

Symptoms.—During the passage of the foreign body through the larynx and trachea urgent symptoms may occur which leave no doubt as to what has happened; but this is not invariable, and the patient may not be sure whether he has inhaled or swallowed it. In any case, after a bronchus has been reached, there may be a latent period which engenders a sense of false security and leads to delay in treatment. In most cases pain, discomfort and cough develop rapidly. The cough may lead to the expulsion of the foreign body, or may cause dyspnœa if it forces it up to the larynx. The cough soon becomes noisy, often paroxysmal, and if local septic changes are set up expectoration occurs, sometimes mucoid and copious, at others muco-purulent. Hæmoptysis is not uncommon. Pain may be absent, but is often severe. The temperature is generally normal for the first few hours, but soon rises, especially if bronchitis, pneumonia or broncho-pneumonia

develops. The further symptoms are those of the reactive changes and complications which ensue.

The physical signs naturally depend upon the bronchus affected and upon the degree of obstruction. They are at first those of deficient air entry. The affected side may show less movement, and there may be some recession of the lower intercostal spaces in young people. If a large bronchus is involved and collapse results, there is some displacement of the heart to the affected side. Vocal fremitus may be diminished or absent, the percussion note impaired, and the breath-sounds and voice-sounds weak or absent over the whole or part of one lung, almost invariably the lower lobe. When bronchiectasis, empyema or other conditions develop, their characteristic signs become apparent.

Complications and Sequelæ.—These have been enumerated in describing the pathological results. Sometimes septic meningitis or cerebral abscess develops.

Course.—Spontaneous relief may occur in two ways, either by the foreign body being coughed up, as may happen within a few hours or days or after an interval of months or years, or the foreign body may track through the lungs and pleura, and be discharged in an abscess bursting through the chest wall. In both cases, if an interval of more than days occurs, irrecoverable damage may have resulted. Apart from these occurrences and from successful treatment the course is very variable. Death may occur quickly from some of the septic complications, or after a longer or shorter interval from bronchiectasis, gangrene or cerebral abscess.

Diagnosis.—The history of disappearance of some article from the mouth in the act of laughing, breathing, yawning, coughing or sighing, should always arouse suspicion of an inhaled foreign body. If signs indicating bronchial obstruction are found, the diagnosis is almost certain. In every suspicious case radiograms of the chest should be taken in two different directions, in case the shadow may be merged in that of the scapula or of the ribs. The possibility of a foreign body should always be borne in mind in cases of unilateral basic bronchiectasis, especially if no obvious cause can be found. When such unilateral lung signs develop after an anæsthetic, or after operations on the mouth or naso-pharynx, the possibility of some inhaled material should always be remembered.

Prognosis.—This is grave unless the foreign body is removed within 36 hours, owing to the various dangerous complications that may ensue. Excluding the few cases in which cure occurs by spontaneous discharge of the foreign body, about 50 per cent. of cases left untreated die within 1 or 2 years.

Treatment.—This consists in removal, if practicable, as soon as possible after the diagnosis is established. If the foreign body is in a main bronchus or one of its principal divisions it can usually be removed by means of the bronchoscope and appropriate forceps. In case of failure the question of pneumotomy may have to be considered. If this is decided on, every effort must be made to localise the foreign body by X-ray examination. If intrapulmonary or pleural suppuration has occurred, this must be dealt with surgically, and sometimes the foreign body can be removed at the same time. The medical treatment of the cases consists in that of the various conditions resulting.

(2) Obstruction or Stenosis from Disease or Cicatrisation of the Bronchial Wall

Ætiology.—Primary bronchial new-growths, including adenoma, columnar-celled carcinoma, oat-celled tumour and squamous-celled carcinoma lead to bronchial obstruction at an early stage. These conditions produce symptoms and signs practically identical with those of new-growths in the lung (see p. 1220).

A plug of mucus or a blood clot may cause temporary obstruction of a large bronchus.

The causes of cicatrisation are those leading to ulceration of the bronchial wall, with subsequent healing, such as syphilitic processes in and around the bronchi, ulceration from injury produced by a foreign body or in its removal, or by the inhalation of severe irritants. The fibroid variety of tuberculosis may also produce it.

Pathology.—The stenosis may occur in one of the main bronchi, or in one passing to a lobe or to part of a lobe. At first partial, it may progress until the lumen is almost completely occluded at one point. The changes occurring in the lung beyond the obstruction vary with its degree. At first there is retention of secretion in the bronchi, and air may be forced past the obstruction in inspiration, but not expelled during expiration, producing emphysema, with gradual bronchial dilatation. When the obstruction is more complete the air is absorbed, the lung tissue gradually becomes fibrotic, and the bronchi dilate further.

Symptoms.—Cough, not infrequently of paroxysmal character, is an early symptom and is usually a continuation of that caused by the primary condition. It may be dry or associated with mucoid sputum, sometimes blood-streaked. The expectoration may cause dyspnœa, by obstructing the narrowed bronchus. If bronchiectasis develops, the sputum usually becomes fetid.

The physical signs are those of collapse of a part of the lung and are progressive. Local limitation of movement and flattening, with displacement of the heart to the affected side, may be apparent on inspection. The vocal fremitus is diminished, the percussion note, impaired at first, may progress to complete dullness when fibrosis develops. The breath-sounds are weak or even absent, and the voice-sounds diminished. In the early stages a bronchial stridor may be audible. Compensatory emphysema of the adjacent healthy lung tissue often develops.

Complications.—These are similar to those in stenosis from a foreign body, notably fibrosis and bronchiectasis.

Course.—Unless the primary condition causing the stenosis is one which can be arrested by treatment, the condition is progressive, and eventually the area of lung beyond the obstruction becomes permanently functionless.

Diagnosis.—Bronchial cicatrisation must be differentiated from obstruction due to extrabronchial causes, such as pressure from new-growths, aneurysm and the other mediastinal conditions mentioned in the section below. The history, the physical signs and examination by X-rays and, if necessary, by the bronchoscope may help in distinguishing. The Wassermann reaction should be investigated in every case where the stenosis is proved to be of intrabronchial origin.

Prognosis.—This varies with the cause. It is most favourable in cases due to syphilis submitted to treatment at an early stage.

Treatment.—Vigorous anti-syphilitic treatment should be employed in cases due to syphilis. In other cases the treatment is to relieve symptoms by appropriate measures.

(*b*) External Causes

These may be subdivided into—(1) *Mediastinal conditions*, chiefly enlargement of the bronchial or mediastinal glands from tuberculosis, Hodgkin's disease or malignant growth, aneurysm of the aorta, mediastinal abscess, pericardial effusion and œsophageal new-growths. (2) *Intrapulmonary causes*, generally primary or secondary new-growths.

Symptoms.—These are practically identical with those just described, but in addition there are those of the condition causing the pressure.

Diagnosis.—This has been discussed in the previous section. The bronchoscope should not be employed where there is any suspicion of an aneurysm.

Prognosis.—This is extremely unfavourable, except in cases due to tuberculous glands and pericardial effusion, and in some cases of mediastinal suppuration.

Treatment.—This can only be palliative in the majority of cases. Useless cough may be checked by a sedative linctus of diamorphine (heroin) or morphine. Dyspnœa when due to spasm may be lessened by inhalations of creosote and spirits of chloroform, or by administration of oxygen. Pain may be relieved by aspirin or other analgesic drugs.

ASTHMA

The term asthma has been loosely employed to denote any form of dyspnœa of expiratory type occurring in paroxysms. For all conditions other than that now to be described some descriptive qualification should be employed to avoid confusion.

Asthma or true spasmodic asthma is a paroxysmal affection, occurring most frequently in patients of neuropathic inheritance. It manifests itself in attacks of severe expiratory dyspnœa due to excessive vagal discharges, set free by peripheral irritation, chemical agencies or cerebral influences.

Ætiology.—Probably no other disease shows such a varied and complex causation, but studies of idiosyncrasy and anaphylaxis have served to explain many of the obscurities.

Predisposing causes.—Age.—The first attack may occur at any age, even as early as the period of the first dentition. The majority of cases begin before the age of 25.

Sex.—Asthma is generally stated to be nearly twice as frequent in the male sex as in the female.

Heredity.—Asthma certainly runs in families. The heredity is not always direct, the nervous instability sometimes being evidenced in other generations by migraine, epilepsy or hysteria. The view that hypersensitiveness to certain proteins is inherited is now discredited, and it is believed that an unduly irritable bronchial centre is the factor transmitted by heredity.

Other diseases.—Gout and syphilis are said to predispose to asthma. Bronchitis not infrequently leads to paroxysms in patients with asthmatic tendencies. Tuberculosis of the lung occasionally induces it, but here again it is probably in patients with the asthmatic diathesis.

Climate and locality.—Asthmatics seem very sensitive to both of these, but no general relationship can be proved, as the effects are most variable. Some patients are better in dry, others in damp, foggy climates, and in regard to locality each patient is a law to himself.

Conditions of the nose and naso-pharynx.—Nasal obstruction from swelling of the turbinates, deflection of the septum, spurs and polypi, and conditions of the naso-pharynx, such as adenoids and enlarged tonsils, undoubtedly predispose to asthma, and may also be exciting causes of the actual paroxysm.

Exciting causes.—Chemical substances.—The emanations from certain animals may be the determining cause. The best known of these are the horse and cat, but rabbits, hares, guinea-pigs, deer, dogs and monkeys may have a similar effect. Even human hair appears capable of discharging the paroxysm. The dust from some substances, such as corn, rice or oats, the smell of certain drugs, such as ipecacuanha, and the scent and the pollen of grasses and flowers may act in a similar fashion, as also may articles of diet, and many drugs. This factor in causation has attracted much attention —in this country by Freeman, Coke and Bray, and in America by Walker. It is claimed that at least 50 per cent. of asthmatics show hypersensitiveness to various protein antigens obtainable from animals, grains, bacterial bodies, foods and drugs, and over a hundred are now available for routine testing of these patients. The analogy with the causation of hay fever and paroxysmal sneezing is obvious. This group has been referred to as "allergic" asthma.

Peripheral irritation.—As already mentioned, irritation of the nose, naso-pharynx and bronchi may be asthmogenic in those of asthmatic tendency.

Gastro-intestinal disturbance.—This is well recognised as a cause, and most asthmatics find by experience the penalties of a heavy late meal and of indigestible articles of diet. It is possible that actual metabolic errors may be a factor, as in the so-called "week-end asthma," due to altered conditions of diet and exercise at this period.

Genito-urinary conditions, particularly in women, notably ovarian or uterine disorders, sometimes act in inducing asthma.

Cutaneous.—Asthmatics are peculiarly liable to urticaria and eczema, although these conditions usually alternate with the asthmatic attacks.

Nervous factors.—Fatigue, emotion and nervous shock may precipitate an attack. This factor cannot be ignored, even in cases due to protein hypersensitiveness, as is shown by a well-known case in which a patient susceptible to roses developed asthma when handed an artificial rose.

Pathology.—Numerous theories have been propounded to explain the asthmatic paroxysm. Among these may be mentioned vascular turgescence of the bronchial mucous membrane, spasm of the bronchial muscle and increased secretion of the mucous glands. Spasm of the diaphragm or of the inspiratory muscles has also been suggested. That bronchial spasm plays the major part seems to have been established by the experiments of Brodie and Dixon, and this view is strongly supported by their observations on the effects of drugs on the bronchial musculature. Muscarine, pilocarpine and physostigmine produce bronchial constriction and asthmatic symptoms

in animals, while atropine, hyoscyamine and chloroform abolish these effects.

There can now be little doubt that the broncho-constrictor fibres of the vagus are the channel by which the impulses discharging the asthmatic paroxysm reach the bronchi, although the possibility that impulses leading to vaso-dilatation and to increased bronchial secretion are also concerned, must be admitted.

ANAPHYLAXIS.—The important part played by extraneous proteins in the genesis of asthma and the obvious analogy between the asthmatic paroxysm and the symptoms of anaphylactic shock have suggested that in many cases, if not in all, asthma is an anaphylactic phenomenon. Evidence is accumulating in support of this view. It has been shown that the lungs of the guinea-pig killed in anaphylactic shock show extreme constriction of the bronchioles. Asthmatics are well known to show anaphylactic tendencies, and especial care in the administration of antitoxic serums is necessary with them. It is of some interest to note that the Eppinger and Hess group of vagotonics show urticaria, dermatographia, eosinophilia and liability to anaphylactic shock, all conditions which occur in asthmatics. It is tempting, therefore, to assume that the foreign protein or toxin produces the asthmatic attack by inducing vagotonicity. Lastly, the observations of Freeman, Coke and the American workers have demonstrated the cutaneous hypersensitiveness of many asthmatics to special foreign proteins. Further research is needed before it can be accepted that anaphylaxis accounts for all cases of asthma, but it is almost certainly an important factor in many.

Symptoms.—The asthmatic paroxysm most commonly commences about 2 a.m. or later, but it may sometimes develop in the daytime. There are often preliminary indications some hours beforehand, constituting the "asthmatic aura." These include restlessness, irritability, mental exaltation, less frequently depression, itching of the nose or chin, flatulence or polyuria. Some attacks are ushered in by coryza. Such warnings are not constant, and the sufferer usually wakes from sleep with a feeling of suffocation. In early attacks great restlessness, anxiety and alarm occur. The difficulty in breathing and the sense of suffocation increase; the patient sits up in bed, or gets up to throw open the window, and fixes his arms to bring into action all possible muscles of respiration. Respiration, although laboured and difficult, is often slow, inspiration being short while expiration is greatly prolonged. Both are accompanied by loud wheezing sounds, audible at a distance from the chest. The patient appears pale, but the lips are dusky and the expression is anxious and distressed. The jugular veins are distended and prominent. The accessory muscles of respiration are seen to be in violent action, notably the sterno-mastoids, scalenes and pectorals. The skin is moist and there may be marked sweating. The chest is much distended, and at each violent attempt at inspiration very little further enlargement occurs, while there is often sucking-in of the supra-clavicular and lower costal regions.

Percussion reveals marked hyper-resonance and encroachment on the cardiac and hepatic dullness. On auscultation inspiration is short and high-pitched, expiration very prolonged, and both are obscured by abundant sonorous and sibilant rhonchi, and later by bubbling râles at the bases. The

pulse is small, quick and sometimes irregular. There is usually marked epigastric pulsation. A differential blood count during an attack may show an eosinophilia of as much as 35 per cent. Cough does not develop until late in the paroxysm, and is quickly followed in many cases by the expectoration of small pellets, called "perles" by Laennec, and often likened to boiled sago or tapioca. These were carefully studied by Curschmann, and when examined on glass on a black background, prove to consist of a central highly refractive mucinoid coil, with masses and threads of mucin wrapped spirally around it. Microscopically leucocytes, mostly eosinophils, may be seen entangled in the mucus. The sputum frequently contains Charcot-Leyden crystals, which are now accepted as spermin phosphate. With the onset of expectoration the dyspnœa quickly lessens, and the attack subsides. The patient often passes a large quantity of pale urine and then may sleep until morning, awaking in apparent comfort. More frequently he appears pale, tired and anxious.

Course, Complications and Sequelæ.—Such an attack may last from a few minutes to several hours, and may remit and then return. When the spasm is very severe and prolonged into hours, with little or no remission, the condition is often termed "status asthmaticus." The patient may be extremely ill, and death may occur unless the attack remits spontaneously or as a result of treatment. More often the attacks recur at the same time each night for a considerable period extending to weeks, and then pass off, after which the patient may enjoy a period of freedom of weeks or months. The intermissions may become shorter with successive attacks, and increasing emphysema may develop. This in turn leads to secondary bronchitis, which persists, together with some degree of permanent œdema of the bases. Later still the cardio-vascular changes incidental to emphysema occur as sequels, namely, engorgement of the right heart, tricuspid regurgitation, venous stasis, ascites and œdema. Chronic asthmatics frequently present a characteristic appearance. Of thin build, with sallow complexion, anxious expression and nervous manner, they often have a long neck, high straight shoulders, and a forward stoop. Asthma necessarily imposes limitations upon those who suffer from it at all severely, although many asthmatics lead active, useful lives in spite of their disease.

Diagnosis.—This involves the differentiation from other forms of dyspnœa, particularly those of spasmodic expiratory type. The chief forms of paroxysmal expiratory dyspnœa are:

1. *Bronchial asthma or spasmodic dyspnœa complicating chronic bronchitis and emphysema.*—This condition is sometimes a late result of true asthma, but may occur independently. The dyspnœa is more persistent and is more definitely related to the bronchitic attacks, being therefore more common in the winter.

2. *Cardiac dyspnœa or cardiac asthma.*—This, like true asthma, is usually nocturnal, but the signs of failure of compensation in association with valvular or myocardial disease usually make the nature of the dyspnœa clear.

3. *Uræmic dyspnœa or renal asthma.*—This is also not infrequently nocturnal and may be almost indistinguishable from true asthma. Examination of the urine, the urea and non-protein nitrogen content of the blood, usually enable the distinction to be made with certainty. Cardio-vascular changes with high blood pressure are frequently but not invariably present.

4. *Hay asthma* is probably only a severe form of hay fever and is to be regarded as a variety of true asthma.

5. *Pulmonary tuberculosis may be associated with asthmatic dyspnœa.*—The differentiation may not be easy during the attack, but the persistence of apical signs in the interval may give a clue. It is a wise precaution to examine the sputum for tubercle bacilli in all cases of asthma. A low blood pressure in an asthmatic should also arouse suspicion of tuberculosis.

The dyspnœa of laryngeal or tracheal obstruction and of mediastinal pressure can usually be recognised by the fact that it is chiefly of inspiratory type, and may be associated with stridor, instead of wheezing. In all cases of doubt the chest should be examined with the X-rays to exclude aneurysm or new-growth.

Prognosis.—When the disease starts in childhood or in early adult life it may stop spontaneously or be relieved permanently when some causal condition is discovered and treated. During a severe attack the aspect of the patient may be so alarming that a fatal issue may seem imminent, yet death rarely occurs. In chronic cases, the ultimate prognosis is made more serious by the complicating emphysema and bronchitis, and in spite of popular belief, the asthmatic has less than the normal expectation of life.

Treatment.—(*a*) *During the attack.*—The list of anti-spasmodic drugs and measures employed is a long one, and it is impossible to foretell which will be efficacious, for asthmatics vary as widely in their response to drugs as they do in regard to asthmogenic causes. Drugs may be administered for this purpose by inhalation, by nasal sprays, by the mouth or by hypodermic injection. Adrenaline hydrochloride, in doses of 2 to 5 minims of a 1 in 1000 solution hypodermically, may act with dramatic efficacy if administered sufficiently early, but it should be given cautiously to elderly asthmatics. It may also be combined with pituitary extract, as in the special preparations evatmine, pitrenalin and asthmolysin. In status asthmaticus, the procedure suggested by Sir Arthur Hurst may give relief. A syringe of 1 c.c. capacity is filled with adrenaline solution 1 in 1000. This is slowly injected over a period of several minutes to half an hour or until the spasm relaxes. Ephedrine hydrochloride, in tablets of gr. $\frac{1}{4}$ to $\frac{1}{2}$, has proved itself a useful substitute for adrenaline in some cases and can be given by the mouth. Pseudo-ephedrine in doses of $\frac{1}{2}$ to 1 grain is often helpful where ephedrine fails. Ephetonin, a synthetic preparation of similar character, is also sometimes employed. Adrenaline often proves helpful as a nasal spray, especially in combination with chloretone. A weak solution of cocaine and atropine in an oily excipient has been much employed as a nasal spray, but it is not devoid of risk if used indiscriminately. The fumes of burning nitre paper, or of a powder composed of tobacco, stramonium and nitre, sometimes help to relieve the distress, but they should be avoided in cases with bronchitic complications. Smoking a cigarette or a cigar may be helpful in patients who do not smoke habitually; others are helped by cigarettes containing stramonium. Inhalations of amyl nitrite, ethyl iodide or chloroform may be tried in some cases. Various drugs have been employed, of which potassium iodide and bicarbonate with tincture of stramonium, hyoscyamus, lobelia or belladonna are the most useful. Twenty minims of liquid extract of grindelia every 20 minutes for three doses have been found useful in some cases. Other drugs which have been recommended are chloral hydrate, phenacetin and the other coal

tar antipyretic drugs, elixir of caffeine tri-odide (eupnine) in 60 minim doses, and an emulsion of benzyl benzoate, 120 minims every 2 hours. Other measures include drinking a cup of strong coffee, the application of a mustard leaf over the sternum, and placing the feet in hot water and mustard. In very severe cases, if all else fails, it may be necessary to inject morphine or diamorphine (heroin), but this should only be done after careful consideration, owing to the danger of inducing habit particularly with heroin. It is especially dangerous in cases of status asthmaticus.

(*b*) *Between the attacks.*—The greatest care should be taken to discover and deal with any predisposing or exciting cause. The patient should live in that locality which his experience shows to be most suitable for him, and at present no rules can be formulated in advising on this matter.

Diet requires careful consideration. Any article of diet to which the asthmatic is susceptible should be entirely eliminated, and only the lightest of meals should be taken after midday. Dextrose has proved to be helpful in some cases of asthma in childhood. It is recommended to give 3 teaspoonfuls in lemonade or orange juice 3 times a day, with extra sugar and sweets at meals. Alkalis may also be given at the same time. Fatigue, overwork and emotional stress are to be avoided. Care should be taken to see that the bowels act efficiently. The general health should be maintained by every possible means. Arsenic may be given by the mouth or intravenously or intramuscularly as sodium cacodylate (gr. $\frac{3}{4}$ in min. 15 sterile water). When the patient is having a series of attacks, iodide of potassium with one or more of the anti-spasmodic group of drugs such as stramonium, lobelia, belladonna and grindelia, may be given regularly with great benefit. Any local source of irritation in the nose or naso-pharynx should be dealt with adequately. Sometimes touching the nasal septum with the galvano-cautery may alone be efficacious. In cases complicated by bronchitis, the sputum should be examined bacteriologically, and a vaccine may be made from the predominating organisms, but small doses and very gradual increments should be employed, since asthmatic patients are frequently hypersensitive to vaccines. If these prove to be *Micrococcus catarrhalis*, or Friedländer's pneumobacillus, great benefit may result, but the patient should be told that the vaccine can only help the asthma by lessening the accompanying catarrh. Some cases associated with marked emphysema obtain considerable relief from compressed air baths, at first on alternate days, then daily, the course extending to 1 or 2 months.

Careful investigation of the question of protein hypersensitiveness should be undertaken, and the method of testing by means of the cutaneous application of various antigens is worth a trial. For this purpose, the particular protein antigen, or a series of such antigens, may be applied to the skin of the forearm in the form of powder, solution or paste, and superficial scarification is then effected by means of a sterile needle or scalpel. A positive reaction is shown by the development of an urticarial wheal surrounded by a hyperæmic area. A control scarification with normal line or a paste free from protein should be made at the same time. A sitive result may be expected in about 50 per cent. of asthmatic patients. such a condition is established to one or more such substances, they should be avoided if possible; if not, the methods of desensitisation may be tried, but the results are frequently disappointing. The specific antigen

may be employed in very minute doses by injection, starting, for example, with 1 minim of a $\frac{1}{100,000}$ solution and gradually increasing. Peptone given by the mouth or by hypodermic injection is sometimes employed as a shock desensitising agent.

A variety of "shock" treatment which has given good results is the intramuscular injection of sulphur oil (*huile soufrée*), 0·03 gramme in 1 c.c. This is given in doses up to 1 c.c. once or twice weekly over a period of weeks or months.

A gold salt, allochrysin, has been given intramuscularly in doses of 0·05 gramme, followed in a week by 0·1 gramme, and then, if tolerated, up to 0·2 gramme at weekly intervals till a total amount of 2 grammes has been given.

Breathing exercises of expiratory type such as those recommended by the Asthma Research Council are often of great value.

BRONCHIECTASIS

Definition.—Bronchiectasis is a condition of permanent dilatation of one or more bronchi. When it occurs in the finer divisions it is sometimes described as bronchiolectasis.

Ætiology.—Bronchiectasis is invariably secondary, and may result from disease of the bronchi, the lung parenchyma or the pleura. Even the rare congenital cases are probably consequent on malformation, atelectasis or intra-uterine disease.

1. The bronchial conditions which may progress to dilatation are bronchitis, and any affection leading to partial bronchial obstruction, such as inhaled foreign body, tumour (simple or malignant), stenosis from cicatrisation and external pressure from new growth or aneurysm. Localised pulmonary collapse thus induced seems to be the commonest antecedent condition. In children, measles and whooping-cough are not uncommon causes, especially when they follow one another in rapid succession, although either alone, if severe, may lead to it.

2. Conditions of the lung parenchyma which may cause bronchiectasis are unresolved pneumonia, broncho-pneumonia, collapse, syphilis and tuberculosis. Syphilis is rare and usually acts by leading to bronchial obstruction or stenosis. Fibroid tuberculosis is a common cause, but the clinical manifestations are as a rule masked by the primary condition. The pulmonary complications of influenza are not infrequently followed by bronchiectasis.

3. The pleural conditions which are followed by bronchiectasis are those which lead to pleural adhesion and those which are associated with pulmonary fibrosis, notably chronic pleural thickening, or empyema leading to prolonged or permanent collapse of the lung.

In a lesion with such diverse antecedents the age relations are necessarily indefinite. It may occur at any age, but is commonest in the third and fourth decades. It frequently commences in childhood, although the characteristic clinical manifestations may not develop until adult life.

Sex.—In most recorded statistics there is a striking preponderance in the male.

Social state.—It is noteworthy that bronchiectasis in its more severe form is more common in the poor than in the well-to-do.

Pathology.—Four factors in the pathogenesis of bronchial dilatation have to be considered. (1) The most important is the localised collapse which leads to secondary bronchial dilatation. (2) Weakening of the bronchial walls. Most of the conditions preceding bronchiectasis tend to induce severe bronchitis and peribronchitis, and thus render the walls more yielding. Where stagnation of secretion occurs, septic and putrefactive organisms develop, producing tryptic ferments which may act injuriously upon the lining membrane. The importance of the infective factor has been stressed by Moll. (3) Increased pressure on the walls thus weakened is the determining factor. This is generally expiratory in origin and due to the strain of cough. The actual pressure of secretion accumulating behind an obstruction may promote yielding of the bronchial walls. In cases of bronchiectasis following on collapse of the lung the force of inspiration has been regarded as contributory, but this is doubtful and in any case is less important than the expiratory strain of cough. (4) The fourth possibility is the traction exerted upon the walls of the bronchi by contracting connective tissue in the surrounding fibroid lung. This obviously postulates the existence of pleural adhesion, which is not invariably present. While this must be admitted as a possible contributory factor, its importance is certainly less than that of the preceding ones.

Congenital bronchiectasis is a pathological rarity and may be confused with congenital cystic disease of the lung (see p. 1222). It is usually unilateral, and the bronchi involved are of small size, although in some cases the lung may show a large central cavity, with smaller spaces around it. Bronchiolectasis is also more of pathological than of clinical interest It occurs chiefly in children, as the result of acute broncho-pneumonic processes. It is said sometimes to follow influenza and possibly tuberculosis. The lung has a peculiar spongy appearance, to which the name "honeycomb" has been applied.

Bronchiectasis of the larger tubes may be either cylindrical or saccular. In the former condition several of the bronchi are more or less uniformly dilated, and when opened out they appear like the fingers of a glove. Sometimes the dilatations are fusiform, at others they show a beaded arrangement, described as moniliform. These forms of dilatation are usually associated with emphysema and chronic bronchitis. Saccular bronchiectasis is generally localised and may be found in any part of the lung, but is most common in the lower lobes and near the base. This is partly due to the fact that the antecedent processes fall with special stress on the bases of the lung, and partly to the influence of gravity in leading to retention of secretions in these parts. Although it may be unilateral in origin, it often spreads and may involve both bases or even all the lobes. There may be one large irregular cavity, or a series of smaller globular dilatations involving the whole or part of the walls of one or more bronchi. The cavities are usually filled with the fetid secretion, to be described under expectoration. When this is washed away the walls are found to be thin, smooth and formed of thinned-out mucous membrane. In places this may have ulcerated, owing to the tryptic action of the secretion, and the lung tissue is thus exposed. An abscess may then form, and an aneurysm sometimes develops, as in a tuberculous cavity. The openings of the smaller bronchi, derived from the dilated bronchus, can often be recognised in its walls. In doubtful cases the

histological demonstration of cartilage and muscle in the walls establishes the bronchial origin of a cavity. The surrounding lung tissue is usually airless and fibroid, and sometimes is almost of leathery consistence. Occasionally, however, it is emphysematous, congested or pneumonic. In the great majority of cases there is a dense pleural adhesion over the area of lung involved.

Other morbid conditions found post mortem include lardaceous disease, gangrene of the lung, empyema, pyo-pneumothorax, suppurative pericarditis and cerebral or spinal cord abscess. Owing to the obstruction of the pulmonary circulation which may result, engorgement and dilatation of the right side of the heart, tricuspid regurgitation and the results of systemic venous stasis are often found.

Symptoms.—The onset is usually insidious, the symptoms developing during the course, or as a sequel, of one of the acute or chronic affections mentioned above. In some few cases, however, they develop rapidly in patients previously in good health. This is particularly the case where bronchiectasis results from an inhaled foreign body or after general anæsthesia, and a rapid onset should lead to the suspicion of this. The cough in well-developed cases is somewhat characteristic and occurs in paroxysms. These are frequently induced by change of posture—for example, bending forward or lying down. They occur with special frequency on rising, and are usually associated with the expectoration of large quantities of sputum, due to the overflow of the secretion, accumulated in the cavities during the night, into a sensitive or relatively healthy bronchus, which excites cough reflexly. They also occur on retiring to bed and at long intervals during the day. The sputum frequently amounts to as much as 20 or 30 ounces in the 24 hours. It is generally extremely fetid, although in the earlier stages it is not invariable. The patient's breath is often also malodorous, and the stench may pervade the room or even the house in which he lives, although it is not persistent. The patient is himself much distressed by the unpleasant character of the sputum, of which he is, as a rule, acutely conscious. On standing in a glass vessel it can be seen to settle into three layers—a surface scum of light frothy mucus, an intermediate stratum of thin, turbid, greenish fluid, and a deep layer of brownish colour consisting of muco-pus, bacteria, anaerobes, spirochætes and putrefactive products, including foul-smelling organic acids. Fetid yellow bodies called Dittrich's plugs can usually be found in the deep layer. Elastic tissue is only present when erosion of the wall has occurred. Hæmoptysis is not infrequent, and may occasionally be fatal. It may be the first and only symptom in some cases, which are referred to as dry or silent bronchiectasis. Dyspnœa is not, as a rule, apparent unless the condition is widespread, or unless the pulmonary or cardiac complications are present. The general condition of the patient is at first but little affected, and there may be no fever for long periods. As the disease progresses, lassitude, anorexia and some wasting slowly develop, while bouts of fever occur, due to retained secretions or to some complication.

Physical signs vary with the extent and degree of dilatation, and also with the amount of secretion present. In the early stages there is at most slight dullness at one base, with diminished air entry, peculiar sticky, "leathery" râles, and diminished vocal resonance. When bronchiectasis is well developed the signs are almost characteristic. The patient may appear well nourished and of good colour, although on cold days, especially

in children, duskiness or cyanosis is often noticeable. There is well-marked clubbing of the fingers, generally of drum-stick character, and pulmonary osteo-arthropathy, involving many joints, sometimes develops. There may be localised flattening or retraction of the chest wall over the affected area, with diminished movement, and the heart is drawn over to this side. The remaining signs vary with the state of the cavity. If this is full, there is diminished vocal fremitus, dullness and weak or absent breath-sounds and voice-sounds. If the cavity is empty or partly empty, the vocal fremitus is increased, the percussion note is boxy or dull, while the breath-sounds are bronchial or cavernous. Adventitious sounds are then generally audible, the most characteristic being sharp metallic or "leathery" râles. Bronchophony and pectoriloquy are marked, and occasionally the "veiled puff" of Škoda can be heard. Signs of bronchitis are often apparent in the adjacent lung tissues; compensatory emphysema may be demonstrable in the unaffected parts of the lung, and on the opposite side. X-ray examination before and after the injection of lipiodol or neo-hydriol serves to define the extent of the disease and the degree of fibrosis. Tomography may also be useful.

Complications and Sequelæ.—The chief pulmonary complications are septic broncho-pneumonia, gangrene and abscess. The pleura may become involved, giving rise to dry pleurisy, which sometimes progresses to empyema and rarely to pyo-pneumothorax, while in other cases pleural adhesion and contraction result. Septic pericarditis may develop and prove fatal. Septicæmia and pyæmia sometimes occur as terminal results. Cerebral abscess constitutes a serious and somewhat common complication, and may be found in the frontal, parietal or temporal regions, the cerebellum or cord. Occasionally multiple abscesses form. Lardaceous disease sometimes develops, especially in the liver, kidneys and intestines.

Course.—This is progressive, but is often slow unless fever or complications develop, though the morbid process may eventually involve the other lung. The sputum at first may be simply purulent, then becomes unpleasant and finally fetid. The disease may start in childhood and not lead to death until well on in adult life. The course is slower in cases due to bronchitis and fibroid lung conditions than in those due to foreign bodies, new growths or aneurysm.

Diagnosis.—In well-developed basic cases this is, as a rule, easy. The history of cough, influenced by posture and associated with copious sputum, is suggestive, especially when variable physical signs are observed. The development of the characteristic sputum with these signs renders the diagnosis almost certain, and the X-rays usually serve to confirm. Radiological investigation after an intra-tracheal injection of 10 to 20 c.c. of lipiodol or neo-hydriol, through the crico-thyroid membrane or between two rings of the trachea, under local anæsthesia, or with care directly between the vocal cords, has greatly facilitated the diagnosis of bronchiectasis. Franklin has recommended the nasal route for the introduction of the lipiodol. One nostril, the oro-pharynx and the larynx are cocainised, then a gum-elastic catheter is passed along the floor of the nose into the larynx. Some cocaine is injected down the catheter and then the lipiodól follows. An attempt should be made to direct the lipiodol towards the affected side by turning the patient towards that side. The injection should be carried out in the X-ray room and the patient instructed to restrain cough if possible until the films have

been taken. The pictures obtained are strikingly characteristic and of great value. In cases with less characteristic symptoms and signs the distinction has to be made from chronic bronchitis, especially the fetid variety, pulmonary tuberculosis, gangrene or abscess of the lung, and fetid empyema. The distinction from chronic bronchitis may be difficult, especially in the early stages when the sputum is not fetid, but the paroxysmal cough, the copious expectoration with signs including bronchial breathing and sticky râles at the base, may be strongly suggestive. In fetid bronchitis the fœtid sputum is not constant, and the cough and sputum may occur only during exacerbations of the bronchitis. Pulmonary tuberculosis may give rise to difficulty, particularly in cases of apical bronchiectasis. Repeated examinations for tubercle bacilli and also for elastic tissue in the sputum should be made. The history, the mode of spread, and X-ray examination may all assist. It should be remembered that the two conditions may coexist and, this may be suspected in some cases of fibroid tuberculosis with basic excavation. Abscess and gangrene of the lung have a more acute onset and course, but the chronic cavities left by these conditions may give rise to difficulty. In such cases the history may be an important aid in diagnosis. In fetid empyema rupturing through the lung, particularly when of interlobar origin, the patient is generally acutely ill, there may be a history of pleurisy at the onset and possibly some evidence of mediastinal pressure or cardiac displacement. The rare condition of congenital cystic disease of the lung may give rise to some difficulty (see p. 1223).

Prognosis.—This varies with the cause. If due to aneurysm or growth, the duration is determined by these conditions. Bronchiectasis induced by a foreign body is generally permanent, even when the latter is removed, but it is not progressive. If the foreign body is not removed, complications generally supervene, and the course may be rapid. In bronchiectasis due to bronchial or pulmonary disease the course may extend into years, particularly if treatment is followed strictly, but sooner or later toxæmia and general or local complications supervene, with the result that the duration of life is inevitably considerably shortened.

Treatment.—Prophylactic treatment in cases of chronic bronchitis, delayed resolution in pneumonia and other conditions tending to fibrosis is of the utmost importance. This comprises respiratory exercises, climatic treatment, inhalations and vaccines.

The medical treatment of bronchiectasis consists in measures to promote the general health and well-being of the patient, to secure efficient emptying of the cavity, and to lessen or control the putrefactive processes occurring in it. The first of these involves a careful mode of life, adequate rest and change, a good and digestible diet, and medicines such as cod-liver oil, iron, quinine, strychnine or arsenic. The evacuation of the cavity may be promoted by postural methods, such as bending over the edge of the bed or stooping forwards. This can now be effectively secured by treating the patient on a Nelson bed. By X-ray and iodised oil (lipiodol) the exact position of the cavities in relation to the trachea can be determined, and the patient placed in the position best adapted to secure effective drainage. Expectorants, especially of antiseptic character, may be given, such as creosote, terebene, tar preparations, balsam of tolu or Peru, compound tincture of benzoin or the benzoates. If the sputum is tenacious, or if much bronchitis coexists iodides

and alkalis may be given in an ordinary expectorant mixture. To lessen the fetor, creosote is most frequently given in perles of 3 to 5 minims three times a day after food, or in an emulsion with cod-liver oil. Guaiacol carbonate and other creosote derivatives may also be tried. Syrupus allii, in 60 minim doses, is sometimes given, and is of value; but it is not always well tolerated by patients on account of its taste and tendency to repeat. Although these drugs are helpful, the amount of antiseptic reaching the cavity by the blood must necessarily be small. Attempts to secure more direct application by intratracheal injection and by inhalation have been made. The former method is now seldom used.

For inhalation purposes, solutions of volatile antiseptics are employed on a Burney-Yeo mask, such as creosote, terebene, menthol or eucalyptol in spirits of chloroform. The mask may be worn almost continuously or at intervals during the day. The creosote vapour bath is, however, the most satisfactory form of inhalation treatment, and is of great value. This should be given in a concrete-floored room without furniture. The patient is covered with a smock, the eyes are protected by closely-fitting goggles, and the nostrils by cotton wool plugs. A small quantity of creosote is heated in a metal dish, on a tripod over a spirit lamp. When the patient inhales the vapour, which quickly fills the room, violent cough is excited and the cavity is emptied. The ensuing deep inspirations carry down creosote-laden air into the air passages. The baths should be at first given on alternate days and last from 10 to 15 minutes. When the patient becomes accustomed to them, they may be given daily for half an hour or longer. The results are often strikingly beneficial. Vaccines made from the predominant organisms found in the sputum have been given with benefit in some cases. Surgical treatment is now more often employed than formerly. Repeated washing-out through a bronchoscope, at weekly intervals, is often helpful, giving comfort to the patient by diminishing the amount of sputum, and lessening or abolishing its fetor. Induction of artificial pneumothorax is sometimes of value, especially in early cases, in which it may be successful. Unfortunately it is often impracticable, owing to adhesions, and even in cases in which it is carried out, the beneficial effect only persists as a rule while the collapse is maintained. Temporary or permanent paralysis of the phrenic nerve has also proved helpful, especially in localised basal cases and in those secondary to abscess of the lung. Lebectomy or pneumonectomy is proving a satisfactory and effective method of cure in unilateral cases. The mortality from these operations is rapidly lessening with recent improvements in technique.

INJURY

External trauma applied to the chest-wall may cause rupture of a main bronchus. This is especially liable to occur after severe crushing accidents. One or other of the main bronchi may be completely severed from the trachea. The chief clinical feature presented in such a case is emphysema of the neck and upper portion of the chest-wall. Death usually ensues in 2 to 3 days.

R. A. Young.
G. E. Beaumont.

DISEASES OF THE LUNGS

HYPERÆMIA AND ŒDEMA

Hyperæmia of the lungs may be either active or passive. In the former there is an increased supply of arterial blood through the pulmonary and bronchial arterioles. In passive hyperæmia there is engorgement of the pulmonary venous radicles and capillaries. With both forms there is frequently œdema, due to the exudation of serous fluid into the lung alveoli. The term "congestion" is sometimes employed as an alternative to hyperæmia, but owing to its erroneous popular use it is best avoided.

(*a*) Active Hyperæmia

Ætiology.—This may occur in association with any acute inflammatory process affecting the bronchi, lungs or pleura. It sometimes results from the inhalation of pulmonary or bronchial irritants, such as poisonous gases or heated air. Severe muscular exertion and exposure to extreme cold are described as causes, but the former at least is doubtful. An important variety is that known as *collateral* or *fluxionary hyperæmia*, which occurs when there is obstruction to the circulation in the whole or part of one lung, from conditions such as a large or rapidly developing pleural effusion, an extensive and spreading pneumonia, or in association with pneumothorax. This may develop in the sound lung, or in the unaffected parts of that diseased. A primary form of acute hyperæmia, the "maladie de Woillez," has been recognised by French authors, but this is generally regarded as a mild or abortive pneumonia.

The clinical manifestations of acute hyperæmia are merged in those of the processes with which it is associated, and therefore do not need separate description.

(*b*) Passive Hyperæmia

Ætiology.—Passive hyperæmia may be produced by (1) conditions impeding the venous return from the lungs; (2) those leading to increased resistance to the passage of blood through the pulmonary capillaries, and (3) failure of the driving power of the right ventricle. The commonest causes of impeded return are left-sided heart lesions causing overfilling of, and increased pressure in, the left auricle. In mitral stenosis it may occur early and sometimes almost acutely, but aortic and myocardial lesions also lead to it, when the left ventricle fails and the mitral valve yields. Direct obstruction of the pulmonary veins sometimes results from external pressure by aneurysm, mediastinal tumour or enlarged bronchial glands, or from obstruction of the lumen by thrombosis. The passage of blood through the pulmonary capillaries may be impeded by emphysema, chronic bronchitis, pulmonary tuberculosis and fibrosis of the lungs. Failure of the right ventricle occurs in the late stages of right-sided heart lesions, with tricuspid regurgitation, and as a late sequel of left-sided failure.

Passive hyperæmia is obviously in the main dependent on mechanical

factors; it is not surprising, therefore, that gravity seems to play a part in the localisation of its effects, which are usually most marked in the bases or most dependent parts of the lungs. In bedridden, enfeebled or old patients, particularly if myocardial weakness or degeneration coexists, this factor becomes of great importance. Not infrequently some degree of œdema of the bases develops, and the condition is then called hypostatic congestion. If such an area becomes infected the resulting process is known as hypostatic pneumonia. Basal hyperæmia and œdema of the hypostatic type also result from toxæmia due to diseases such as enteric fever, from poisoning by drugs such as morphine, and as a terminal event in many cerebral lesions causing increased intracranial pressure.

Pathology.—The pulmonary veins and capillaries are engorged, with the result that the lung is darker in colour and heavier, while the alveolar walls and septa are swollen. If the condition persists for some time, pigment derived from the hæmoglobin of red corpuscles escaping by diapedesis is deposited in the epithelium of the alveoli and in the fibroblasts in the interalveolar septa. In long-standing cases the lung is firmer than normal and brownish-red in colour, a condition described as *brown induration*. If any degree of œdema is present, serous fluid is found in the alveoli on post-mortem examination, and on section of the lung frothy serous fluid exudes, which may contain some of the pigmented alveolar cells, constituting what are called "cardiac cells." Although congested and œdematous lung is heavier than normal, it usually floats in water.

Symptoms.—In slight degrees of hyperæmia these may be absent or negligible. In more advanced cases, they are those resulting from the impeded circulation through the lungs and the deficient aeration which this entails. Dyspnœa is the most prominent symptom, and it is generally a measure of the degree of hyperæmia. It is markedly increased by exertion of any kind, and in extreme degrees it is distressing and eventually alarming. It may be inspiratory or expiratory in type, and in the latter case it is sometimes described as cardiac asthma. In severe cases there is usually orthopnœa. Cough is almost invariably present, and there is usually some expectoration of frothy fluid, which may be blood-stained. The pigmented cells referred to above as "cardiac cells" may be found in it. Cyanosis is common and indicates the degree of anoxæmia. This may be associated with distension of the jugular veins, and there is often obvious distress. As in other forms of cyanosis there is usually some increase in the number of red corpuscles. The vocal fremitus at the bases may be diminished, the percussion note impaired, the breath-sounds weak and accompanied by rhonchi, crepitations or bubbling râles, although these signs are for the most part due to the associated œdema. In addition, the signs of the primary condition in the lungs or heart will be apparent.

Complications.—Pulmonary œdema and infarction are the chief complications.

Course.—If the venous engorgement cannot be removed, it usually tends to become progressively worse, whereas when it results from temporary cardiac embarrassment, recovery is usually complete as soon as the heart function is restored.

Prognosis.—This condition has to be distinguished from (1) chronic bronchitis, in which case there may be some rise of temperature and the

physical signs are more variable and more disseminated; (2) infarction, in which pain and hæmoptysis of sudden onset are the rule.

Prognosis.—This is so entirely dependent upon the nature and degree of the condition responsible for the engorgement that no general rule can be formulated.

Treatment.—In elderly patients, or those likely to be confined to bed for long periods, attention should be directed to the decubitus. This should be changed frequently, and if possible the patient should be permitted to sit up or to get into a chair, and encouraged to take a few deep breaths several times during the day. If the hyperæmia is associated with cyanosis and engorgement of the right heart, bleeding to the extent of 8 to 12 ounces may be helpful. If this is not practicable, the application of 6 leeches over the liver, or dry cupping of the bases of the lungs may be tried. Free purgation and the administration of diuretics, notably injection of mersalyl (salyrgan) or neptal may also help indirectly to relieve the engorgement. In cases associated with cardiac failure, the administration of cardiac tonics, such as digitalis, strophanthus or squills, the injection of strychnine, camphor in oil or niketha mide (coramine) may all be of assistance. Moderate hæmoptysis should not be checked, and cough, if effective, may be promoted by suitable expectorants. In cardiac cases a "régime lactée" or strict milk diet is advocated by some French physicians.

(c) Acute or Hyperacute Pulmonary Œdema

In this condition flooding of the alveoli with the serous exudate from the pulmonary capillaries occurs with great rapidity.

Ætiology.—It is more commonly met with after the age of 40 than before, although cases have been recorded in children. It is considerably more frequent in the female than in the male sex. Arterial disease and hypertension are the most common antecedents, but acute or chronic renal disease and pregnancy may all act as predisposing factors. It sometimes occurs in diabetes. The actual exciting cause is often obscure, and probably varies in different cases. A heavy meal, an epileptic fit, or the administration of an anæsthetic may be the immediate cause in those predisposed. In other cases it may be a manifestation of angio-neurotic œdema. Sometimes paracentesis of a pleural effusion is quickly followed by œdema, no doubt as a result of a collateral hyperæmia. It has occurred after "gassing" by chlorine. In diabetes the lipæmic condition which sometimes occurs has been suggested as the determining factor, possibly causing multiple fat embolism. Coronary occlusion and acute left ventricular failure are noteworthy causes. In some cases dissociation of the action of the two ventricles has been supposed to be the cause, the right contracting forcibly while the left is in an enfeebled or asystolic condition. In support of this contention may be adduced the fact that acute pulmonary œdema has been observed after rupture of the chordæ tendineæ of the mitral valve.

Pathology.—The alveoli are found to be flooded with a thin serous exudate. The lungs are heavier than normal, sodden, and on squeezing exude large quantities of greyish-yellow or pinkish fluid. Frothy fluid of similar character is found in the bronchi and even in the trachea and naso-pharynx in hyperacute cases.

Symptoms.—The onset is sudden, and generally occurs when the patient is lying down, hence being most frequently observed at night. The patient awakes with intense dyspnœa, and a sense of suffocation, then frequently rolls or rushes about in the endeavour to breathe, even clutching at the throat. Cyanosis is present, and the aspect is one of anxiety and alarm. Frothy fluid, often pink in colour, may soon stream from mouth and nose, or be brought up in great gulps. The chest movements are hurried, and the accessory respiratory muscles are in violent action. Vocal fremitus is diminished over the lower lobes. The percussion note soon becomes impaired over the lungs, commencing at the bases. The breath-sounds are at first vesicular or harsh with prolonged expiration, then become faint and may be obscured by bubbling râles or crepitations, audible all over the chest. Voice conduction is diminished.

Complications and Sequelæ.—Owing to its acute and rapid course, complications do not occur. Bronchitis may result as a sequela.

Course.—The malady usually lasts only minutes or hours. Unless it remits, or treatment affords relief, the patient rapidly becomes unconscious and death follows, the heart continuing to beat after respirations have ceased.

Diagnosis.—The affection is usually so characteristic that the diagnosis is obvious. In the more protracted cases the dyspnœa and the physical signs are not unlike those of acute suppurative bronchitis or suffocative catarrh and broncho-pneumonia; but in both of these there is some degree of fever and the expectoration is less copious, and when it occurs is usually of purulent or muco-purulent character. The nocturnal onset of œdema may suggest asthma; but the physical signs and the late and scanty expectoration in the latter suffice to distinguish it.

Prognosis.—The prognosis is always very grave; but prompt treatment has saved some cases. Death may occur in less than 10 minutes, or be delayed for 24 or 48 hours. In the angio-neurotic type repeated attacks may occur.

Treatment.—The most successful treatment is the immediate subcutaneous injection of gr. $\frac{1}{4}$ morphine. Good results have also followed the injection of gr. $\frac{1}{100}$–$\frac{1}{50}$ atropine sulphate hypodermically. These are often given together. Oxygen inhalation by nasal catheter or special mask such as the B.L.B. variety may be used. Prompt venesection has been recommended, and should be tried if possible.

(*d*) Chronic Pulmonary Œdema

This is usually the sequel of chronic passive hyperæmia, and the causes and symptoms are those of that condition. It may also occur in chronic renal disease. In marked degrees of œdema, however, the signs may closely simulate those of pleural effusion, save for the displacement of the cardiac impulse. It is important to remember that some degree of hydrothorax may occur as a complication, and increase the difficulty in diagnosis.

INFARCTION OF THE LUNGS

Infarction of the lungs or "pulmonary apoplexy" results when a branch of the pulmonary artery becomes occluded by embolism or thrombosis.

Ætiology.—*Embolic forms.*—The obstructing plug may originate in any part of the systemic venous system, in the right side of the heart or on its valves or in the pulmonary artery itself. The commonest peripheral cause of embolism is detachment of a thrombus in cases of thrombo-phlebitis. This may occur in the veins of the lower extremity, or in those of the uterus after childbirth. Thrombosis with embolic detachment may also develop in prolonged or wasting diseases, such as enteric fever, tuberculosis and cancer; in acute processes, such as influenza, septicæmia and pyæmia; and in localised septic lesions, such as otitis. Pulmonary embolism is not infrequently observed after abdominal or pelvic operations, and after the radical cure of hernia or hæmorrhoids.

Intracardiac thrombi from the right auricle or ventricle, becoming detached, lead to embolism, and this occurs especially in cases of right-sided heart failure secondary to left-sided valve lesions. Vegetations forming on the tricuspid or pulmonary valves in septic endocarditis on detachment produce pulmonary infarction. Rarer causes are fat embolism after injury to bone or to a fatty liver, the entry of pieces of new-growth or hydatid daughter-cysts into systemic veins, and even air embolism.

The exciting cause of embolism is not infrequently sudden movement or strain leading to detachment of a thrombus or vegetations.

Thrombotic forms.—Thrombosis occurs as a secondary process around pulmonary emboli; but it is probable that some cases of infarction are due to a primary thrombosis. This condition may be produced by some acute or chronic pulmonary disease, such as gangrene, tuberculosis and fibrosis, and by atheroma of the pulmonary artery. Any process leading to chronic venous hyperæmia may also cause it. A rare cause is thrombo-phlebitis migrans.

Pathology.—Although the pulmonary arteries are not strictly speaking end arteries, since there is some degree of anastomosis between them and the bronchial arterioles, yet the result of their obstruction is to produce infarcts comparable with those in other organs. The origin of the blood in the obstructed area has been much discussed. Cohnheim regarded it as the result of regurgitation from the veins, a view subsequently disproved, since the infarct is hæmorrhagic even when the veins are also obstructed. It is now regarded as due to influx from the anastomosing bronchial capillaries into the pulmonary capillaries, and the escape of this blood from the latter owing to their altered nutrition. It is generally accepted that embolism is much more common than thrombosis. It has been suggested that some infarcts are not obstructive, but are the result of hæmorrhage *per rhexin* in cases of extreme passive hyperæmia, and that the shape is due to the alveolar distribution of the bronchial area affected. If a large embolus has caused sudden death, it will be found arrested at the bifurcation of a large branch of the pulmonary artery, or even in one of the main divisions of that vessel. In such cases there has not been time for pulmonary changes to occur, and the chief post-mortem condition found is engorgement of the right side of the heart.

In post-mortem examination of cases where smaller emboli have led to infarction, the infarcts are usually found in the lower lobes, more commonly in the right lung. They extend to the surface in the majority of cases, and can be seen before section as slightly raised, dark red areas, with the over-

lying pleura a little roughened from inflammatory exudate. They feel hard and firm, and on section are typically wedge-shaped, with the base on the surface and the apex centrally placed. In the rare deep-seated infarcts a spheroidal form is the rule. When recent, an infarct is dark red in colour, and suggests hæmorrhage with clot formation, hence the term "pulmonary apoplexy." In some cases infarcts have a purplish hue, and are said to resemble the colour of damson cheese; later they change to brownish-red. Infarcted areas sink in water. There may be a single large infarct almost occupying one lobe, sometimes only a small one, or several of varying size and age scattered throughout the lungs. In some cases a fortunate section may reveal the embolus with its ensheathing thrombus, but sometimes a thrombus only is found. Microscopically, the alveoli and finer bronchioles are filled with red blood corpuscles, and there is a sharp delimitation from the healthy lung. If the embolus is infective, suppuration occurs, and abscess or empyema ensues.

Symptoms.—If a large embolus blocks one of the main divisions of the pulmonary artery, there is sudden intense dyspnœa, pain in the chest, distress, cyanosis, and rapid unconsciousness, death resulting in a few minutes from asphyxia. In other cases the patient gives a short cry, and falls unconscious, death occurring almost immediately from syncope. In some cases unconsciousness develops so rapidly, and the respiratory symptoms are so little apparent, that a cerebral vascular lesion may be suspected. On the other hand, life may be maintained for several minutes or even hours, the patient being unconscious or in acute distress and anxiety with urgent dyspnœa, lividity and cyanosis. Respiration is deep and laboured, but fails to give relief to the sense of suffocation. In such cases also, death may result eventually from asphyxia or syncope, or the patient may slowly recover. In less severe forms, such as occur in cardiac and in some post-operative cases, there is sudden pain with difficulty in breathing, followed in a few hours or in a day or two by cough with hæmoptysis or by the expectoration of deeply blood-stained mucus persisting for some days, and slowly clearing up. If the embolus is infective, fever, often of hectic type, results, sometimes delayed for a day or more.

In the severe cases there is cyanosis, distension of the veins of the neck, acute anxiety with exophthalmos and cold, clammy skin. The only physical signs apparent are the deep, laboured breathing, the harsh breath-sounds, and the evidence of cardiac embarrassment with feeble, failing pulse.

In less severe cases the signs are also not characteristic. There are evidences of cyanosis and distress of less urgent character, possibly some limitation of movement on the affected side, increase of vocal fremitus, localised dullness, with weak or absent breath-sounds, and sometimes a pleural rub. In some cases definite bronchial or tubular breath-sounds may be audible. A few fine râles are sometimes present in the adjacent lung areas.

Complications and Sequelæ.—Localised dry pleurisy is almost invariably present. With infective emboli, abscess or gangrene, and later empyema may result. In organisation an infarct leads to a localised area of fibrosis.

Course.—As already described, death may occur from asphyxia or syncope in the course of a few minutes or hours, although recovery occurs in some very severe cases. In the less severe forms, after the initial urgent symptoms

have passed off, recovery is often rapid and uneventful, save for pain, cough and bloodstained expectoration.

Diagnosis.—The dramatic onset, the history and the associated lesions of the veins or heart render diagnosis easy as a rule; but it may be necessary to eliminate other causes of hæmoptysis, notably pulmonary tuberculosis and chronic venous hyperæmia.

Prognosis.—This depends largely upon the initial shock. The prognosis is very grave when the patient rapidly becomes unconscious. As there is less likelihood of sepsis in cases due to cardiac lesions than in those due to localised venous thrombosis, the prognosis is rather better in the former; but, on the other hand, organisation of a clot in a vein may completely remove the source of the emboli, while the source often persists when they are derived from the heart.

Treatment.—The coagulability of the blood may be lowered by the administration of 30 grains of sodium citrate three times daily. This is a wise prophylactic measure in prolonged illness, especially when a milk régime is being enforced. When thrombosis has occurred in a peripheral vein, such as in the leg, the affected limb should be immobilised until organisation of the clot has taken place. Morphine is useful in quieting a patient if there is much mental distress when a pulmonary infarct forms; but usually the patient is collapsed and stimulant measures are indicated. An injection of morphine gr. $\frac{1}{6}$, atropine gr. $\frac{1}{100}$, and strychnine gr. $\frac{1}{30}$ is found of value in some cases. If there is dyspnœa oxygen should be administered. Venesection to the extent of 10 or 12 ounces may be tried in cases where there is marked lividity with a forcibly acting heart. Hæmoptysis, when it occurs, should not be checked. Pain may be relieved by leeches, cupping or by application of iodine. In cases with heart failure the appropriate treatment by cardiac tonics should be administered. A few cases are on record in which immediate surgical aid has been available and the operation of embolectomy has been successful.

COLLAPSE OF THE LUNGS

In collapse of the lungs the alveoli are completely or partly devoid of air. The condition may be congenital, and due to non-expansion of the lung, when it is referred to as atelectasis. On the other hand, collapse may be the result of removal of the air from lung tissue previously expanded, when it is called apneumatosis or acquired collapse. The three terms—collapse, atelectasis and apneumatosis—are, however, used as synonyms by many writers.

Atelectasis or Congenital Collapse

Ætiology.—This condition occurs in still-born and in premature infants, and probably persists to some degree for weeks or even months in weakly children. It may result from immaturity or from weakness of the inspiratory muscles, and from obstruction of the air passages by mucus and meconium. It may be a consequence of disease, such as congenital syphilis or lesions and developmental defects of the nervous system.

Pathology.—Atelectasis is due to failure of the respiratory mechanism

to draw air into the alveoli and expand them, as occurs normally with the first few inspiratory efforts of the newborn infant.

Atelectatic lungs are solid, airless and small. They are usually described as presenting appearances similar to those of adult liver as regards colour and consistence. In partial atelectasis the lung appears mottled, and small expanded areas of pinkish colour may project from the surface. The condition is chiefly of medico-legal and pathological interest.

Apneumatosis or Acquired Collapse

Collapse of previously expanded lung may be active or passive, the former being due to active shrinking of the lung owing to defects in the inspiratory musculature, the latter to conditions disturbing the pressure relations within the thorax.

1. Active Pulmonary Collapse.

Synonyms.—Active Lobar Collapse; Massive Collapse.

Ætiology.—This condition was first described by William Pasteur in 1890 in cases of diphtheria associated with paralysis of the diaphragm. In 1908 he pointed out that it occurred also as a sequel of operations, especially of those upon the abdominal organs, less frequently of those upon the neck and pelvis. It is highly probable that many post-operative lung conditions formerly recorded as pneumonia were in reality due to active collapse. It may also follow after injuries, such as those resulting from falls from a bicycle or a horse. During the War of 1914–1918, when chest wounds were collected in special hospitals, it was found that massive collapse was not infrequently an important complication of penetrating and non-penetrating wounds of the chest. It was also noticed in some cases after severe wounds of the buttocks and pelvis.

Pathology.—The mechanism by which deflation results is obscure, and is the subject of controversy. Pasteur regarded the condition in the diphtheritic cases as due to paralysis of the diaphragm through the phrenic nerves or their nuclei, and in the post-operative and traumatic cases as a consequence of reflex inhibition of this muscle. Briscoe, on experimental, pathological and clinical evidence discards Pasteur's explanation. He maintains that the deflation is caused by an exaggeration of the normal phenomena of breathing in the supine position, in which he states that the crural portion of the diaphragm alone contracts, the costal portion being in abeyance. In the supine position, with quiet breathing, deflation of the lower lobes occurs, and this is promoted by conditions of debility, toxæmia or operation. The clinical manifestations described by Pasteur are regarded by Briscoe as the result of superadded pleurisy, or of inflammation of the crura of the diaphragm.

Boland and Sheret have put forward the suggestion that massive collapse is due to obstruction of the bronchi, followed by removal of the air in the corresponding lung areas by absorption into the blood stream. The obstruction is supposed to be due to increased secretion and the inhibition of the cough reflex.

Post mortem, the lower lobe of one lung is usually found to be deflated and retracted towards the spine. Sometimes the whole of one lung may be affected, or both lower lobes. The collapsed area is bluish-red, firm, does not crepitate and sinks in water. Pleurisy or pneumonic changes may be

seen, and these are regarded by Pasteur as secondary to infection of the deflated lung, the resistance of which is lowered, and by Briscoe as the essential factor in the production of the symptoms. In massive collapse the heart and mediastinum are displaced towards the affected side, and the sound lung is often bulky and distended.

Symptoms.—The symptoms commonly commence within 24 or 48 hours of the injury or operation, although they may rarely be delayed for 5 to 7 days. The onset is generally sudden, with pain in the lower part of the thorax or behind the sternum. Severe dyspnœa quickly follows, and the patient appears dusky, cyanosed and alarmingly ill. Cough, with viscid mucoid expectoration, generally develops in a few hours. The latter may become copious and muco-purulent if pneumonic changes ensue. The pulse and respirations are markedly increased in rate, and the temperature not infrequently rises to 103° F. Occasionally the onset is more gradual with pain and cough, and in some cases of wounds it may give rise to few symptoms and be discovered only on routine examination.

Examination of the chest shows diminished movement on the affected side, and often absence or reversal of epigastric excursion with respiration, whereas the movement on the other side may be exaggerated. In other respects the signs usually simulate those of lobar pneumonia. Over the collapsed lung the vocal fremitus is increased, the percussion note is dull, the breath-sounds are tubular, and bronchophony and whispering pectoriloquy are present; but as a rule there are no adventitious sounds, although occasionally rhonchi and a few fine râles may be heard. In some cases the breath sounds are very weak or almost absent, and voice conduction is diminished. Over the healthy lung, loud and harsh breathing is audible. The displacement of the cardiac impulse towards the collapsed lung is a point of cardinal importance. It is noteworthy that in certain cases of gunshot wounds of the chest the collapse affects the contra-lateral lung.

Complications and Sequelæ.—Bronchitis, lobar pneumonia, or pleurisy may occur as complications. There are usually no sequelæ, except that pleural adhesions may occur.

Course.—The course of the affection is rapid. After periods extending from 2 to 5 days the temperature falls to normal, the symptoms disappear, the lung quickly re-expands, the heart returns to its normal position, and there is complete recovery.

Diagnosis.—The most important conditions from which this malady has to be distinguished are lobar pneumonia, pulmonary embolism, pneumothorax and pleural effusion. The position of the cardiac impulse is often the deciding factor: in collapse it is displaced towards the lung involved, in pleural effusion and pneumothorax it moves away from the affected side, whereas in lobar pneumonia there is usually no cardiac displacement, although there may be dilatation. Labial herpes and blood-stained expectoration are frequently seen in pneumonia, but not in collapse. When in right-sided collapse there is marked distension of the left lung with obliteration of the normal cardiac dullness, the signs superficially resemble those of a left-sided pneumothorax; but with careful examination no such error should be made. The distinction from pulmonary embolism may be difficult at first, but the localisation of the signs, and the blood-stained expectoration, may give useful indications.

Treatment.—PROPHYLACTIC.—The administration of morphine and atropine before the anæsthetic, propping up of the patient in bed as soon as possible after it, and the insistence upon periodic deep breaths are useful measures in preventing the onset of lobar collapse. When the "collapse attack" develops oxygen should be administered and pain relieved by local applications, such as leeches or poultices, or by an injection of morphine, atropine and strychnine. Expectorants may be given if the cough is ineffective, and cardiac tonics, such as digitalis, strophanthus and caffeine if there is much cardiac embarrassment. Injections of strychnine or coramine are useful if the patient is collapsed at the onset. Bronchoscopic aspiration has been recommended in cases of post-operative massive collapse.

2. PASSIVE PULMONARY COLLAPSE.

This form of collapse may affect the whole of one lung, or be confined to one lobe or to groups of lobules.

Ætiology.—Total collapse is generally the result of pleural effusion, empyema, pneumothorax or obstruction of a main bronchus. In a large effusion and in pneumothorax collapse is complete, unless the shrinkage is prevented by adhesions. In a smaller effusion, the process may be limited to the lower parts of the lung. Other causes of lobar or partial lobar collapse are conditions leading to complete obstruction of a main bronchial division, particularly new-growth, aneurysm or foreign body. It also occurs in aged or bedridden patients, or in those with enfeebled inspiratory muscles, when prolonged fever has enforced a dorsal decubitus. Abdominal distension from tympanites or ascites can also cause collapse of the bases of the lungs.

Lobular collapse results from any condition impeding the air entry to the smaller bronchi or bronchioles, such as bronchitis, broncho-pneumonia, pulmonary tuberculosis, whooping-cough and diphtheria. Obstruction of the naso-pharynx by enlarged tonsils and adenoids may cause partial collapse, especially in the upper lobes.

Pathology.—The deflation of the lung area may be produced in three ways—(1) By complete obstruction to the air from blocking of a bronchus or bronchiole, the residual air being absorbed; (2) by enfeeblement of the inspiratory mechanism similar to the process in active collapse; and (3) by disturbance of the intrapleural pressure by fluid or air, the lung at first contracting in virtue of its elasticity until the intrapleural pressure becomes equal to that of the atmosphere, when any further accumulation of fluid or air causes positive pressure and compression of the collapsed lung.

Post mortem, in complete or lobar collapse the appearances are similar to those in active collapse. In lobular collapse the deflated areas are contracted and depressed below the level of the healthy lung. They are dark red or slaty in colour, while the adjacent areas are pinkish and often emphysematous. The collapsed areas do not crepitate.

Symptoms.—Total collapse of the lung or of a lobe being usually a secondary process, the symptoms and signs are masked by those of the primary condition, such as pleural effusion, pneumothorax, growth or aneurysm. It can, however, usually be demonstrated by X-ray examination, the collapsed lung being apparent as a fairly dense shadow lying alongside the vertebral bodies. Not infrequently, however, in pleural effusion definite tubular breath sounds, with bronchophony and pectoriloquy, may

be audible in the relatively dull area above the level of the fluid posteriorly, and these signs are due to the collapsed lung. In aortic aneurysm, or less commonly in mediastinal, pulmonary and bronchial neoplasms, distinctive signs due to the local collapse may be apparent. These consist of slightly diminished movement of the corresponding part of the chest wall, with diminution of vocal fremitus and impairment of percussion note or actual dullness. Breath-sounds are weak, as a rule, but may be bronchial or tubular. Voice conduction is increased, and in incomplete collapse crepitations are often audible. The cardiac impulse may be displaced towards the affected side, but this is less apparent than in active collapse, and it is not infrequently displaced to the opposite side by the primary condition. Lobular collapse gives rise to no symptoms which can be differentiated from those of the condition inducing it.

Complications and Course.—The lung usually re-expands wholly or in part when the condition causing collapse has been removed. Thus a lung that has been maintained continuously collapsed by artificial pneumothorax, with repeated refills for as long as 4 years or more, will re-expand when the gas in the pleural cavity is not replaced. In chronic effusion, or in large or neglected empyemata, re-expansion may be incomplete, and some falling in of the chest wall results. Fibroid changes may occur in lung tissue which has been long collapsed.

Diagnosis.—This is frequently a matter of inference, owing to the nature of the primary disease. Valuable help may be afforded by X-ray examination.

Treatment.—No special treatment apart from that of the condition causing the collapse is required. If a pleural effusion is slow to absorb, the necessity for paracentesis or gas replacement, to avoid pleural thickening, may have to be considered.

HÆMOPTYSIS

It should be recognised that hæmoptysis is a symptom, not a disease. It is here considered separately because the accurate diagnosis of its origin is essential to its treatment, which differs widely in different conditions.

Definition.—The term hæmoptysis is arbitrarily restricted to the expectoration of blood, entering the air passages from structures below the larynx or from the larynx itself. When the blood is derived from the naso-pharynx or mouth it is sometimes described as spurious hæmoptysis.

Ætiology.—1. **Pulmonary tuberculosis** is the commonest cause, the blood being derived from an aneurysm in a pulmonary cavity, or from ulceration of a small vessel, or congestive processes around the early lesions.

2. **Chronic venous congestion**, particularly in mitral stenosis. These two conditions account for the majority of cases.

3. **Inflammatory and destructive diseases of the lungs, air passages or pleura**, such as pneumonia, broncho-pneumonia, especially the influenzal variety, abscess, gangrene and bronchiectasis with ulceration of the walls. A latent bronchiectasis without sputum may cause recurrent hæmoptysis (*forme hémoptoïque sèche*). Pneumokoniosis, streptotrichosis and ulceration of the larynx, trachea or bronchi from tuberculosis, gumma or new-growth

may also be associated with hæmoptysis. Breaking down of a caseous or calcareous bronchial gland is a rare cause, as also is rupture of an empyema through a bronchus.

4. Infarction of the lung from embolic or thrombotic obstruction.

5. New-growths of the lung, bronchi or mediastinal glands.

6. An aortic aneurysm may cause hæmoptysis by "weeping" through an eroded bronchus, or by direct rupture, the latter being of course immediately fatal.

7. Traumatic causes.—Injury may cause hæmoptysis, by fractured ribs wounding the lung, by contusion and by breaking down of healed tuberculous lesions. Hæmoptysis occurs frequently in wounds of the chest, both penetrating and non-penetrating. A foreign body, such as a piece of shrapnel, may lie dormant for years, and then cause recurrent hæmoptysis.

8. Certain abnormal blood conditions, chiefly leukæmia, purpura, hæmophilia, scurvy, minor degrees of vitamin C deficiency and occasionally pernicious anæmia. Hæmoptysis occasionally occurs in the malignant specific fevers, especially small-pox and measles.

9. Parasitic causes, such as pulmonary distomatosis and spirochætosis, are common in Asia but rare in Europe. Hydatid disease of the lung may cause repeated slight hæmorrhages.

10. Vicarious menstruation.—Some cases in women have been regarded as vicarious menstruation, and this view dates back to Hippocrates. It is probable, however, that most cases are to be explained as due to leakage from obscure pulmonary lesions.

11. Hæmoptysis occasionally occurs in apparently healthy persons. In some, with high systemic arterial tension, it is probable that the pulmonary arterial pressure is also raised, and the condition may be regarded as analogous to the epistaxis which occurs more commonly in such patients. Sometimes the hæmoptysis is due to leaking from an old arrested tuberculous lesion.

12. Rupture of an hepatic abscess or hydatid cyst through the diaphragm into a bronchus is an occasional cause.

Spurious hæmoptysis is usually due to staining of the saliva or the pharyngeal secretion with blood, generally derived from the gums, which are spongy and congested, often from early pyorrhœa. The condition is common in anæmic girls, and is, as a rule, observed in the morning. Hæmorrhage from an enlarged pharyngeal vein is often suggested as a cause, but is rarely seen. Hæmorrhage after tooth extraction, and staining of the mucus expectorated after epistaxis, are other causes of spurious hæmoptysis.

Pathology.—From the list of causes it might be inferred that the origin of the blood differs in different cases. It may come from the pulmonary or bronchial vessels in pulmonary tuberculosis and other lung or bronchial conditions, and also in chronic venous congestion or infarction. It may come from the thoracic aorta direct, or from some of its branches, in aneurysm and mediastinal new-growth, and from the hepatic vessels in abscess of the liver. In cases due to disease of the trachea and larynx it comes direct from the vessels supplying them.

Post mortem, the larynx, trachea and bronchi may contain clots, or blood-stained froth and mucus, and their walls may be stained in places. Dark reddish areas of lobular distribution, due to inhaled blood, may be seen

in various parts of the lungs, particularly at the bases. Sometimes this may induce bronchitic changes, described as hæmoptoic bronchitis. Careful search in cases of profuse hæmoptysis will usually reveal the source of the hæmorrhage, and in pulmonary tuberculosis this is generally a ruptured aneurysmal dilatation in a cavity or an ulcerated vessel. The aneurysm may be small and escape notice unless many cuts are made into the lung.

Symptoms.—In hæmoptysis, the patient often experiences a tickling in the throat, followed by a gush into the mouth with a salt taste, and on expectoration notices blood. The alarm and anxiety this occasions lead to restlessness and rapid action of the heart. If the bleeding is profuse, cough is frequent, and large clots, together with liquid alkaline blood, may be expectorated to the extent of 20 or 30 ounces in a few hours. The bleeding may cease temporarily, to recur at intervals for several days, until the patient becomes blanched, weak and syncopal, with rapid, weak pulse. In any profuse hæmoptysis, death may occur in a few minutes, either from asphyxia or syncope. In the former case, the blood, at first bright and arterial, is soon dark and frothed, while the patient becomes cyanosed and livid. In slighter degrees of hæmoptysis there may be only streaks, small clots or liquid blood mixed with ordinary sputum. After the actual bleeding has ceased, the sputum may be blood-stained for some days, owing to the expectoration of blood inhaled into other parts of the lungs. This can be recognised by its colour, which varies from dark red to brown, owing to the changes undergone by the blood pigment.

Diagnosis.—This involves two problems—first the differentiation from hæmatemesis and spurious hæmoptysis, and secondly the recognition of the cause of the hæmorrhage. If the patient is seen at the time of the bleeding the first of these is easy. The nature of the blood, and its association with cough and possibly with pulmonary or cardiac signs, are conclusive. When the diagnosis has to be made upon the history given by the patient or by friends it may be difficult, especially in the absence of physical signs.

In hæmatemesis there is frequently gastric pain and faintness before the vomiting, the blood is acid in reaction, dark in colour, even brown from acid hæmatin, and is sometimes mixed with food. The fact that in hæmoptysis blood may be swallowed and subsequently vomited increases the difficulty. Patients often give very dubious answers to questions as to whether the blood was coughed or vomited up. They should then be questioned as to whether sputum was brought up on the following day, and, if so, whether it was blood-stained. In cases of doubt the investigation of the pulmonary and abdominal physical signs, when the patient's condition permits, may decide the diagnosis.

The utmost caution should be exercised to exclude tuberculosis before making a diagnosis of "spurious hæmoptysis." Only when there are no pulmonary symptoms, signs or X-ray indications, and when some obvious cause, such as anæmia or pyorrhœa, is found, is it safe to do so.

While distinguishing between the various causes of hæmoptysis it is well to regard and to treat it as due to pulmonary tuberculosis until some other cause is conclusively established. The sputum should be examined for tubercle bacilli on several occasions, the temperature recorded and the physical signs including X-ray appearances most carefully watched.

The presence of a valvular lesion, especially mitral stenosis with signs of

pulmonary engorgement, may render the cause of hæmoptysis clear. When tuberculosis and cardiac disease can be excluded, a careful study of the history, the symptoms and signs, may throw light on the diagnosis or suggest some investigation which will serve to establish it, *e.g.* examination of the sputum for parasites and hydatid hooklets, the cytological examination of the blood and an X-ray examination.

In other cases, as in bronchiectasis, abscess or gangrene, the history, the physical signs and the nature of the sputum are often characteristic.

In the latent or silent form of bronchiectasis (forme sèche), the condition may be revealed only by lipiodol injection.

Bronchoscopy may be of great value in revealing the presence of adenoma or carcinoma.

Prognosis.—Apart from hæmoptysis, which is rapidly fatal, due to aneurysm or pulmonary tuberculosis, the immediate prognosis in cases of pulmonary hæmorrhage is not unfavourable, even when it continues for days. The ultimate prognosis depends upon the cause.

Treatment.—This is so entirely dependent upon the cause and origin of the bleeding that reference should be made to the corresponding diseases.

EMPHYSEMA OF THE LUNGS

Emphysema of the lungs, or alveolar-ectasis, is a condition of distension of the alveoli; it is usually progressive and is associated with definite changes in the inter-alveolar walls. The following varieties are generally recognised—(1) Large-lunged or hypertrophic; (2) small-lunged or atrophic; (3) compensatory; (4) acute vesicular; and (5) acute interstitial emphysema. The last-named condition has no relation to true emphysema except in name, but will be described in this group for convenience.

1. Large-Lunged or Hypertrophic Emphysema (Substantive or Idiopathic Emphysema)

This is a chronic affection and is usually bilateral.

Ætiology.—*Predisposing causes.*—It may occur at any age, even in childhood, but is most frequently seen in middle and late adult life. It is commoner in men than in women, probably because they are more exposed to the conditions inducing it. Although not strictly hereditary, it often shows a familial incidence. Certain occupations are credited with being concerned in its production, notably those involving violent or prolonged muscular effort with closed or partially closed glottis, such as blowing wind instruments and lifting heavy weights. Dusty occupations also favour its onset by leading to bronchitis and cough.

The common *exciting cause* seems to be the strain of prolonged and repeated cough, induced by chronic bronchitis, bronchiectasis, asthma, whooping-cough, cigarette smoke inhaling, and other causes of irritation of the upper air passages.

Pathology.—The pathogenesis of emphysema has been much debated and various explanations have been offered. (1) **Primary degeneration theory.** Villemin suggested that the essential lesion was a fatty degenera-

tion of the alveolar walls, while Cohnheim believed that there was a congenital defect of the elastic tissue of the lung. (2) The inspiratory theory, first suggested by Laennec and developed by Gairdner, postulates the force of inspiration as the distending agent. (3) The expiratory theory, first enunciated by Mendelssohn, was independently brought forward and established by Jenner. The distension of the alveoli is regarded as due to the effect of forced expiration and cough. Jenner pointed out the special and early involvement of the apices, the anterior and lower margins of the lungs; in other words, the parts least supported by the thoracic cage. (4) Freund regarded the changes in the lungs as secondary to calcification of the costal cartilages, the chest becoming fixed in the inspiratory position and the lung permanently expanded in consequence. The expiratory explanation is now generally accepted, and emphysema is regarded as the result of increased intra-alveolar tension, due to violent expiratory efforts, acting on walls weakened by congenital defects, by inflammatory processes or by toxic agents, such as alcohol (Nothnagel).

The characteristic conformation of the chest is usually apparent (see Symptoms), the costal cartilages are often calcified, and on opening the thorax post mortem, the lungs bulge instead of retracting, so that the pericardium may be almost completely obscured. They are pale in colour, even in town-dwellers, a condition called albinism of the lung by Virchow. They are soft and pit on pressure, and, as described by Laennec, give the sensation of a down pillow. The surface of the lung under the pleura shows a finely vesicular appearance, due to the distension of the alveoli, the vesicles often being nearly as large as pins' heads. Not infrequently large bullæ or blister-like protuberances, varying in size from a pea to a Spanish olive, occasionally much larger, may be seen projecting from the surface, particularly at the apices and margins. These bullæ when incised show fine fibrous bands crossing them, the remains of inter-alveolar walls and of atrophied blood vessels. It was formerly customary to refer to such cases as bullous or marginal emphysema and to describe those in which the dilatation is less obvious but more widely diffused as general emphysema; but the conditions are so commonly associated together in varying degrees that little is gained by so doing. On section the lungs are pale and dry, except at the bases, where there is frequently some œdema in advanced cases. The bronchi may show some general dilatation, although less commonly than might be expected from the close similarity of the causal factors of emphysema and bronchiectasis. When bronchitis coexists, muco-pus can be squeezed from the cross-sections of these tubes. As pointed out by Fowler, pleural adhesion is relatively uncommon. The infundibula and alveoli are dilated, and the inter-alveolar walls are thin and atrophic, even disappearing wholly or in part. The distension and coalescenec of adjacent alveoli result in the formation of bullæ. The calibre of the pulmonary capillaries is diminished by stretching of the alveolar walls, and where atrophy of the inter-alveolar septa occurs the capillaries are destroyed. These two processes result in a considerable diminution in the total aerating surface, and cause the dyspnœa and cyanosis characteristic of the disease. Moreover, the normal anastomoses between the terminal bronchial and pulmonary capillaries increase considerably, and some of the blood in the latter may therefore fail to reach the alveoli and so escape aeration. Atrophic changes in the elastic tissue

have been described. In order to maintain the circulation through the diminished capillary area, the right ventricle hypertrophies and the resultant raised blood pressure sometimes induces atheroma of the pulmonary artery. Emphysema being a progressive lesion, and the defective aeration of the blood perhaps interfering with the nutrition of the heart muscle, cardiac failure eventually ensues, causing tricuspid regurgitation, engorgement of the right auricle, and the visceral effects of venous engorgement, such as "nutmeg" liver. Cabot states that true emphysema is often not found post mortem in cases so diagnosed during life, and prefers to designate the clinical entity here described as "the Barrel Chest."

Symptoms.—Dyspnœa of varying degree is the most characteristic symptom. In uncomplicated cases of moderate extent it is only present on exertion, unless bronchitis coexists. In advanced emphysema, dyspnœa is marked and becomes extreme in the bronchitic or "asthmatic" attacks and in foggy weather. Cyanosis is common, and is to some extent a measure of the degree of emphysema. Varying degrees of polycythæmia may be observed. The patient may walk about with a more extreme degree of cyanosis than in any other condition except congenital heart disease. Clubbing of the fingers of moderate degree is common. Cough is usually due to the associated bronchitis, and is worse in the winter and in foggy weather. It is frequent, noisy and often hacking and paroxysmal. Expectoration is also the result of the bronchial catarrh, and varies from a few grey mucoid pellets to copious muco-pus.

The chest is enlarged, particularly in the anteric-posterior diameter, the upper thoracic spine is rounded and kyphotic, the sternum protrudes forward, and the angle of Louis is prominent, the general effect being the so-called barrel-shaped chest. The ribs run forward more horizontally and the intercostal spaces are wider than normal, the chest being as a whole in the inspiratory position. The respiratory movements are much restricted, the patient elevating the rigid thorax with little expansion on taking a deep breath, so that the inspiratory increase at the level of the nipples may be only half to 1 inch, instead of the normal 2½ to 3 for an adult. There is often filling and even bulging of the supra-clavicular hollow, while the neck appears short, the sternomastoids stand out, and the jugular veins are full. A zone of dilated venules, the "emphysematous girdle," is often present along the line of the costal attachment of the diaphragm, but is not pathognomonic. The cardiac impulse is not visible as a rule, and may only be felt with difficulty, but epigastric pulsation is usually apparent. Vocal fremitus is diminished, and the percussion note is hyper-resonant. The superficial cardiac dullness is greatly diminished or even absent, and the lower limit of pulmonary resonance may extend to the costal margin, back and front, the hepatic dullness being encroached on or obliterated.

It is said that in bullous emphysema the breath-sounds are harsh over the outer part of the upper lobes in front, and weak at the bases. In general emphysema the breath-sounds are weak everywhere, inspiration is short, and expiration is greatly prolonged. A loud rumbling, from contraction of the thoracic muscles, may entirely obscure the breath-sounds. A few fine bubbling râles may be heard at the bases or at the sternal margins. If bronchitis is present, scattered rhonchi may be audible. Vocal resonance is generally slightly diminished. The heart-sounds are weak and distant,

and in late stages a tricuspid systolic murmur may develop. The "vital capacity" of the lungs, measured by a spirometer, is often reduced to one-half or less. Examination by the X-rays shows increased extent, and undue transradiancy of the lung tissue. They show the diaphragm lower in position and flattened, and the costophrenic angle widened. The liver is sometimes palpable, possibly from downward displacement by the bulky lung, but more often from enlargement due to passive hyperæmia. The spleen may also be depressed and enlarged.

Complications.—Bronchitis is the commonest, and often constitutes a vicious circle. Asthmatic attacks, so-called "bronchial asthma," are common in later stages; on the other hand, spasmodic asthma may be the cause of the emphysema. Pneumothorax and interstitial emphysema may occur from rupture of the bullæ, although these accidents are surprisingly rare. Pulmonary tuberculosis is an occasional complication of emphysema, which, contrary to popular opinion, is not antagonistic to it, although it may mask and obscure the early stages. Right-sided cardiac failure, with its train of consecutive changes, is a late and often terminal complication.

Course.—Emphysema is progressive, unless the cause is removed or the effects of the disease are mitigated by residence in a warm, dry climate, especially in the winter. Conversely, residence in unsuitable districts, persistence in detrimental employment, and repeated attacks of bronchitis accelerate its course.

Diagnosis.—This is never difficult in advanced cases. The slighter degrees may be more difficult, and the diagnosis is then largely a matter of inference from the association of chronic cough and dyspnœa, with physical signs of hyper-resonance and prolonged expiration.

Confusion may occasionally arise in regard to pneumothorax and pulmonary tuberculosis. Careful record of the symptoms and signs and the investigation of the sputum generally suffice to distinguish these conditions. In doubtful cases the X-rays may assist.

Prognosis.—This depends upon the degree of emphysema and the circumstances of the patient. If progressive, it exerts an increasingly crippling effect, and it certainly shortens life under urban conditions. A "vital capacity" of less than 50 per cent. of the normal is of serious import. The advent of severe bronchitis or of cardiac complications may affect the prognosis gravely.

Treatment.—Emphysema may be arrested but cannot be cured. Attention must be directed to prevention of the causes of chronic cough and increased intra-alveolar tension. In any person with hereditary tendency to emphysema or to winter cough, the questions of occupation and place of residence should be carefully considered. When the disease is established, the patient, if in a position to afford it, should spend the winter in a warm, more equable climate, either abroad or at the south-west coast of England.

Various attempts have been made to increase the respiratory ventilation of the lungs, *e.g.* by compression of the chest during expiration, by expiring into rarefied air, by breathing compressed air or by expiratory breathing exercises. The patient enters a special iron chamber fitted with a window, and the air pressure is raised during the course of half an hour to $1\frac{2}{3}$ atmospheres. He remains at this pressure for an hour, and is then decompressed to normal during the nest half-hour. These baths may be given every other

day and gradually increased in duration and frequency. This treatment is often helpful in cases of emphysema associated with bronchial spasm or with bronchitis. Cases with marked arterial disease or with much rigidity of the chest-wall are unsuitable for this form of treatment.

The diet should be simple and easily digestible, especially in the later stages. If there is spasmodic dyspnœa or asthma, no late meal should be permitted. Cod-liver oil or halibut liver oil in the winter seems to help some patients. Clothing should be warm, but the excess of under-garments, often worn in fear of chill, is harmful.

In other respects treatment is largely symptomatic. In acute bronchitic attacks the measures to be adopted are in no way different from those in bronchitis uncomplicated by emphysema. In the more chronic bronchitis so commonly present in the winter, iodides with alkalis and balsamic expectorants seem beneficial. Terebene (min. 10) in emulsion or in capsule has been recommended. Counter-irritation to the chest by liniments, such as the lin. terebinthinæ aceticum, is often comforting to the patient, when cough is troublesome. When asthma or paroxysmal dyspnœa occurs, antispasmodic drugs and measures similar to those used in spasmodic asthma may be employed. When cardiac failure supervenes, the appropriate treatment must be vigorously applied. If there is marked cyanosis and venous engorgement, oxygen administration, venesection, leeching, purgative and diuretic drugs may be employed, and digitalis and other cardiac tonics administered. American authorities have suggested the use of an abdominal belt to increase the intra-abdominal pressure and raise the diaphragm.

2. Small-Lunged Emphysema (Atrophic or Senile Emphysema)

Ætiology.—This condition occurs in old age and forms part of the general atrophy of the tissues.

Pathology.—The alveolar walls become thinned and disappear, so that adjacent alveoli coalesce. The condition is primarily atrophic, and therefore differs from true emphysema, although the result is to produce a diminished area for aeration. Post mortem the lungs are small and do not bulge or obscure the pericardium. They are often deeply pigmented, and are more spongy than normal, but although bullæ occur they are small. On section the lung tissue is bloodless and friable. The bronchi may be slightly dilated and show catarrhal changes.

Symptoms.—These are slight and are masked by the enfeeblement due to the general atrophy and debility. There is shortness of breath only on exertion, or on exacerbation of the chronic bronchitis which is frequently present. The chest is small, flat and thinly covered, the movements are poor and there is elevation of the chest as a whole, with poor expansion. Kountz and Alexander maintain that there is very little diminution in vital capacity, that the movements of the diaphragm are increased and that the intervertebral discs are abnormal. There is little cyanosis, and no clubbing. The vocal fremitus is unaltered or slightly diminished. The percussion note is hyper-resonant, but there is no encroachment on the cardiac and hepatic areas of dullness. Breath-sounds are weak, and there is but little prolongation of expiration. Rhonchi and râles may be heard, especially if bronchitis is present, or if the heart is failing.

Diagnosis.—The condition is generally so obvious that no difficulty arises.

Treatment.—This is chiefly a matter of careful regimen and diet, with treatment of coexisting bronchitis or cardiac failure.

3. Compensatory Emphysema (Localised or Secondary Emphysema)

Ætiology.—Localised emphysema is a sequel to some process inducing collapse, contraction or destruction of areas of lung tissue. It may be lobular in distribution in bronchitis, broncho-pneumonia, tuberculosis and diphtheria. It may affect one or more lobes, or the whole of one lung, especially in cases of fibrosis following tuberculosis, pneumonia, chronic pleural effusion and empyema.

Pathology.—It is generally conceded that the inspiratory theory of Laennec and Gairdner satisfactorily explains the genesis of this condition. When shrinkage of an area of lung occurs, the chest wall may fall in, if there is pleural adhesion, but otherwise inspiration tends to expand the normal parts of the lungs. None the less, it must be admitted that the expiratory strain of cough may assist in its production.

Although it may be compensatory and physiological at its inception, it is doubtful whether a true hypertrophy takes place after adolescence. In any case it soon leads to atrophy of the alveolar walls, as in true emphysema, and thus becomes pathological and harmful. Post mortem the condition may be found in an upper lobe around contracted scarred lung tissue, or in a lower lobe when the upper lobe is contracted or disorganised. In cases where one lung is fibroid and contracted, compensatory emphysema may be found throughout the sound lung. The resulting adaptations caused by enlargement of one part and shrinking of another may produce some striking displacements, the lower lobe extending upwards nearly to the clavicle, or the anterior margin of the sound lung crossing the mid line. The general appearances are closely similar to those of ordinary emphysema, except that bullæ do not occur, at any rate until the process is advanced and definitely pathological.

Symptoms.—This condition does not produce symptoms that can be differentiated from those of the primary disease. When it affects a lobe or the whole of one lung, there is hyper-resonance over the area involved, which often contrasts strikingly with the dullness due to the primary lesion. The hyper-resonance may extend across the sternum and even for an inch or more beyond it. The heart is displaced towards the side where fibrosis is in progress. Vocal fremitus and vocal resonance are little altered, but may be increased at first and subsequently diminished. In the early stages, when there is alveolar dilatation without degenerative mural changes, the breath-sounds are exaggerated, harsh or puerile, but when such processes develop, they become weak and there are indications of dyspnœa and cyanosis on exertion.

Diagnosis.—This is easy, owing to the difference between the diseased and "compensatory" areas, and to the indications of contraction and displacement.

Treatment.—No special treatment apart from that of the primary condition is required.

4. Acute Vesicular Emphysema

Although custom has included this condition with emphysema, it is in reality only a temporary acute distension of the alveoli resulting from any condition causing widespread obstruction of the smaller bronchi. It is sometimes observed after death in cases of acute bronchitis, whooping-cough or asphyxia and in anaphylactic shock, and its existence may be inferred in severe asthma. Post mortem the lungs are bulky and the alveoli distended.

The symptoms are dependent upon the primary condition, although dyspnœa is invariably present. The chest is found to be fully expanded, the vocal fremitus is diminished, the percussion note is hyper-resonant, and the breath-sounds vary with the condition inducing it.

5. Acute Interstitial Emphysema

In acute interstitial emphysema air is present in the stroma of the lungs, and in the subpleural connective tissues. It may follow external trauma, such as fractured ribs, or wounds penetrating the lungs. The alveoli may rupture with violent expiratory efforts, as occur in whooping-cough or influenzal broncho-pneumonia. It may occur in diphtheria. The air sometimes tracks along the pulmonary roots to the mediastinum, and appearing in the neck or on the chest-wall gives rise to surgical emphysema.

Post mortem, subpleural bullæ may be seen containing air, and on section of the lung minute air bubbles may be found in the inter-alveolar connective tissue. A diagnosis cannot be made unless the physical signs of surgical emphysema are present. The air is usually completely absorbed, and a perfect recovery takes place. No special treatment is required beyond keeping the patient at rest, and giving sedative drugs to allay cough.

ABSCESS OF THE LUNG

Definition.—Abscess of the lung includes any circumscribed collection of pus formed in the lung tissue, but softened tuberculous areas and bronchiectatic accumulations are usually excluded.

Ætiology.—*Predisposing causes.*— These include any diseases producing general cachexia or malnutrition, notably diabetes and chronic alcoholism, also any conditions leading to diminished resistance locally in the lung, such as injury, disease or exposure.

Exciting causes.—These are pyogenic organisms, which reach the lung by inhalation, by extension from adjacent suppurative processes, or by the blood stream, either directly or in septic emboli. The common organisms found are streptococci, staphylococci, the pneumococcus, Friedländer's pneumo-bacillus, *Bacillus welchii* and the *Bacillus coli*—sometimes acting in conjunction with putrefactive bacteria. Spirochætes, *Bacillus fusiformis*, treponemata and anaerobic organisms are often present, especially after rupture has occurred. Pulmonary abscess may form under the following conditions:

(1) After inhalation of foreign material into a bronchus. This may be a foreign body, or may occur in association with septic conditions in the nose,

nasopharynx and larynx, or during and after operations in these regions. These are referred to as inhalation abscesses, though some post-operative cases are regarded as due to embolism and not to inhalation. (2) As a result of lobar or lobular pneumonia, especially after the deglutition and aspiration varieties of the latter. Such abscesses are sometimes called metapneumonic. (3) Embolic causes—in pyæmia, or following on septic pulmonary emboli due to right-sided septic endocarditis, or derived from distant septic processes, such as otitis media, and infective thrombo-phlebitis. Amœbic abscess occurs occasionally after dysentery, and pulmonary abscess may be found as a rare complication of enteric fever. (4) From infection of the lung tissue due to spread from adjacent disease. This may occur in bronchiectasis, in ulcerating new growths of the lung, bronchi, œsophagus or mediastinal glands, in caries of the vertebræ or ribs, and in suppurating mediastinal glands. Rupture of an empyema, of a subphrenic abscess, of a liver abscess, or of infected hydatid cysts of the lung or liver may also lead to pulmonary suppuration. Ten per cent. of cases of abscess are due to new growths. (5) As a sequel of perforating chest wounds, or of fractured ribs piercing the lung.

Pathology.—Abscess of the lung is generally single and basic when consequent on pneumonia, whereas embolic abscesses are often small and multiple and may be found in any part of the lung. Abscesses due to extension from adjacent disease are generally solitary, and are often large and irregular. The walls of acute abscesses are generally formed of congested and œdematous lung tissue, or of a zone of unresolved pneumonia. Since acute abscesses commonly rupture quickly into a bronchus, a fibrous capsule is unusual, but in chronic abscess there is often considerable fibroid change in the neighbouring lung tissue. The pleura may become involved over superficial abscesses, leading to empyema, or to pyo-pneumothorax if rupture follows.

Symptoms.—Abscess may develop insidiously, with comparatively slight symptoms. More commonly they are an intensification of those due to the primary or antecedent condition. The patient often appears seriously ill, the fever becomes of septic type, remittent or intermittent in character, and of a high range. Rigors and sweating are common. The pulmonary symptoms at first may be only slight cough with scanty muco-purulent expectoration. Dyspnœa may be present and pain of acute character develops if the pleura is involved. Hæmoptysis occurs in 70 per cent. of cases of abscess. A considerable leucocytosis, up to 20,000 or 30,000 may be found, and occasionally the breath may be offensive, even before rupture into a bronchus occurs, followed by the sudden expectoration of a large quantity of pus. The pus is sometimes unpleasant or offensive-smelling, but has not the extreme fetor of gangrene. Microscopical investigation will demonstrate the presence of pulmonary debris, especially elastic tissue, together with pus cells and micro-organisms. After the expectoration of the pus, the temperature usually falls and the general condition of the patient is much improved, though cough and expectoration persist. In chronic cases after rupture the temperature may become irregular and periodic, a few days of normal temperature being followed by a period of fever and later by increased expectoration. The physical signs in a deep-seated or small abscess are often inconspicuous, and comprise slight dullness over a small area, weak breath-sounds and possibly a few râles in the surrounding infiltrated or œdematous lung tissue. With a large or a

superficial abscess, the signs before rupture may be those of consolidated or collapsed lung. After evacuation occurs, the characteristic signs of excavation usually develop at once. In multiple embolic abscesses the signs are usually those of disseminated broncho-pneumonia.

Complications and Sequelæ.—The commonest complication is dry pleurisy. This may progress to empyema, or to pyo-pneumothorax, if rupture into the pleura occurs. In some cases mediastinitis or pericarditis may develop. Gangrene is described, but is a rare sequel. Metastatic abscesses may be produced in other parts of the body, especially in the brain, and meningitis is a rare and serious complication. The most important sequelæ are fibrosis of the lung, with bronchiectasis, pleural adhesion, and rarely indurative mediastinitis.

Diagnosis.—This is difficult before rupture, but abscess may be suspected from the gravity of the symptoms in relation to the history and signs, especially if leucocytosis and fetor of the breath are present. X-ray examination may be helpful, by demonstrating a localised shadow before rupture, and excavation afterwards, and also by establishing the situation of the abscess. A fluid level can often be seen in films taken in the erect position. The sudden expectoration of pus, followed by retrogression of symptoms and signs of excavation is very suggestive of abscess. After rupture has occurred the differential diagnosis has to be considered from:

1. *Interlobar empyema.*—This may be very difficult or even impossible. In this condition the signs are generally most marked in the region of an interlobar septum, there may be some cardiac displacement, and the sputum, though purulent, does not contain elastic tissue.

2. *Bronchiectasis.*—The history, the characteristic cough and sputum, and the variation of the physical signs with the state of the cavity usually suffice to distinguish this condition. An X-ray examination after lipiodol or neo-hydriol will distinguish in doubtful cases, since they do not as a rule enter the abscess cavity and the appearances in bronchiectasis are characteristic.

3. *Gangrene of the lung.*—The distinction is not always easy in acute abscess, since the two processes are closely related. The extreme gravity of the patient's general condition and the horrible fetor of the breath and sputum are the most characteristic features of gangrene.

4. *Tuberculous excavation.*—The history, the distribution of the signs, and the characters of the sputum, including the presence of tubercle bacilli, are the distinguishing indications.

5. *Purulent bronchitis.*—The history, the widespread physical signs, and the absence of elastic tissue from the sputum usually serve to establish the diagnosis, and lipiodol or neo-hydriol investigations may be helpful.

In multiple or pyæmic abscesses, it is often impossible to recognise the condition, though it may be suspected from the severity of the symptoms and signs. In any doubtful case an X-ray examination or tomography should be carried out, if the condition of the patient permits. The possibility of malignant growth as a cause of abscess should be borne in mind and, when necesssary, bronchoscopy as well as lipiodol investigation carried out. Exploratory puncture as a means of diagnosis is dangerous and should be avoided.

Prognosis.—The prognosis, though grave in many cases, is better than

might be anticipated. Many of those in which rupture into a bronchus occurs recover. Death is inevitable in the pyæmic cases.

Treatment.—(1) *Medical.*—In acute abscesses medical measures should be employed, since in a considerable proportion of cases, recovery may occur after rupture, especially when the abscess is in the upper lobe. Before rupture the treatment should be similar to that for acute pneumonia. After rupture, evacuation should be promoted by "tipping," or postural drainage. The Nelson bed is of great value in this connection when the relation of the abscess to the nearest patent bronchus has been determined by X-ray examination. Expectorant drugs and antiseptics, such as creosote, should be employed. Antiseptic inhalations may also be used on a Burney-Yeo mask, as for bronchiectasis, or creosote vapour baths may be given. In like manner intratracheal injections of menthol, guaiacol and olive oil have been employed with benefit. In cases with spirochætes, treponemata and anaerobic organisms in the sputum, intravenous injections of salvarsan or neo-arsphenamine may be administered with benefit.

(2) *Surgical.*—If spontaneous rupture does not occur after the abscess has become localised and encapsulated, operation is indicated in order to prevent the walls becoming thick. Repeated bronchoscopic aspiration is sometimes employed after rupture, and at times gives satisfactory results. If, after rupture, there is not satisfactory progress towards cure within 6 weeks, clinically and radiologically, surgical treatment should be considered. Thoracotomy and open drainage is the operation generally employed. This is now usually carried out in two stages: (*a*) a preliminary exposure of the pleura by rib resection and packing with gauze, to ensure adhesion of the pleura; (*b*) some days later the abscess is opened along the course of an exploring needle. Artificial pneumothorax has been recommended, especially in deep or centrally placed abscesses. There is a risk of rupture into the pleura, more particularly when re-expansion of the lung is permitted. For this reason, this form of treatment is rarely advisable. Phrenic evulsion may aid in the evacuation of a chronic abscess. either alone or after thoracotomy. Pneumolysis, lobectomy, and thoracoplasty are also used in the treatment of chronic abscess. Lobectomy seems likely to be the most satisfactory in chronic cases in which it is practicable.

GANGRENE OF THE LUNG

In this condition localised or diffuse areas of lung tissue undergo putrefactive necrosis.

Ætiology.—*Predisposing causes.*—These include old age, over-indulgence in alcohol, general debility, diabetes and insanity. In certain rare cases, especially after broncho-pneumonia complicating measles, gangrene of the lung is met with in children.

Exciting causes and associated conditions.—These are, in the main, identical with those of pulmonary abscess (see p. 1183). In addition, the pressure of aneurysm or of new-growth on branches of the pulmonary artery may lead to gangrene. The causal organisms are also very similar to those found in abscess of the lungs, and include staphylococci, streptococci, sarcinæ, the *Micrococcus tetragenus*, the *Bacillus coli communis*, the *B. pyocyaneus*, the

B. fusiformis with its associated spirochæte, and various anaerobes. In some instances acid-fast bacilli, classed as streptothricæ, occur. Some of these organisms yield putrefactive products, with the liberation of phenol, indole and skatole compounds in the lung.

Pathology.—It is not quite clear what are the factors determining whether abscess or gangrene occurs in an infected area of lung. Doubtless the general resistance of the body, the degree of local vascular disturbance, and the virulence of the infecting organisms all play their part. Laennec first described the two varieties of gangrene, the circumscribed and the spreading or diffuse. Around the former there are indications of a line of demarcation, formed by congested lung tissue, which may present the appearance of red hepatisation. The surrounding lung tissue is invariably somewhat œdematous. The gangrenous area is soft and pulpy, and its colour varies from reddish-brown to greenish-black. As the necrosis advances, putrefactive liquefaction occurs, with the formation of a horribly reeking fluid, containing shreds and masses of necrotic lung tissue. When this is discharged, excavation results, and isolated vessels may be seen running across the resulting cavity, the walls of which are rough and covered with fetid pus. The diffuse variety of gangrene is less common; there is no attempt at a zone of demarcation, and the whole of a lobe or of one lung may be affected. In both forms, the overlying pleura is intensely inflamed, and empyema or pyo-pneumothorax may be produced.

Symptoms.—These are similar to those occurring in abscess of the lung, but are more acute. The patient is desperately ill, rigors are more common and sweating is more profuse. The breath has a peculiar fetor, which, on account of the presence of the skatole group of putrefactive products in the gangrenous lung, has an almost fæcal odour. The sputum is intensely offensive, and on standing separates into three layers, similar to those of the expectoration in cases of bronchiectasis. Elastic tissue is usually present, but it may undergo rapid disintegration. Hæmoptysis is not infrequent and may prove fatal. In rare cases gangrene is not accompanied by fetid expectoration, especially when developing in the insane, in young children, and in diabetics, or after pulmonary embolism. The physical signs closely resemble those present in cases of pulmonary abscess, and are those of consolidation before liquefaction occurs, and of excavation afterwards. The signs of the antecedent condition such as bronchiectasis, aneurysm, or malignant disease may also be present.

Complications and Sequelæ.—These are similar to those met with in pulmonary abscess, but owing to the rapid course and greater fatality of gangrene, they are not so common. Cerebral abscess may occur.

Course.—The course is usually rapid, unless the diseased area is small and circumscribed. In rare cases of localised gangrene of small extent, resolution and subsequent fibrosis occur.

Diagnosis.—The differential diagnosis is as for pulmonary abscess, the distinguishing features being the extremely critical condition of the patient and the revolting fetor of the breath and expectoration. X-ray examination may give great assistance if the patient's condition permits it to be made.

Prognosis.—This is always extremely grave, though a few cases of localised gangrene recover spontaneously. The prognosis is improved by

early operation in suitable cases. The outlook is said to be worse if the condition is apical, and diffuse gangrene is invariably fatal.

Treatment.—Operation is indicated when the general condition of the patient permits, if the gangrenous area can be localised by physical signs or X-ray examination. Exploratory puncture should not be carried out. The other operative procedures are similar to those for abscess of the lung. Operation is contra-indicated in cases of diffuse gangrene. The medical treatment is in all respects similar to that for pulmonary abscess. Injections of neo-arsphenamine, in doses of 0·3 g., have given good results, especially in cases due to fuso-spirochætosis.

PULMONARY FIBROSIS

Synonyms.—Fibroid Disease of the Lung; Chronic Interstitial Pneumonia; Cirrhosis of the Lung.

Definition.—Pulmonary fibrosis is a late sequel of many acute and chronic inflammatory or irritative processes affecting the bronchi, lungs and pleuræ. It is therefore rather of pathological than of clinical interest, and in no sense constitutes a separate disease, although the end-results are remarkably similar in different forms. It is described here partly in deference to tradition, and partly to point out the methods of diagnosis between the various causes producing such strikingly similar effects.

Ætiology.—(1) The commonest cause is pulmonary tuberculosis, particularly the fibroid and fibro-caseous varieties. (2) The group of pneumokonioses contributes a considerable number of cases, and possibly some varieties of gas poisoning may induce fibroid changes. (3) Bronchopneumonic processes, particularly the forms associated with measles and whooping-cough, may be followed by widespread fibrosis, especially in children. (4) Although fibroid induration is commonly described as a sequel of lobar pneumonia, this disease is one of the rarer causes. (5) Localised fibrosis may occur around any circumscribed pulmonary or bronchial lesion, such as that produced by syphilis, leprosy, glanders or streptotrichosis. Similarly it occurs about infarcts, pulmonary abscesses and parasitic cysts. (6) Chronic venous congestion, if prolonged, leads to fibroid change, which is referred to as "brown induration." This is usually of moderate degree and does not affect the clinical manifestations. (7) Chronic pleural affections, particularly those leading to adhesions or causing pulmonary collapse, may induce fibroid changes within the lung, and these forms are described as "pleurogenous cirrhosis." (8) Any condition causing obstruction of a bronchus and leading either to collapse or to bronchiectasis may, if long continued, cause fibrosis of the corresponding lung area. Among such may be mentioned inhaled foreign body, new-growth, cicatricial contraction and thoracic aneurysm.

Pathology.—The fibroid overgrowth may be: (1) Massive or lobar; (2) localised or insular; (3) peribronchial; and (4) reticular.

Any part of the connective tissue framework of the lungs and bronchi may contribute to the fibrosis. In the massive form, which generally affects the whole or the major part of a lobe or even of one lung, the appearances in cases due to tuberculosis differ from those due to other causes. In the

tuberculous variety the primary distribution is usually apical, and evidence of other tuberculous processes may be apparent in the form of large or small dried-up cavities, inspissated caseous material or calcareous masses enclosed in fibrous strands. In non-tuberculous processes, the early localisation is commonly basic, and although the primary cause may be obvious in the form of bronchial obstruction or some pleural condition, this is not always the case. On the other hand, non-tuberculous processes may involve the upper lobe primarily and fibroid tuberculosis may fall with special stress upon the lower lobe. In both forms of fibrosis, bronchiectasis may result, although this is more common in the non-tuberculous cases. Apart from the special tuberculous lesions, the end results are very similar in both forms. The affected area of the lung is shrunken and often devoid of air except for that in the bronchi and in the cavities. It is dark in colour, very firm and hard. On section it presents a mottled appearance owing to the strands of blue-grey fibrous tissue traversing it, contrasting with the pigmented, condensed, airless lung tissue. The fibroid area may be honeycombed by cavities or may present one large excavation, due either to tuberculous cavitation or to bronchiectatic dilatation. There is nearly always thickening and adhesion of the pleura. The contraction of the abnormal fibrous tissue leads to marked displacement of the heart and mediastinum.

The localised form is commonly due to healed tuberculous processes at an apex. There may be simple puckering with or without pleural thickening and adhesion, or a dense mass enclosing dried-up caseous matter or calcareous spicules. In bronchitic or broncho-pneumonic processes a patchy fibrosis may occur, described as insular fibrosis by Fowler.

Reticular fibrosis is a rare condition in which the fibrous tissue in the interlobular septa seems to become increased as well as that around the bronchi. It is at present only of pathological interest.

Symptoms.—The symptoms of pulmonary fibrosis are, in the main, expectoration and dyspnœa together with those of the primary affection. In the non-tuberculous cases, bronchiectasis is so frequently associated that the symptoms and signs found are practically those of this condition. Even in tuberculous cases, some degree of bronchial dilatation is the rule, although the sputum is rarely offensive. The cough is generally periodic and associated with change of posture. The expectoration is abundant, and if bronchiectasis is present, it has the usual characteristic features. The dyspnœa is proportional to the extent of lung involved. It may be extreme in the later stages, when the heart becomes embarrassed and begins to fail. Fever is usually absent, except when complications occur.

The patients are generally spare, although nutrition may sometimes be well maintained until late. They may show signs of deficient aeration in duskiness, cyanosis and congested cheeks. Polycythæmia of some degree is the rule. Clubbing of the fingers is almost constant. Evidence of contraction is generally forthcoming in the flattening and retraction of the affected side, with the dropped shoulder and compensatory spinal curvature. Movement is greatly restricted, contrasting with the increased expansion of the other side. The cardiac impulse is sometimes much displaced, especially in left-sided cases, when it may be in the left posterior axillary line or even under the angle of the scapula. In right-sided cases, it is drawn

to the right of the sternum, even sometimes under or outside the right nipple. Vocal fremitus is usually diminished and percussion gives dullness of varying degree over the fibroid area, while the unaffected parts may be hyper-resonant from "compensatory" emphysema. The diaphragm may be drawn up, and the liver or stomach correspondingly displaced. The breath-sounds are often weak or inaudible unless there is bronchiectasis or cavitation, when the characteristic signs of these conditions can be recognised. The vocal resonance is diminished if there is much pleural thickening, increased if cavities are present. Adventitious sounds may be entirely absent, and when present vary from rhonchi and bubbling râles to coarse metallic râles, according to the presence or absence of excavation. X-ray examination gives useful confirmation, showing displacement, excavation and pleural thickening.

Course.—The course is invariably chronic, and may extend to years, even ten or twenty.

Diagnosis.—The diagnosis is usually easy. The evidence of contraction and of mediastinal displacement towards the affected side, especially if signs of cavitation are also present, is highly suggestive. In the absence of the cavitation some difficulty may arise in regard to chronic pleural effusion or empyema. In the earlier stages the contra-lateral displacement of the cardiac impulse should prevent any mistake, but where partial absorption has occurred, this may be very slight or absent. In such cases an exploratory puncture or an X-ray examination may be helpful.

When the diagnosis of pulmonary fibrosis has been made, the differentiation of the cause is an essential to prognosis and treatment. If the condition is apical, there is a presumption in favour of tuberculosis; if basic, some other cause is more probable. Repeated examinations of the sputum should be made for tubercle bacilli, and if these prove negative, X-ray examination may reveal some cause such as new-growth, aneurysm or even foreign body. In some cases a careful consideration of the history may afford a clue to the diagnosis.

Prognosis and Treatment.—These depend upon the primary condition, but in most cases the latter is mainly symptomatic.

PNEUMOKONIOSIS

Synonyms.—Pneumonokoniosis; Dust Disease of the Lung.

Definition.—Pneumokoniosis comprises all the pathological changes induced in the bronchi, lung and pleuræ by the inhalation of dust particles.

Ætiology.—*Predisposing causes.*—Pneumokoniosis is one of the occupational diseases. It is practically limited to men, and usually develops between the ages of 25 and 40. Defective ventilation, bad hygienic conditions and alcoholism promote its incidence.

Exciting causes.—Various forms of dust, both inorganic and organic, serve to produce pneumokoniosis, and in general the harder and more gritty the particles, the more marked are the changes induced. Organic forms of dust lead especially to bronchitic changes, the inorganic forms to pulmonary fibrosis.

The following varieties are recognised:

1. *Anthracosis* from coal dust (coal-miners' phthisis).

2. *Siderosis* (silico-siderosis), from the inhalation of fine particles in tin, copper, lead and iron miners, and in grinders of steel goods (grinders' rot).

3. *Silicosis* or chalicosis, met with in workers in quartz, gannister and slate quarries, also in potters (quarts-miners' phthisis, and potters' asthma). Gold-miners' phthisis, the most serious form of pneumokoniosis, and especially prevalent in the South African gold mines, is due to the fine dust caused by the rock drills.

4. *Byssinosis*, a rare variety, is met with in cotton workers, felt-hat makers, and the employees in shoddy mills.

5. *Asbestosis.*—A condition found occasionally in those working in the manufacture of asbestos articles. Asbestos is composed of compound silicates of iron and magnesium.

Pathology.—The lungs of persons living under rural conditions are practically free from deposited pigment. A certain amount of carbon is invariably present in the lungs of town-dwellers, giving them a dark-grey mottled appearance, but producing no pulmonary fibrosis. In coal-miners this occurs to such an extent that the lungs are black (anthracosis), although even here little fibrosis occurs, except in miners of hard coal or anthracite. In siderosis and silicosis, fine sharp particles of metallic oxides or silica are deposited in the lung tissue. According to Stewart, siderosis is in effect silico-siderosis, the damaging agent being silica inhaled at the same time. In asbestosis, curious irregular discoid structures of golden yellow colour and containing iron, now called "asbestosis bodies," are found in the lungs and in the sputum. There is also much fibrosis in pneumokoniosis, and tuberculosis is liable to be a later development.

It is generally accepted that these particles are conveyed to the bronchi and alveoli by inhalation. In normal breathing, most of the coarse particles are detained in the nose, and are discharged with the nasal mucus, whereas in mouth-breathers they readily gain access to the trachea and bronchi. Even then, the coarser particles may be discharged, in the expectoration through the agency of the ciliated epithelium, but, owing to the catarrhal processes induced by the irritation of the inhaled dust, this epithelium may be desquamated and the absorption of the particles is promoted. As a further consequence of this initial bronchitis, the finer particles may reach the alveoli, and passing between the epithelial cells, gain access to the tissue spaces, or in some cases they may be taken up into special "dust cells." In silicosis, particles of crystalline silica become deposited in the connective tissue, and chronic peribronchial and perialveolar fibrosis develops. The bronchial glands also become enlarged by the deposition of similar particles conveyed by the lymphatics. Other changes more or less constantly present are emphysema, pleural adhesion and bronchiectasis.

The relationship to tuberculosis has been much debated. It is now established that pneumokoniosis is non-tuberculous in origin, and that it may remain so throughout its course. On the other hand, certain forms undoubtedly favour the development of tuberculosis. In England and Wales coal-miners suffer less from tuberculosis than do all other males. On the other hand, gold-miners are extremely liable to it. It would appear that the determining factor is the presence of particles of silica. Silicates, as

in clay, do not induce tuberculosis. Workers in freestone develop this disease, limestone workers do not. Slate quarries do not acquire tuberculosis very readily, while metalliferous miners working in quartzite very frequently suffer from it. The Miners Phthisis Bureau recognises two types of silicosis. (1) Simple silicosis, the damage found being due to dust alone. It is non-progressive if exposure ceases. (2) Tuberculo-silicosis, in which most of the damage is due to dust, and tuberculosis is secondary. Haldane and Mavrogordato demonstrated that particles of coal are absorbed by the "dust cells" whose movements are thereby stimulated, with the result that they appear in the black spit, which is therefore a healthy sign. The particles of silica are also absorbed by these "dust cells," but no stimulus to their movement is induced and they remain *in situ*. Kettle and Gye have shown that a silica colloid is slowly formed, which leads to breakdown of the tissue defences and thus favours the activity of tubercle bacilli.

Post mortem, the lungs are generally firm and pigmented, the colour varying with the cause, being black in anthracosis, reddish-brown in siderosis, and greyish-black in silicosis. The pleura is generally adherent, especially at the bases. On section the lungs are firm, and often gritty. Small hard nodules may be felt with the finger. Fibroid changes are especially marked in silicosis. The bronchi are inflamed and sometimes dilated. Soem degree of emphysema is usually apparent. If tuberculous lesions are also present, these vary from fibroid areas to miliary nodules. Destructive processes resulting in cavitation may also be seen. Microscopically, the alveolar walls are thickened, the connective tissue is everywhere found to be increased, the "dust cells" may be seen in the connective tissue or in the alveoli, and particles of pigment or silica are found widely deposited in the connective tissue cells.

Symptoms.—The onset is insidious, bronchial irritation and cough, especially in the morning, may be the first indications, but increasing shortness of breath and debility are frequently early symptoms. The expectoration, at first scanty and mucoid, becomes more abundant and may present characteristic features as in the "black spit" of anthracosis. Tinging of the sputum and later hæmoptysis occur, but these suggest the possibility of superadded tuberculosis. The patient may appear healthy and be but little troubled except by the shortness of breath, but later emaciation and an appearance of premature old age are not uncommon.

The physical signs are not characteristic; at first they are simply those of persistent bronchitis, then emphysematous changes may become apparent. Later, signs of fibrosis appear, very similar to those described in the preceding section. Even when tuberculosis develops the signs are often but little characteristic, and repeated sputum tests may be necessary to establish the diagnosis. Examination by X-rays may be helpful; at first there is an increase in the reticulation and later nodulation, somewhat like that of miliary tuberculosis. At a still later stage, the nodules become larger, and there is increased fibrosis. The changes characteristic of tuberculosis may be super-added.

Complications and Sequelæ.—The most important complication is tuberculosis, which forms the terminal stage of many cases of silicosis. This may be suspected when fever, night sweats, hæmoptysis or emaciation develop. Bronchiectasis of considerable degree sometimes results as a

consequence of the fibrosis, and leads to the symptoms and signs characteristic of that condition.

Course.—This is progressive, unless the sufferer is removed from the exciting causes. Anthracosis runs a very chronic course, siderosis somewhat less so, while gold miners only live a few years (5 to 6—Oliver) after the onset of the disease.

Diagnosis.—The diagnosis can usually be made from the history of shortness of breath, cough and expectoration, developing in a worker in a dusty occupation. In the early stages, cigarette-smoker's cough and bronchitis may give rise to difficulty. In the later stages, the possibility of a primary fibroid tuberculosis has to be considered.

Prognosis.—This is unfavourable except in anthracosis. Lyle Cummins suggests that the finely divided carbon particles absorb the toxins of the tubercle bacillus. If recognised early, and if the patient is taken from the dusty conditions, recovery may be anticipated. The development of tuberculosis affects the outlook very gravely.

Treatment.—*Prophylactic.*—Every means should be adopted to avoid the dusty conditions leading to the disease. Mines should be well ventilated, and respirators should be worn where practicable in dusty occupations. Factories and workshops should be provided with apparatus to draw away dust. Sprays or jets should be used with drills to moisten the dust produced.

Curative.—Directly the condition is diagnosed, the patient should be advised to change his occupation. Nutrition should be kept at a satisfactory level. Symptoms and associated conditions, such as bronchitis or tuberculosis, should be treated on general principles.

PULMONARY TUBERCULOSIS

Synonyms.—Phthisis; Consumption; Decline.

Pulmonary tuberculosis embraces all the abnormal conditions induced by infection of the lungs, pleuræ and bronchial glands with the tubercle bacillus.

Ætiology.—Predisposing Causes.—Age.—The maximum age incidence is between the 15th and 45th years, although the disease may be encountered at any age. Senile tuberculosis is more common than is generally recognised.

Sex.—The disease is more frequent in males, but between the ages of 5 and 15 the female sex shows a preponderance.

Heredity.—Pulmonary tuberculosis certainly occurs with undue frequency in certain families. Since the direct transmission of the tubercle bacillus to the infant is extremely rare, two explanations seem possible—(1) Children born of tuberculous stock may inherit an increased susceptibility or diminished resistance, the tuberculous diathesis; or (2) they may contract tuberculosis on account of their exposure to massive infection in early life.

Race.—Differences in racial susceptibility probably depend upon the degree of inherited resistance acquired by the race from infection of previous generations. Native races suffer severely when first exposed. In Europe the Irish are particularly susceptible, whereas the Jews are relatively immune.

Climate.—Tuberculosis occurs in all climates. The prevalence of strong

rainy winds and defective subsoil drainage may tend to increase its incidence.

Occupation.—The highest mortality from tuberculosis occurs in England amongst the workers in dusty occupations, thus Cornish tin miners head the list. On the other hand, coal miners are notably free from the disease. Any conditions leading to overwork or to underfeeding increase the liability to tuberculosis.

Environment.—Overcrowding, defective sanitation, dampness, dirt, lack of sunlight and insufficient ventilation are most potent factors in the spread of the disease, causing both lowering of the resistance and increased facilities for direct infection.

Trauma.—Trauma, involving the chest-wall, may be followed by active pulmonary tuberculosis. This is probably because the injury leads to activity of previously arrested disease, rather than to fresh infection at a spot of lowered resistance.

Gassing.—In certain cases the inhalation of poison gases causes rapid activity and spread in latent disease, or it may possibly prepare the ground for reinfection, but it is not a factor of great ætiological importance.

The influence of other diseases and conditions.—The following diseases predispose to the development of pulmonary tuberculosis: measles, especially when complicated by broncho-pneumonia, whooping-cough, influenza, pneumokoniosis, alcoholism, diabetes, syphilis, congenital heart disease and insanity. Tuberculosis may manifest itself for the first time during prolonged lactation or after repeated pregnancies; when previously existent it often remains quiescent during pregnancy, but it may spread rapidly after childbirth. Contrary to the usual belief, pulmonary tuberculosis not infrequently coexists with mitral stenosis. Cases apparently following pneumonia, pleurisy or bronchitis are usually tuberculous from the onset.

Exciting Causes.—The causal organism is the *Bacillus tuberculosis*, discovered by Koch in 1882. It exists in four main forms, human, bovine, avian and reptilian; only the two former usually occur in man, but avian infection has been recorded. The human type is found in over 97 per cent. of pulmonary tuberculous lesions, though a higher proportion of the bovine type has been found in Scotland. In glandular tuberculosis up to the age of 5 years, over 80 per cent. of the bacilli isolated conform to the bovine variety. In tuberculosis of bones and joints up to the same age, 29 per cent. of the cases are of bovine origin.

The bacilli may gain access to the body by inhalation, by alimentary ingestion, through the tonsils, through the skin, or possibly, in rare instances, by hereditary transmission. It is probable that in the majority of cases of pulmonary tuberculosis in adults, the organisms are carried direct to the lungs in the inspired air, and Ghon showed that in children, who had died of tuberculosis of the lungs, a primary focus was present in the lungs in 92·4 per cent. As, however, extensive tuberculous lesions are frequently found in the bronchial glands in cases of pulmonary tuberculosis, it is believed by some that the glands are primarily affected, and that the bacilli pass from them to the lungs, either against the lymphatic flow or in the blood stream. Calmette and others have demonstrated that the bacilli may gain access to the bronchial glands from the alimentary tract through the

thoracic duct, or from the tonsils through the cervical and mediastinal glands. Cases have been recorded in which primary cutaneous infections have been followed later by active pulmonary tuberculosis. Direct transmission of the tubercle bacillus is believed to occur only when the mother is suffering from advanced tuberculosis, and even then is of great rarity.

The incubation period tuberculosis of is uncertain, owing to the difficulty in determining when infection takes place. It is now believed by many authorities that the majority of individuals are originally infected in infancy or early childhood, either from the ingestion of tuberculous milk, or by the inhalation of bacilli from dried sputum. Pulmonary tuberculosis is thus regarded as a late manifestation comparable with the tertiary stage of syphilis. On this hypothesis, active pulmonary disease in adult life may result either from reinfection or from the activation of a dormant lesion in the body. As the organisms found in early life are frequently of the bovine type, whereas in pulmonary tuberculosis they are almost invariably of the human variety, it is probable that reinfection is the more common, since mutation of type has not so far been proved.

Provided that the proper precautions are taken, the risk of infection from adult to adult is not great, and only exists in " open " cases of tuberculosis, *i.e.* in cases with tubercle bacilli in the sputum. The occurrence of conjugal disease, which is less common than might be expected, has been explained by mating of those with hereditary diathesis.

Pathology.—The earliest lesion in the lung is the formation of tubercles, whose structure is described in the general article on tuberculosis. They usually appear first near the apex. This may be due to the relative immobility of this portion of the lung, possibly as the result of calcification of the first costal cartilage (Freund), but in some cases the bacilli may spread from the cervical to the supraclavicular glands and thence to the adjacent lung. In some cases the earliest lesion is found in the subclavicular region well below the apex. It may commence in a subacute manner. In such cases, an area of localised deposit may be seen on radiological examination—known as Assmann's focus (Redecker's "*früh infiltrat*"). The initial deposit is usually in or around the small bronchioles of the third to fifth degree (Hirschfeld's bronchioles). The inflammatory swelling of the bronchioles obstructs their lumen, leading to collapse of the alveoli beyond and the formation of bronchopneumonic areas. At the same time peri-bronchiolar inflammation develops. In children there is, in the majority of cases, a primary lung focus (Ghon's focus), with secondary deposits in the bronchial glands.

Secondary Changes.—1. *Caseation.*—The tubercle is avascular, and owing to this, and possibly also to the action of tubercle toxins, coagulation necrosis and fatty degeneration frequently ensue. This combined process is known as caseation and results in the formation of a structureless, cheesy mass. Further changes may now occur, either softening, with the development of a " cold abscess " filled with tuberculous " pus," or calcification, with the subsequent formation of gritty masses known as " pneumoliths."

2. *Cavitation.*—Cavities result from the liquefaction of caseous areas, and the expectoration of the resulting debris. They may be no larger than a pea, or may occupy the whole of one or more lobes. A recent cavity has an irregular outline, with rough, shaggy walls and a vascular line of demarcation. It is often traversed by trabeculæ, formed by bronchi and vessels

which may be partly or completely obliterated, while sometimes the trabeculæ consist of condensed lung tissue which originally separated adjacent cavities. In chronic cases, the cavity is surrounded by fibrosed lung tissue forming a pseudo-capsule, and its interior becomes lined by a thin, smooth, false membrane. Small aneurysms may be found, arising either from vessels running in the walls or in the trabeculæ of the cavity, the former being the more common. In some cases, where hæmoptysis has occurred, rupture of such an aneurysm is the cause.

3. *Fibrosis.*—Reactive changes in the lung stroma lead to the formation of fibrous tissue. This may occur early or after caseation has taken place. Such changes are often classified as productive, whereas infiltration and the earlier reactive changes are referred to as exudative.

In the majority of deaths from all causes, old tuberculous lesions are found post mortem near the apex of one lung. These consist of small nodules of arrested disease, with thickening and dimpling of the adjacent pleura.

Dissemination in the Lungs.—The disease may spread from the primary peri-bronchial deposit—(*a*) By direct infiltration; (*b*) By the peri-bronchial lymphatics and capillaries, leading to a racemose appearance or to peri-bronchial fibrosis; (*c*) By the subpleural and interstitial lymphatics, with localised miliary dissemination; (*d*) By inhalation into a bronchus of tuberculous material, which is then carried to other parts of the same or to the opposite lung—this not infrequently happens after hæmoptysis and in cavitation; (*e*) By the blood vessels, *e.g.* generalised miliary tuberculosis may result from erosion of a caseous tubercle into a vein.

The pathology of the clinically distinguishable forms of pulmonary tuberculosis will now be described.

1. Acute Miliary Tuberculosis.—A primary caseous focus may be discovered at the apex of one lung, in the bronchial glands, or at some distant spot in the body. Local erosion of a vein may be found, accounting for the dissemination of the disease. The lungs are usually studded with minute grey tubercles, the smaller ones requiring a hand lens for their recognition. In very acute cases death occurs before any secondary broncho-pneumonic changes take place. Miliary tuberculosis may develop as a terminal event in chronic fibro-caseous or fibroid tuberculosis. The tubercles are then found in large numbers around the old foci of disease, but to a less extent in the more remote portions of the lung.

2. Chronic Miliary Tuberculosis.—The lungs are studded uniformly with firm nodules varying in size from one to several millimetres in diameter. They are grey or white, project from the cut surface of the lung, and in some cases are calcified. There may be, in addition, a diffuse fine fibrosis. Miliary tubercles are at times found scantily distributed in the spleen, kidneys and liver. Not infrequently there is evidence of terminal acute miliary tuberculosis involving the brain and meninges.

3. Acute Caseous Tuberculosis.—Large areas of consolidation form rapidly, which differ histologically from the common chronic tuberculous broncho-pneumonia in that the alveolar exudate is more definitely inflammatory and contains fibrin. In the rare lobar cases, the rapid caseation and the presence of tubercle bacilli show that the caseous pneumonia is a specific process. Firm yellowish patches, which may be confluent, are seen,

usually scattered throughout both lungs. The affected areas are airless and sink in water. Softening is generally present in varying forms up to actual cavity formation, which may be extensive, involving even a whole lobe.

4. Fibro-caseous Tuberculosis.—This is the commonest variety of the disease; the appearances of the lung vary with the relative preponderance of the caseous and fibrotic changes. The early lesions are miliary or bronchopneumonic, but areas of caseation in varying stages, including cavitation, are almost always present. The older lesions show considerable fibrosis, the strands of sclerotic tissue being pigmented and glistening. The earliest lesion is usually near the apex of the upper lobe at the back, more rarely a little lower and towards the front. The apex of the lower lobe is next affected, and the disease then spreads in the direction of the interlobar septum; the apex of the upper lobe of the opposite lung is next involved (Fowler's law of spread). Pleural adhesions are usually present over the oldest lesions, and in the interlobar fissures. An open cavity, from which infected sputum is discharged, is a danger, being a frequent cause of spread.

5. Fibroid Tuberculosis.—Fibrosis may be localised around a small arrested lesion, or may spread throughout a lung in which caseation or excavation has occurred. One lobe or the whole lung is then contracted and firm. In the interstices of the fibrous tissue, which is usually pigmented, inspissated caseous material, calcareous patches, or cavities are seen. The shrinkage may lead to bronchiectasis, especially in the lower lobes. The overlying pleura is much thickened and adherent, and the mediastinum is drawn over towards the affected side. The opposite lung, or the sound portions of the fibrosed one, may show compensatory emphysema.

The bronchial glands.—The tracheo-bronchial glands are affected in all forms of pulmonary tuberculosis. They are enlarged, sometimes pigmented, and may present miliary, caseous, calcareous or fibroid changes, in some cases primary, in others secondary to the lesions in the lungs.

The pleura.—This, too, is almost constantly affected. The commonest changes are an early dry pleurisy, and a later thickening with adhesions which may completely unite the visceral with the parietal layers. In acute disease or active spread, the pleura may be studded with miliary tubercles, leading to a large serous effusion.

The post-morten appearances of the lesions situated in the other organs, found as complications of pulmonary tuberculosis, are described in the respective sections dealing with them, and include tuberculous meningitis, peritonitis, enteritis and genito-urinary tuberculosis. There is usually atrophy of the skeletal muscles, sometimes lardaceous and fatty degeneration of the liver, and hypoplasia with fatty degeneration of the heart.

Symptoms.—The symptoms fall into three groups (Pottenger)—(1) pulmonary, such as catarrh, expectoration, hæmoptysis and pleurisy; (2) reflex, such as pain, cough and laryngeal irritability; (3) toxæmic, including malaise, tachycardia, pyrexia and loss of weight.

Onset.—The mode of onset is very variable, but certain forms can be recognised.

(*a*) *Insidious*).—The early symptoms may be malaise, anæmia, amenorrhœa, cardiac irritability, progressive loss of weight, and slight rise of temperature, generally towards evening. Cough and expectoration often appear only when the signs in the chest are quite apparent. When there is intestinal

stasis, the cutaneous pigmentation may suggest the diagnosis of Addison's disease.

(*b*) *Catarrhal*—A series of febrile "colds" may usher in the disease, and such a sequence is always suspicious.

(*c*) *Phthisis ab hæmoptoë*.—Hæmoptysis may first draw attention to the lungs. It may be slight, and is then due to early congestion around the focus of infection. If it is more marked, it indicates breakdown of an old arrested lesion, or may afford dramatic evidence of extensive disease which had not been recognised previously.

(*d*) *Laryngeal*.—Hoarseness or aphonia may be the first symptom, but laryngeal tuberculosis is usually secondary to pulmonary disease, although the latter may have been unsuspected.

(*e*) *Gastro-intestinal*.—Anorexia and flatulence often occur early. When they are accompanied by slight loss of weight and pyrexia, the possibility of pulmonary tuberculosis should be suspected.

(*f*) *Pleural*.—Dry pleurisy is a frequent manifestation of latent pulmonary tuberculosis. When a serous effusion develops, its tuberculous character can be determined by laboratory investigations. Pneumothorax, developing in a previously healthy individual is a rare but often serious clinical mode of onset.

(*g*) *Pneumonic*.—"Galloping" consumption often begins with pneumonic manifestations, especially in the young.

(*h*) *Traumatic*.—Pulmonary tuberculosis may follow injury or "gassing," as described under ætiology.

(*i*) *Neurasthenic*.—Neurasthenia may occur as a complication of tuberculosis; but in some cases an initial neurasthenia dominates the picture, and the pulmonary lesion is only detected on careful examination.

(*j*) *Malarial*.—Regular attacks of sweating and fever may occur, especially in those who are or who have been residing in malarial climates, suggesting malaria, but in reality due to tuberculosis.

(*k*) *Associated with other diseases*.—Tuberculosis may follow immediately on an attack of measles, influenza or whooping-cough, especially if complicated by broncho-pneumonia. In some cases it develops at a later period after the acute disease.

(*l*) *Senile*.—In old people an insidious onset is common. The disease may be of bronchitic type, and the signs are often masked by emphysema. There may be little or no rise of temperature.

THE CHIEF SYMPTOMS of pulmonary tuberculosis are—

Cough.—This varies considerably in different types of disease. It may be very slight or absent in generalised miliary tuberculosis, or in any form in the insane. It is sometimes dry, persistent and ineffective, especially in miliary extension in the lungs from an old focus of disease, in bronchial gland tuberculosis, or in pleurisy. When there is associated bronchitis or caseation, the cough is usually accompanied by expectoration, which, if very tenacious, may lead to retching or even to vomiting, particularly in the morning. In laryngeal tuberculosis the cough is husky and frequently painful.

Expectoration.—In early disease there is usually no sputum, and in some cases, more especially in the fibroid type, widespread lesions may be present with practically no expectoration. When caseation is in progress, or when

there is secondary infection with bronchitis, the sputum may be abundant and amount to as much as 20 or more ounces in the 24 hours. It may be clear or mucoid, or thick tenacious muco-pus. If mucoid, it often contains small particles, the size of a pin's head or larger, of yellow caseous material. Nummular sputum may be met with in active caseous disease, especially with excavation. This consists of flat rounded masses of muco-pus, with a somewhat distant resemblance to coins. In tuberculosis the sputum is usually inoffensive, but may have the characteristic sickly odour which is also noticed to emanate from the patient himself (odor phthisicus). If bronchiectasis or gangrene occurs as a complication, the expectoration becomes typically malodorous. Pulmonary calculi or pneumoliths, composed chiefly of calcium carbonate or phosphate, are sometimes expectorated. They vary in size from a pin's head to a pea, are irregular in outline and sometimes branched, being derived generally from the walls of a cavity. Although the occurrence of these does not necessarily indicate fresh activity in the lungs, yet such a possibility should always be suspected, and a careful watch maintained on the temperature during the next few days. In some cases larger pneumoliths, as big as a cherry, may be coughed up, and those are frequently derived from calcified tracheo-bronchial glands. They may give rise to alarming symptoms at once, and be the forerunner of fresh activity in the lungs.

Microscopical examination.—The presence of tubercle bacilli in the sputum is the most decisive test of the existence of this disease. The small yellowish caseous particles should be selected from the sputum, and appropriately stained. If no tubercle bacilli are found, samples from the whole sputum of the 24 hours, concentrated by the antiformin method, can be examined. Droplets collected on a laryngeal mirror by cough induced by it may be examined for the presence of tubercle bacilli, especially in children or in patients who habitually swallow sputum.

Sputum culture by the Loewenstein method may be of value when tubercle bacilli are not found in smears. The cells present are usually of the mononuclear type, either mononuclear leucocytes or altered alveolar epithelial cells. The presence of elastic tissue indicates that destructive pulmonary lesions are in progress. Secondary infecting organisms may be demonstrated by cultural methods.

Dyspnœa.—Slight dyspnœa occurring early in the disease may be due to diminished movement of the diaphragm on the affected side. In more advanced cases the degree of dyspnœa is proportional to the amount of lung tissue involved. In addition, cough and pyrexia play a part in its production. Complications such as pleurisy, pleural effusion, pneumothorax and cardiac failure increase the shortness of breath. It is rare to find orthopnœa even in acute and rapidly spreading disease. In arrested cases the dyspnœa is proportional to the extent of fibrosis.

Cyanosis.—This is not an early symptom of tuberculosis. It is dependent upon the amount of lung tissue involved, but is increased by the coexistence of emphysema or cardiac failure. The typical "hectic flush" of tuberculosis is a vasomotor effect caused by toxæmia.

Pain.—Not every sufferer from tuberculosis experiences pain, even in the acute stages of the disease. The commonest cause of pain is dry pleurisy. When the diaphragmatic layer of the pleura is affected, pain may be referred to the epigastrium or to the corresponding shoulder. In chronic fibroid

phthisis there is frequently a dull, aching pain in the chest, which is more noticeable in damp weather. This is caused by the contraction of the condensing fibrous tissue. Cutaneous tenderness of the chest-wall is met with in some cases of advanced disease, and is probably due to a cachectic neuritis. A "cold abscess" forming along one of the ribs or costal cartilages is a rare cause of localised pain in the chest-wall. Cough may be painful, especially when paroxysmal or frequent, the pain being referred to the costal attachments of the diaphragm and upper abdominal muscles. The sudden occurrence of pneumothorax may cause such severe pain as to induce collapse; but when of more gradual onset no severe discomfort may be experienced. Tuberculous laryngitis may be the cause of very great suffering.

Night sweats.—Although not pathognomonic, night sweats occur more frequently in tuberculosis than in other diseases. They are met with in all stages of active lesions, and may be of great severity.

Loss of weight.—This is often an early symptom. It is most marked in acute disease and in the late stages of chronic fibro-caseous tuberculosis.

Fever.—Pyrexia is one of the most important indications of activity at any stage of pulmonary tuberculosis, although it does not follow that the disease is arrested when there is no fever. During treatment the temperature should be recorded at certain definite hours in the day. (*a*) On waking. The normal mouth temperature at 7 or 8 a.m. is 97° or 98° F. in the mouth, and 97°·2 to 99° F. in the rectum. This temperature should be taken in bed, before eating or drinking. (*b*) At 1 p.m., after the hour's recumbent rest. (*c*) At 6 p.m. (*d*) At 9 p.m., after retiring to bed. The maximum temperature is usually reached between 4 and 6 p.m., but may be delayed to 8 or 9 p.m. In most Continental sanatoria the rectal temperature is taken, and a centigrade thermometer employed. The temperature is dependent upon the extent and the activity of the disease, and upon the amount of exercise taken.

(*a*) In acute miliary tuberculosis it may be continuous or remittent, and the "typus inversus" is not uncommon, the morning temperature being higher than the evening. This is generally regarded as a sign of grave prognosis.

(*b*) In acute caseous tuberculosis the high temperature at the onset is continuous, and the record resembles a pneumonic chart. When caseation occurs it becomes hectic or intermittent, with a daily swing of 4° or 5° F. This is probably due to the action of tubercle toxins, and not to the presence of a secondary infection.

(*c*) In chronic fibro-caseous tuberculosis there is no characteristic temperature record. There may be only a very slight rise occurring at intervals of a few days. On the other hand, the patient may be afebrile while resting, but febrile when ambulant (Stage 2. Inman's classification). Further an afebrile ambulant patient may over-exert himself, and by excessive auto-inoculation develop a sharp rise of temperature which subsides in a few days with rest. The temperature chart is thus a guide to prognosis and to treatment, and if acute miliary tuberculosis or caseation occurs, a typical temperature variation ensues.

(*d*) In fibroid tuberculosis the temperature is usually normal, unless excessive auto-inoculation results from exercise, or the disease advances. The occurrence of hæmoptysis may have a very definite effect upon the temperature. In some cases it is not followed by pyrexia, but if the inhaled blood leads

to a hæmoptoic bronchitis, there may be a slight degree of fever lasting for a few days. When a definite and persistent pyrexia follows, it usually indicates activity around an old focus of disease, or fresh spread by inhalation of blood containing tubercle bacilli to distant parts of the lung.

A premenstrual rise of temperature may occur; but as it is also met with in healthy women it is not pathognomonic.

Hæmoptysis.—Hæmoptysis occurs at some stage of pulmonary tuberculosis in about 50 per cent. of all cases. With early lesions the sputum is only streaked. This may result from the congestion of tuberculous bronchitis, or from a small area of collapse or broncho-pneumonia. In the pneumonic or broncho-pneumonic forms rusty sputum may be seen. Profuse hæmoptysis generally occurs in chronic disease; but it is occasionally met with in acute caseous forms. Recovery may take place after coughing up 2 or 3 pints, or death may ensue rapidly from suffocation before any considerable quantity of blood has been expectorated. After the cessation of bleeding the sputum may be blood-stained for several days, the colour becoming darker. The source of profuse hæmoptysis is generally an aneurysm of a branch of the pulmonary artery lying in a cavity or in a fibroid lung, although occasionally ulceration without previous aneurysm formation may occur. In the majority of cases hæmoptysis begins while the patient is lying down or resting, so that exercise or work are not frequent exciting causes.

The patient notices a salt taste, feels a warm gush in the mouth, and then expectorates the blood. He is usually greatly alarmed, flushed and sweating, with rapidly beating heart. The blood at first is as a rule bright and frothy but some clots may be present; later it is mixed with muco-purulent expectoration, in the form of clots or streaks.

Circulatory system.—The heart may be small, but the right side often hypertrophies in chronic fibroid cases. Tachycardia may be due to nervousness, but when constant it generally indicates active disease or over-exertion on the part of the patient. The blood pressure is usually low in the stages of activity, and a steady rise during treatment is a favourable sign. If tuberculosis is coexistent with other diseases, such as atheroma, which raise the blood pressure, higher readings are naturally obtained.

The blood.—The red cells are usually normal in number, but there may be a slight anæmia. On the other hand, when there is much cyanosis, or after sanatorium treatment, the red cells may be increased. The colour index is usually low. In the early stages the leucocytes may be slightly increased. A polymorphonuclear leucocytosis occurs in caseation and in early cavity formation, and at times with secondary infection of the lungs. A special differential count of the polymorphonuclear leucocytes themselves may be made by subdividing them into groups, according to the number of their nuclear lobes, as suggested by Arneth. An increase in number of immature cells with only one or two nuclear lobes constitutes a deviation to the left from the normal, and raises the Arneth index. This lævo-deviation is said to indicate toxæmia, and if it is not present, the disease will probably be chronic. The von Bonsdorff modification in which the number of lobes of the nuclei in one hundred polymorphonuclear leucocytes is counted, is sometimes used. The normal figure is 274, a figure less than this suggests activity. The lymphocyte monocyte ratio is said to be of prognostic value, an absolute and relative increase in the monocytes being unfavourable.

Alimentary system.—The tongue is usually clean and the appetite good even in cases with marked fever. When tuberculosis of the larynx is present, there is frequently severe dysphagia. Dyspepsia may be complained of, usually of a nervous type. Anorexia, flatulence, distension with nausea are the commonest symptoms, pain being rarely noticed. There may be marked intolerance of fat in the diet. Atonic dilatation of the stomach may occur in some cases towards the end of the disease. Constipation is common; on the one hand, diarrhœa may occur apart from intestinal ulceration or lardaceous disease.

Nervous system.—The classical "spes phthisica" is distinctly rare, but when present is very striking from its contrast with the realities of the disease. It is most commonly seen in acute caseous tuberculosis. More often the patient becomes emotional and self-centred, depression is common and hard to combat, and melancholia with delusions occasionally develops. Neurasthenia is frequent and, as mentioned above, may lead to errors in early diagnosis. Insomnia may be due to cough, pyrexia, night sweats or pain, especially in laryngitis. With marked cachexia, a definite peripheral neuritis may occur.

Genito-urinary system.—In the early stages there is often an increased sexual desire, and this may recur when arrest is taking place. This is probably in part due to the therapeutic régime, the rest, abundant food and lack of interesting occupation reacting upon the nervous system of young adults. In advanced disease, all sexual desire is lost. Menstruation often ceases early, and the patient may seek advice for amenorrhœa. Women remain fertile even in advanced disease. The urine is normal in the early stages, later a febrile albuminuria may occur, or in advanced cases an amyloid nephrosis with generalised œdema may develop.

The Physical Signs of Early Disease.—The general appearance of the patient may be healthy, or may be that of malnutrition with the characteristics of the "habitus phthisicus," the hair being lank and lustreless, the skin white, thin, dry and shiny. and the thorax of the alar or phthinoid type. Certain stigmata are described, which although useful, are not pathognomonic. The eyelashes may be long, dark and curling, the back hairy and the thoracic cutaneous venules dilated. When present around the upper thoracic vertebral spines, they are sometimes known as "the varicose zone of alarm." Deficient movement may be observed below one clavicle, at the point of one shoulder, or at the lower costal margin. The corresponding shoulder may be slightly drooping, with flattening above or below the clavicle, and slight hollowing of the supra-spinous fossa with wasting of the trapezius muscle may be observed. Pottenger regarded these shoulder signs, when not due to scoliosis or kypho-scoliosis, as reflex, and comparable with the fixation of a tuberculous joint and wasting of its adjacent muscles. In women it may be noticed that the breast on the affected side is smaller and hangs at a lower level.

Palpation confirms the diminished expansion, and reveals a slight increase of vocal fremitus over the affected area of the lung, usually at one apex. The normal increase in fremitus of the right apex over the left must be borne in mind, in order to prevent mistakes.

With light percussion slight dullness and a small increase in the sense of resistance can be detected. This is usually most apparent in the

supra-spinous and upper interscapular regions. The extent of pulmonary resonance above the clavicle, known as "Krönig's isthmus," may be diminished by ½ to 1 inch on the affected side.

Various types of breath-sounds may be heard over the affected portion of lung. They are—(*a*) weak inspiration, with expiration vesicular or inaudible; (*b*) cog-wheel inspiration, with expiration vesicular, prolonged or rarely jerky; (*c*) the "granular" breathing of Grancher, the breath-sounds being somewhat coarse and irregular, suggesting fine or distant râles, although none can be definitely detected; (*d*) harsh inspiration, with expiration vesicular or prolonged; (*e*) broncho-vesicular breathing; (*f*) definite bronchial breathing when early consolidation is in progress.

Often there are no adventitious sounds. Occasionally a few small rhonchi or fine crackling or bubbling râles may be heard with the first few deep breaths, or only with the inspiration immediately following coughing. If râles are constantly heard, it indicates that the lesion is already of some extent. Care must be taken to differentiate them from atelectatic râles, emphysematous râles audible along the sternal margin, and pleural friction or fascial creaks. There is usually a slight increase in the conduction of both the spoken and whispered voice, and the more definitely this extends away from the trachea in front, and from the vertebral spines behind, the more reliable is the sign as an indication of disease.

Mensuration is seldom practised in routine examination, but graphic records of the chest contour, which are of interest in following the progress of a case can be obtained by cyrtometry.

Physical Signs of Acute Miliary Tuberculosis.—If the condition develops acutely from breaking down of an infected bronchial gland or small lung focus, the physical signs are generally those of an acute generalised broncho-pneumonia, unless there is meningeal involvement as well, in which case the pulmonary symptoms and signs are masked or obscured by those of the cerebral involvement. When miliary tuberculosis occurs as a terminal event in a chronic case, marked dyspnœa, cyanosis and tachycardia are early symptoms. There may be crepitations or fine crepitant râles widely distributed over both lungs, and sometimes areas of tubular breath-sounds especially in the lower lobes. The original signs are often masked or less apparent. This is especially the case if meningeal involvement occurs also.

The Physical Signs of Consolidation.—Limitation of movement and flattening over the affected part of the lung, usually the apex, is now more noticeable.

The diminution of movement is confirmed on palpation, and vocal fremitus is found to be definitely increased.

The pulmonary resonance is diminished to definite dullness and the sense of resistance is correspondingly increased.

The breath-sounds are bronchial, or in acute caseous disease may even approximate to tubular.

Adventitious sounds may be absent, but usually fine or medium crackling râles are heard with inspiration, especially after coughing. When active softening is in progress the râles frequently become coarse and sticky. The voice conduction is much increased, bronchophony and whispering pectoriloquy being audible.

Mensuration may confirm the presence of flattening.

THE PHYSICAL SIGNS OF EXCAVATION.—Flattening of the chest-wall and diminished movement over the cavity are now more marked; if the cavity is apical there is in addition notable dropping of the shoulder, and wasting of the shoulder-girdle muscles.

The diminution of movement is confirmed by palpation. Vocal fremitus is generally increased owing to the surrounding consolidation, but if the cavity is full or there is much pleural thickening, it is diminished.

The percussion note is dull when the cavity is small or filled with secretion. A peculiar boxy or "cracked-pot" note, the "bruit de pot fêlé," is obtained over large superficial cavities, especially when communicating with an open bronchus. This is best heard on percussing with the mouth open, and Wintrich showed that the note may be altered in pitch over such cavities when percussing with the mouth open or closed, apart from the actual presence of the cracked-pot sound. Gerhardt's sign (alteration of note with the position of the body) is supposed to indicate a cavity of oval shape. It is rare, and of little value.

The breath-sounds are bronchial, broncho-cavernous, cavernous or amphoric, according to the size of the cavity, and to the amount of its contents. When it is full the breath-sounds may be distant, weak or even absent, and this is especially noticeable in basal bronchiectasis.

With a dry cavity there may be no adventitious sounds. Usually râles are audible; they may be medium or large, and bubbling or crackling in character. Over a large cavity a metallic tinkle and amphoric echo may be heard. With a very large cavity, extending through the whole of one lung, a typical *bruit d'airain* is at times obtainable. Voice conduction is increased, bronchophony and whispering pectoriloquy are present, and in some instances post-tussive suction is heard. Some cavities are only revealed by X-ray examination or by tomography.

Mensuration affords a graphic representation of the flattening of the chest-wall.

THE PHYSICAL SIGNS OF FIBROSIS.—The chest is asymmetrical, the affected side being flattened and moving little, while compensatory scoliosis or kypho-scoliosis is often present. The cardiac impulse is seen to be displaced towards the affected lung and may be higher or lower than normal. It may be drawn over to the right axilla, or on the left side as far back as to the posterior axillary line, or even to the angle of the scapula. The intercostal spaces may be retracted, and dilated venules are sometimes seen over the front of the chest as the result of obstruction, caused by displacement of the mediastinum and traction on the deeper veins.

Diminution of movement is confirmed by palpation, and the cardiac impulse can be more accurately localised. Vocal fremitus may be increased or diminished; the former occurs when the lung is consolidated and the large bronchi patent, the latter when there is much pleural thickening.

The percussion note over fibroid lung is dull and the sense of resistance increased, unless cavities are present. The opposite lung may be hyper-resonant, and its resonance extend across the mid-sternal line. The cardiac dullness is often continuous with that of the fibroid lung, and its area can only be determined by the cardiac pulsation.

The breath-sounds are weak and distant, unless modified by the presence of a cavity.

Often there are no adventitious sounds, although fine or medium râles of a sticky or metallic nature may be heard. The voice conduction is usually diminished, and there is no pectoriloquy unless excavation has occurred, when bronchophony and pectoriloquy are audible.

It must be borne in mind that in actual disease the lesions are not so clear-cut and well-defined. In a case of some duration different stages of disease can be found in the same individual, thus infiltration, consolidation with softening, excavation and fibrosis may be present in different lobes of the lungs, and thus it may be possible to determine the site of origin and path of spread of the disease.

Certain other signs are occasionally seen in pulmonary tuberculosis.

Myoidema is an undue irritability of the muscles to direct mechanical stimulation, revealing itself by a flickering fibrillary contraction on tapping with the finger, and may occur in tuberculosis at all stages. It is best seen over the pectoralis major on the affected side. It may be present quite early, but is not pathognomonic, as it may occur in any cachectic state.

Clubbing of the fingers is commonly seen in chronic cases, the nails are curved and present a parrot-beak appearance, the thumb, index and middle fingers being most affected. Drum-stick clubbing is only seen in fibroid lesions with bronchiectasis.

Chronic Miliary Tuberculosis.—*Clinical features.*—Chronic miliary tuberculosis affects males and females equally. The age incidence is between 6 and 40 years, but usually the patient is between 11 and 30. The early symptoms include cough, shortness of breath, pain in the chest, expectoration and at times hæmoptysis. Constitutional disturbance is usually slight with low-grade fever. In some cases the spleen is palpable and in others tuberculous lesions are present in glands, bones or joints. Tubercle bacilli may be found in the sputum, gastric contents or pleural fluid. X-ray examination reveals small symmetrical, rather ill-defined opacities throughout the lung-fields. In some cases they may be limited to one portion of the lung. The course of the disease is more prolonged than that of miliary tuberculosis, being never less than three months and usually considerably longer. Death may occur in about six months, or eventually the disease may be arrested.

The differentiation of chronic miliary tuberculosis from the acute variety depends rather upon the clinical than the radiological findings. The fact that the pulmonary lesions are tuberculous is established in many cases by the finding of tubercle bacilli in the sputum or stomach contents. When tubercle bacilli cannot be detected, other conditions giving rise to scattered opacities throughout the lung-fields must be considered. Thus in secondary carcinomatosis, sarcomatosis or chorio-epitheliomatosis, the opacities are usually larger. Multiple opacities are also found in pneumokoniosis, congestive heart failure, sarcoidosis and more rarely with periarteritis nodosa, xanthomatosis, bilharziasis, leukæmia and disseminated broncho-pneumonia.

Hilum Tuberculosis.—The existence of a special type of pulmonary tuberculosis commencing at the root of the lungs and extending thence in a fan-shaped manner along the bronchi has been postulated by some authorities, chiefly on X-ray evidence. While lesions in the middle zone of the lung are sometimes revealed by X-ray examination, it is more than doubtful whether this condition merits recognition as a separate variety of the disease.

EPITUBERCULOSIS.—This term was applied by Eliasberg and Neuland in 1920 to a condition of consolidation in tuberculous infants, often affecting a whole lobe. In spite of definite physical signs and characteristic radiological appearances, there are few symptoms, and recovery is the rule, with fairly rapid clearing of the X-ray shadows, from the periphery inwards. It is probably due to atelectasis of a lobe in whole or part, due to bronchial obstruction from enlarged hilar glands.

HILAR FLARE is the name given by Burton Wood to a similar condition affecting the right middle lobe, or the upper part of either lower lobe in childhood. The X-ray shadow is generally triangular in shape, the base being at the hilum or mediastinum. This, like epituberculosis, is probably due in many cases to localised bronchial obstruction, but in both conditions it is possible that there may be an allergic factor.

It is important to note that in both epituberculosis and hilar flare, the chief evidence is radiological, and that the prognosis is good.

PULMONARY OSTEO-ARTHROPATHY.—In cases with bronchiectasis the joints may be affected, swelling occurring especially in the wrist, ankles and knees, and rarely in the hips and shoulders. A serous effusion into the joints may be present. Pain is usually slight, but there is much deformity and functional impairment. X-ray examination reveals productive periosteal changes, which may also affect the long bones and the spine (see p. 1376).

RADIOGRAPHY OF THE CHEST.—If possible, the chest should be examined in every case with the fluorescent screen, and a photograph taken on a film. Certain important points can only be determined by a screen examination. The chief of these are the respiratory movements of the diaphragm, lighting up of the apex of the lung with inspiration, and the cardiac pulsation. Unilateral restriction of diaphragmatic movement not infrequently occurs in early apical tuberculosis, but as it may be observed under other conditions, notably with pleural adhesions, it is not diagnostic. The film will show the extent of the disease and in some cases it may suggest the existence of activity; thus areas of consolidation, caseation or excavation can be demonstrated, and thickening of the pleura, pleural effusion and pneumothorax give their characteristic appearances. In films taken in the erect position a fluid level is often apparent in cavities. A curious rounded shadow may be apparent in early disease called Assmann's focus, in which rapid changes, such as softening, may occur. The tomograph sometimes shows unsuspected cavities.

The significance of "root shadows" is still debatable. Although the presence of calcareous deposit in the glands at the roots of the lungs is usually obvious, the interpretation of the radiating shadows is a matter still under discussion. They may be due to peribronchial thickening, caused by the formation of fibrous tissue, or may merely represent the shadows cast by the branches of the pulmonary artery.

A film is often of crucial value in determining the presence or absence of early disease, but slight diminution of translucency of one apex may be due to an old arrested lesion, or, on the other hand, there may be definite physical signs of active disease, without abnormalities being found on X-ray examination. The heart shadow is often narrow and vertical in tuberculosis. Displacement of the heart due to pulmonary fibrosis or to affections of the pleura is clearly indicated. A good film may also give valuable information as to the

extent of lung involved and as to the presence of complications, such as effusion, pneumothorax or bronchiectasis. As the X-rays only cast shadows lacking in all pictorial details, tuberculous shadows cannot always be distinguished from those due to other pulmonary lesions. It is thus clear that the X-ray findings should always be interpreted in connection with the history, symptoms and physical signs of the case. The X-rays, although often of great help, do not afford a simple road to diagnosis or supply infallible evidence in determining the nature of an obscure case. On the other hand, they are absolutely essential in the determination of the suitability of a case for artificial pneumothorax or other collapse treatment and in controlling its application.

Complications and Sequelæ.—Compensatory emphysema is common in chronic fibroid disease, but bronchiectasis occurs less frequently. Gangrene of the lung is not often observed. Colds and catarrhal affections of the respiratory passages are frequent in sufferers from tuberculosis, and lobar pneumonia may develop as a complication. Bronchitis often occurs, due either to spread of the tuberculous process or to a secondary infection. In some instances asthma appears for the first time after tuberculosis has become manifest. A tuberculous abscess occasionally forms about a rib or costal cartilage.

Small areas of dry pleurisy are present at some stage in nearly every case; a serous pleural effusion is common, and an empyema may develop as the result of a mixed infection, or from the tubercle bacillus alone. Pneumothorax may occur as an early complication, or late in the disease, generally from rupture of a caseous focus just under the pleura; this frequently progresses to the formation of a pyo-pneumothorax. The implantation of tubercle bacilli from the expired air or sputum may lead to secondary foci in the larynx, trachea and epiglottis, or more rarely in the pharynx, tonsils, base of the tongue or nose. Swallowing of sputum containing tubercle bacilli gives rise to gastro-intestinal complications in many cases. The most common site of tuberculous ulcers, is the terminal portion of the small intestine, but the appendix may be affected, and the connective tissue around the cæcum is sometimes matted and thickened to form a palpable mass (hypertrophic tuberculoma). Tuberculous peritonitis is not common in adults and is usually secondary to intestinal lesions. The stomach is very rarely ulcerated, but an atrophic gastritis may occur in advanced cases. Fistula-in-ano and ischio-rectal abscess are comparatively common complications and tubercle bacilli may be found in the discharges.

Small vegetations may be found post mortem in the heart on the aortic and mitral valves, but these are usually due to some terminal infection. Fatty degeneration of the myocardium occurs as a result of toxæmia, and infection by direct spread along the lymphatics may lead to pericarditis. The peripheral circulation is not infrequently poor, chilblains are common, and cachectic purpura may be seen. Lardaceous degeneration as a consequence of chronic tuberculosis is not so common nowadays as formerly, but when present may affect the liver, spleen, intestines, lymph glands and kidneys.

The genito-urinary complications include lesions in the kidneys, bladder, epididymis and prostate. If the suprarenal body is affected Addison's disease will usually develop. Spinal caries is occasionally observed. A peripheral neuritis may form part of the lesions occurring with marked

cachexia. Generalised dissemination of the tubercle bacilli by the blood stream is followed by tuberculous meningitis.

Course.—The course pursued by pulmonary tuberculosis is variable, depending upon the clinical type of the disease. In acute miliary tuberculosis, death may occur in from 1 to 3 weeks from toxæmia or generalisation of the lesions. In acute caseous tuberculosis, death usually results in from 1 to 6 months. In chronic fibro-caseous tuberculosis, the disease may be completely arrested, or after a temporary arrest may become active at intervals and again become arrested under suitable treatment; in other instances it progresses steadily to a fatal termination. In fibroid tuberculosis the disease may become completely arrested or smoulder quietly for many years.

Apart from the question of the expectation of life, various stages of tuberculosis are described based upon anatomical lesions, toxæmia and functional disablement. The most important of these are as follows:

1. The Turban-Gerhardt Classification.—An anatomical classification based upon the extent of lung tissue involved. Three stages are described. *Stage* 1. Early cases in which physical signs, if unilateral, only extend from the apex to the second rib, and, if bilateral, are limited to the supra-clavicular and supra-spinous regions. *Stage* 2. The signs, if unilateral, do not reach lower than the fourth rib, and, if bilateral, are situated above the second ribs. Excavation is not present in this stage. *Stage* 3. This includes more extensive lesions or localised ones in which excavation is present.

2. Sir Robert Philip's Classification.—Both the extent of lung tissue involved and the degree of toxæmia present are taken into consideration. Twelve stages are described, which are indicated by the following signs:

L_1, L_1s, L_1S, and 1_1S; L_2, L_2s, L_2S, and 1_2S; L_3, L_3s, L_3S, and 1_3S. L_1, L_2, and L_3 represent lung involvement to the extent of stages 1, 2 and 3 respectively, according to the Turban-Gerhardt scale. s applied to these letters indicates that there is only slight systemic disturbance, whereas S signifies marked systemic disturbance; and the signs 1_1S, 1_2S and 1_3S show that the systemic disturbance is excessive in relation to the lung involvement.

3. Inman's Classification.—This is based solely on the temperature in relation to exertion.

Stage 1. The patient is febrile when resting. Stage 2. The patient is resting afebrile, but ambulant febrile. Stage 3. The patient is ambulant afebrile. Stage 4. The patient is working afebrile.

The course taken by tuberculosis of the lung may lead to several terminations. These are: (1) permanent arrest, either by fibrosis prior to caseation, or if the latter has occurred, by calcification and fibrosis; (2) incomplete arrest, as shown by the persistence of tubercle bacilli in the sputum, or by slight degrees of pyrexia on over-exertion; (3) rapid extension, here the disease spreads, and the toxæmia is out of all proportion to the extent of the lesions; (4) death, this may result from the pulmonary lesion or from complications. The former may prove fatal as the result of progressive asthenia or cardiac failure, from asphyxia due to acute miliary tuberculosis or hæmoptysis, or in a small proportion of cases directly from loss of blood in repeated hæmoptysis. The complications that most often prove fatal are meningitis, enteritis, laryngitis leading to dysphagia and starvation, or

pneumothorax. Intercurrent diseases, such as pneumonia, influenza or diabetes, are occasionally the cause of death.

Diagnosis.—This is easy when definite signs are present in the lungs, and when tubercle bacilli are found in the sputum. On the other hand, the diagnosis of early cases may present one of the most difficult problems in clinical medicine. Tuberculosis may be suspected on account of symptoms, although the physical signs are indefinite. The conditions which most frequently lead to doubt are dyspepsia, neurasthenia, debility, visceroptosis and intestinal stasis, oral sepsis, tachycardia associated with early Graves's disease or heart disorders, affections of the nose and throat, and in children enlargement of the bronchial glands or acidosis. The history and symptoms are of great importance in these cases, and a careful examination should be made of each system. A test meal, opaque meal, or blood examination may be required before the correct diagnosis is established.

On the other hand, there may be definite signs of disease in the lungs which have to be differentiated from those produced by other conditions simulating tuberculosis. The cases included in this group embrace the majority of pulmonary lesions, especially chronic bronchitis, fibrosis, bronchiectasis, asthma, emphysema, apical catarrhs and collapse, pleurisy, new-growths and cysts. Diagnosis depends upon the history and course of the disease, together with a careful record of the physical signs in the chest, investigation of the sputum for infecting organisms, X-ray examination and in some cases the determination of the Wassermann reaction.

A condition of special difficulty is that of the variety of sarcoidosis known as Boeck's sarcoid. The lesion is a benign lymphogranuloma or reticulosis. It affects the lymph glands, lungs, bones especially those of the fingers, and the skin (see pp. 1478–1480). The parotid and lachrymal glands are sometimes involved and irido-cyclitis has been recorded in 10 per cent. of the cases. The intestines, spleen and liver may be affected. The chief diagnostic points are the character of the skin lesions and the chronicity and tendency to spontaneous arrest. Tubercle bacilli are not found and the Mantoux reaction is often negative. The radiological appearances in the lungs are those of a diffuse mottling—coarser than that of miliary tuberculosis. The hilar glands are often markedly enlarged.

When the diagnosis still remains doubtful the patient should be placed under observation, and a series of examinations carried out, the object of which is to determine whether or not active tuberculosis is present. The temperature should be observed with the patient in bed, a daily rise to 99° F. or a swing of 1°·5 to 2° below normal being suspicious. The sputum should be examined repeatedly for tubercle bacilli by the ordinary method, and if not found the antiformin process should be carried out.

Before applying any tuberculin tests the blood may be examined serologically. The use of the Arneth or von Bonsdorff blood count in diagnosis has been referred to on page 1196. The complement-fixation test has proved disappointing, and in the present form does not afford reliable criteria of activity or quiescence.

The sedimentation test of the blood (stability reaction), *i.e.* the rate of settling of the erythrocytes in blood diluted with sodium citrate solution, is affected in this disease. In active cases the sedimentation rate is increased, but this reaction is not specific. It is also increased in other conditions such

as pregnancy, carcinoma, syphilis, rheumatism and acute infections. The test is therefore of little or no value in diagnosis, but it affords valuable indications of the degree of activity, and may assist in determining the form of treatment.

It has also been used as a guide to prognosis, since it is affirmed that arrest should not be considered as firmly established until the sedimentation rate has returned to normal. This may not occur until some time after the usually accepted clinical symptoms and signs of activity have disappeared.

THE TUBERCULIN TESTS.—1. *Cutaneous (the Pirquet reaction).*—Scarifications are made on the skin of the forearm through a drop of Koch's old tuberculin, human and bovine, and through a drop of saline as a control. A positive reaction is shown by the formation of a slightly raised, reddened papule at the site of the scarification through one or other varieties of tuberculin, whereas the control is not affected. Unfortunately, except in the first two years of life, this affords no indication of active disease, but only reveals the presence of previous infection with resulting tuberculin sensitiveness. A positive reaction is therefore given by the majority of adults.

2. *Mantoux's intradermal test.*—An injection of 0·1 c.c. of a 1 in 10,000 dilution of old tuberculin (0·01 mgrm.) is injected intradermally. If no reaction occurs, the injection is repeated in a week, with 0·1 c.c. of 1 in 1000 dilution (0·1 mgrm.). A positive reaction is shown by a red areola, with some œdema and occasional vesiculation.

A modification of this test consists in the use of Purified Protein Derivative (P.P.D.). This is supplied in tablets of two strengths, which must be dissolved in a buffered solution immediately before use. The advantage of this preparation is its constant potency.

3. *Vollmer's patch test.*—A strip of adhesive plaster is applied over the sternum, previously cleaned with ether. To this strip are attached three small squares of filter paper, the central one is a control of untreated paper, the other two have been saturated with undiluted old tuberculin and allowed to dry. The plaster is removed in 48 hours and 12 or 24 hours later a positive reaction is shown by redness, infiltration and sometimes by papules or vesicles.

4. *The subcutaneous test.*—The patient must be apyrexial, and must be kept in bed—$\frac{1}{10}$ mgrm. of old tuberculin is injected subcutaneously, and its effect determined. The reactions that may develop are—(*a*) local, an inflammatory swelling at the side of the injection; (*b*) focal, an increase of the signs observed at the seat of disease in the lungs, such as the temporary appearance of a few râles at one apex. This is the most important; (*c*) general, as judged by a rise of temperature and sense of malaise. The temperature should be charted 4-hourly after the injection, and a rise to over 99° F. indicates a positive reaction. If no reaction follows this initial dose, larger injections are given at intervals of 2 or 3 days, in this sequence: $\frac{1}{5}$, $\frac{1}{3}$, 1, 5 and even 10 mgrms.

This test has the drawback that it does not indicate activity of disease, and it has the additional disadvantage that it may cause a quiescent pulmonary focus to light up and spread, and so cause irreparable damage.

Finally, the X-rays afford most valuable assistance in the diagnosis of early cases with doubtful signs, and also help in the differential diagnosis of tuberculosis from other lung diseases with well-marked signs.

Prognosis.—A number of factors must be critically considered in the determination of the prognosis in pulmonary tuberculosis.

A marked family incidence generally suggests an unfavourable course, though this rule is not invariable.

Personal history.—Chronic alcoholism is serious, chiefly because the régime of treatment is then peculiarly irksome, while the digestion and powers of resistance are often impaired in alcoholics. Tuberculosis in syphilitics frequently assumes a fibrotic type, and its course may be beneficially influenced by anti-syphilitic treatment. The outlook is grave when tuberculosis is conjoined with diabetes though less so since the use of insulin. Congenital heart disease and pulmonary stenosis are unfavourable factors; but hypertrophy of the heart and mitral stenosis are said to be beneficial.

The prognosis is very grave in infants and young children; but slightly less serious up to the age of 20. Between 20 and 50 age has little influence; but in later years the outlook becomes progressively less favourable.

Apart from the effects of pregnancy and exposure, sex plays no important part.

Freedom from financial embarrassment improves the prognosis, inasmuch as advice can be sought early, and treatment carried through thoroughly.

Marriage often leads to a breakdown in arrested cases especially in women, and induces more rapid spread of active lesions.

Persistence in an unfavourable occupation, or return to it after completion of institutional treatment, affects the prognosis adversely.

Poor chest development and the "habitus phthisicus" are usually bad prognostic signs, although tuberculosis may run a rapid course even in patients with good physique.

Patients with resolute and persistent personality are more likely to persevere with treatment and to recover, than those of weaker moral fibre.

The prognosis is greatly affected by the type of the disease—acute miliary tuberculosis is usually rapidly fatal, whereas in acute caseous tuberculosis, although the prognosis is very grave, recovery may occur. In fibro-caseous tuberculosis the prognosis is most uncertain and difficult to forecast. Every factor must be carefully considered, and the response to treatment noted. The best outlook is in fibroid disease, which often undergoes complete and permanent arrest.

Symptoms in their Relation to Prognosis.—Persistent cough, by exhausting the patient and disturbing sleep, is often unfavourable.

The amount of sputum is usually dependent upon the type of disease and upon the presence of secondary infection, and may therefore be of value in prognosis.

The significance of tubercle bacilli in the sputum.—The figures obtained at the Midhurst Sanatorium, over a period of 8 years, in which the after-history of the patients was traced for the ensuing 6 years, show that the prognosis is best in "closed" cases; but that it is nearly as good in those cases in which the tubercle bacilli disappear from the sputum during the sanatorium treatment. Persistence of bacilli in the sputum is an unfavourable sign. The actual number of bacilli in the sputum and the presence of "beading" have no definite prognostic significance.

Cases commencing with hæmoptysis progress more satisfactorily than

those with other modes of onset, chiefly because they are diagnosed earlier. Hæmoptysis occurring later may exert an unfavourable influence, either indirectly by spreading the disease into previously healthy portions of the lungs, or actually by the loss of blood.

If dyspnœa is not due to attacks of bronchial spasm, it has usually an unfavourable significance.

The temperature affords a clue to the type and activity of the disease, and is thus a valuable aid to prognosis. Profuse and persistent night sweats, or marked anorexia, especially when occurring early in the disease, are grave signs. Tachycardia due to toxæmia, signs of cardiac failure, œdema and albuminuria are of bad omen. The blood pressure is thought by some to be a useful guide, systolic figures below 100 mm. Hg being unfavourable, whereas a rise of pressure may be associated with amelioration of the disease. In fibroid lesions the pressure may be raised throughout.

The Extent of Physical Signs.—The activity of the disease rather than its extent is the important factor in determining prognosis. The development of compensatory emphysema is of value only as an indication of fibrosis in the tuberculous portion of lung, and therefore of chronicity.

The Influence of Complications on Prognosis.—Generally speaking, the presence of complications increases the gravity of the disease. Involvement of the larynx is a serious complication, especially when accompanied by dysphagia; but complete recovery may take place if the pulmonary lesion is quiescent. In early cases spontaneous pneumothorax occasionally acts favourably; but when it develops in association with extensive tuberculosis, and especially if it progresses to pyo-pneumothorax, it is almost invariably fatal though, if the disease is unilateral, surgical measures may prove successful.

Pleural effusion often has a beneficial influence by diminishing the movements of a lung in which there is an early tuberculous focus.

Secondary catarrhal affections tend to increase the cough and expectoration, and may lead to further spread of the disease.

Meningitis is almost invariably fatal. Tuberculous peritonitis or enteritis is a very grave complication, but fistula-in-ano often occurs in chronic cases, and exerts no marked deleterious effect. Involvement of the genito-urinary system increases the severity of the disease, especially if the kidneys or bladder are affected. If the epididymis alone is involved the prognosis is not materially affected, as the lesion can be dealt with surgically, although the administration of a general anæsthetic may cause spread of the pulmonary disease. For this reason when operations are urgently needed on these patients, gas and oxygen, basal anæsthetics, local or spinal anæsthesia should be insisted on.

As shown by the figures obtained at the Midhurst Sanatorium, a fairly accurate guide to prognosis is afforded by observing the condition of the patient on admission to the sanatorium, and his response to treatment. Even in the most favourable cases, which are diagnosed in an early stage, and progress satisfactorily under treatment, the mortality rate is six times greater after discharge from the sanatorium than it is for the remainder of the population of England and Wales for the same age periods; whereas in the cases of advanced disease the mortality rate is thirty-eight times greater than for the average population. As the most critical time is during the two

or three years succeeding discharge from the sanatorium, the prognosis is largely affected by the conditions of life during this period.

The rate of sedimentation of the erythrocytes (see p. 1204) has proved to be a valuable aid to prognosis. A persistently rapid rate is unfavourable.

Treatment.—PROPHYLACTIC.—The prophylaxis of tuberculosis involves a consideration of public health questions dealing with the purity of the milk supply, the infection of meat, sanitation and housing, the early diagnosis of tuberculosis, the examination of contacts, and the segregation of "open" cases. Inoculation with the B.C.G. vaccine (attenuated living bovine bacilli) has not met with favour in this country. All these questions are considered in the general article on Tuberculosis.

CURATIVE.—This varies with the type and stage of the disease. In all acute or febrile cases treatment should be commenced at home or in a nursing home or hospital, where the patient can be under careful observation in bed. The various forms of treatment which may be considered are—(1) sanatorium treatment; (2) home or institutional treatment; (3) dietetic treatment and personal hygiene; (4) climatic treatment; (5) graduated rest, exercise and labour; (6) medicinal treatment; (7) specific measures; (8) operative treatment; (9) symptomatic treatment.

1. SANATORIUM TREATMENT.—This constitutes the best mode of treatment for early and for certain types of chronic disease; but is totally unsuited for acute febrile or very active cases. The advantages obtained are: (*a*) the patient learns the most suitable mode of life, and the methods employed to check the spread of the disease; (*b*) the housing is specially designed and the climatic conditions are good; (*c*) the dietary is abundant and adapted to the patient's needs; (*d*) there is constant skilled medical supervision, and the daily routine is adapted to the actual physical condition of the patient.

On arrival a newcomer is kept in bed for a few days in order that his resting temperature may be observed, and the necessary examinations carried out. If there is pyrexia, rest in bed must be enforced until the temperature falls to normal. If the temperature rises above 99° F. when the patient is up, return to bed is usually necessary. The routine of sanatorium treatment varies in different institutions, the most important divergence being whether or not a system of "graduated exercise" is employed. In nearly all an hour's recumbent rest is enforced before lunch and dinner.

After three months' stay it is usually possible to decide whether the patient is responding to treatment, and, if so, it should, if possible, be prolonged for at least another three months, or until the sputum is free from tubercle bacilli.

2. HOME AND INSTITUTIONAL TREATMENT.—Treatment at home, in nursing homes or in special hospitals, is essential in early cases with fever, and in cases in which it is necessary to establish the diagnosis. Home treatment is also usually necessary on return from sanatorium or climatic treatment, if arrest is incomplete. An endeavour should always be made to carry out the principles inculcated at the sanatorium, and the patient should be under regular medical supervision. Advanced cases are best looked after in special institutions.

3. DIETETIC TREATMENT AND PERSONAL HYGIENE.—It is desirable to graduate the diet in each case so that the patient is restored to the previous maximum weight; but, in order to accomplish this, the food should be slowly

increased and all ideas of enforced overfeeding discountenanced. A total calorie value of 3000 to 3500 is usually ample; but, if the patient is performing heavy work, as much as 4000 may be necessary. Meat, fish, eggs and fats are usually well tolerated. It is not often necessary to give large quantities of milk when the patient is on a full dietary. If extra food is required, the protein may be increased by raw meat sandwiches. Additional carbohydrates with small daily doses of insulin if they are not well tolerated are often helpful.

In all cases in which there is expectoration the patient should be clean-shaven. Great care must be taken in the disposal of sputum to ensure that it does not become dry, and that flies do not have access to it. All patients who are up should carry special sputum flasks, while those who are in bed should have sputum cups suitably covered and containing disinfectant. The sputum should be burnt, or, if this is impossible, it should be emptied into the water-closet after disinfection with carbolic acid or other simple or cheap disinfectant.

Smoking is best avoided in cases of active disease or laryngeal tuberculosis, and in no instance should inhaling be allowed. Woollen under-garments should be worn; but all excess of clothing is harmful. Sun-bathing and injudicious uncontrolled sun exposure are dangerous and often activate quiescent lesions. Patients should be strongly warned of this danger.

4. Climatic Treatment.—This is undoubtedly of value in carefully selected cases. The climatic resorts fall into three groups—mountain, marine and inland.

The mountain resorts.—In Europe the most suitable places are found in Switzerland. Among these are St. Moritz (6090 feet), Arosa (6000 feet), Davos (5150 feet), Montana (5000 feet) and Leysin (4690 feet). In America the most celebrated resorts are in the Rocky Mountains at Colorado Springs (5000 feet) and Denver (5000 feet), or in the Andes or Adirondack Mountains. The advantages of high altitudes consist in the stillness, purity and rarefaction of the air, and the greater diathermancy of the atmosphere to the sun's rays. Metabolism and the general circulation are thereby increased.

High altitudes are suitable for early cases which are afebrile, or for quiescent cases of more advanced type. Contra-indications are recent hæmoptysis, active disease with fever, extensive fibrotic lesions and complications such as emphysema, asthma, cardio-vascular lesions or nephritis.

Marine and coast resorts.—Among the important coast resorts in the British Isles are Hastings, Bournemouth, the Isle of Wight, Torquay, Falmouth, Llandudno, Penmaenmawr, Scarborough, Mundesley and the various seaside towns in Thanet. Farther afield are the French and Italian Riviera, Madeira, the Canary Isles, Morocco, Algiers and Egypt. The climate tends to be warm, moist and equable, and the amount of ozone is probably increased. These resorts are especially suitable for cases of more advanced and active disease, and for those complicated by hæmoptysis, bronchitis, emphysema and laryngitis. Residence by the sea actually at sea-level is undesirable.

Inland resorts.—These are to be found on the English and Scottish moorlands. The climate of California, the South African veldt, and parts of Australia and New Zealand are admirably suited to this disease, especially for arrested or early uncomplicated cases; but the laws against the admission of tuberculous patients are strictly enforced at all of them.

Sea voyages.—These are contra-indicated for all except completely arrested

cases owing to the lack of fresh air in cabins, the possibility of sea-sickness, and the difficulty of obtaining suitable treatment if the disease advances.

5. GRADUATED REST AND EXERCISE.—Treatment in bed is necessary so long as there is fever, and if the raised temperature is persistent "absolute rest" should be enforced. This consists in keeping the patient recumbent in bed, sufficiently well covered to prevent any muscular contraction from chill, while feeding and washing are attended to by the nurse, and the use of the bed-pan and slipper for evacuations is insisted upon. When the temperature becomes normal the patient is allowed up for varying periods, commencing with 1 hour daily, and increasing slowly to 6 or 8. If still apyrexial, walking exercise of 1 or 2 miles or more daily can be allowed.

The system of "graduated exercise" which Paterson instituted at the Frimley Sanatorium has proved of great value. There are six grades, the first and lightest consisting of walking up a slope carrying a light weight such as a basket of earth, while the sixth and heaviest involves hard manual labour with a pickaxe or shovel for 6 hours daily. This system is based on the principle that muscular exercise leads to the discharge of tubercle toxins from the pulmonary focus, and by liberating these in gradually increasing doses, a condition of active immunity is induced. A careful watch must be kept during this controlled process of auto-inoculation to prevent excessive doses of toxin being discharged, which are early indicated by rise of temperature and of pulse-rate, headache, increased cough and expectoration, lassitude and malaise. If such occur, the patient should be put back to bed for a few days, and when the condition has subsided the graduated exercise may be resumed at the grade which induced the over-inoculation or that immediately below it.

6. MEDICINAL TREATMENT.—No specific drug has yet been discovered for the treatment of tuberculosis. Amongst the medicines in most general use are:

(*a*) *Cod-liver oil.*—This may be administered by the mouth in doses up to 2 ounces daily. The cod-liver oil may be of value either on account of its fat-soluble A and D vitamins content, or, as suggested by Rogers, it may assist by dissolving the capsules of the tubercle bacilli and so facilitating their disintegration. Halibut liver oil is now sometimes used instead.

(*b*) *Creosote.*—This may be given in doses of min. 2 to 3 three times a day after food, either in combination with cod-liver oil, or in capsules. It should be discontinued if gastric disturbance or hæmoptysis ensue.

(*c*) *Hypophosphites.*—These are not so generally used as formerly and, beyond their "tonic" effect upon the nervous system, have no demonstrable influence upon the pulmonary lesion.

(*d*) "*Nascent*" *iodine.*—With the idea of liberating free iodine in the tissues, potassium iodide grs. 30 is administered after breakfast in half a pint of water, and throughout the day 3 to 5 ounces of chlorine water are consumed with lemonade. This treatment is of value in certain chronic fibroid cases, but it often produces no appreciable results, and may cause dyspepsia.

(*e*) *Arsenic.*—Liquor arsenicalis min. 2 to 3 by mouth, or sodium cacodylate gr. $\frac{1}{4}$ to $\frac{1}{2}$ subcutaneously, are of value in some cases associated with anæmia. Neoarsphenamine, administered intravenously, is useful in chronic cases complicated by syphilis.

(*f*) *Inhalations.*—Disinfectant drugs when inhaled often check cough lessen expectoration and improve the general condition of the patient. Lees's inhalation is of value. It consists of creosote, parts 2; acid. carbol., 2; liq. iodi mitis, 1; sp. ætheris, 1; and sp. chlorof., 2. About 6 drops an hour are placed upon a Burney-Yeo mask, which should be worn almost continuously throughout the day. A modification now more frequently employed is: menthol, 4; olei cinnamomi, 3; olei limonis, 4; creosote, 10; olei pini, 10; sp. chlorof., 10.

(*g*) Calcium is often given by the mouth in the form of colloidal calcium in doses of 60 minims three times a day; or intramuscularly, as calcium gluconate, 5 c.c. of a 10 per cent. solution once or twice a week. Parathyroid extract is sometimes administered at the same time.

(*h*) There has been a revival of interest in preparations of gold in the treatment of this disease, notably by Møllgaard, who uses sodium aurothiosulphate, to which the name of sanocrysin has been applied. It is now administered in smaller doses than when it was first introduced. The initial dose is usually 0·01 g. dissolved in sterile saline solution and injected intravenously. The second dose is given 5 days later, and is as a rule 0·025 g. If no reaction occur, the dose is increased to 0·1 g., and usually later to 0·25 g., the intervals being extended to a week. The total amount given in a course is usually 3 g., or sometimes up to 5. The course may have to be interrupted owing to reactions, chiefly fever, albuminuria, stomatitis, diarrhœa, peripheral neuritis and skin manifestations.

7. Specific Measures.—(*a*) *Active immunisation.*—Tuberculin and tubercle-vaccines.

The tuberculin treatment has not fulfilled the high hopes held out on its introduction by Koch. There are now numerous forms of tuberculin available, indicated by certain letters, and falling into three groups. (1) Those containing the exo-toxins only. These include Koch's old tuberculin T., O.T., and T.O.A., Denys' bouillon filtré (B.F.) and albumose-free tuberculin, T.A.F. (2) Those containing the endo-toxins chiefly, such as Koch's "new" tuberculin, T.R. (3) Mixtures of endo- and exo-toxins, the most important of which are Koch's bacillary emulsion, B.E., the sensitised bacillary emulsion, S.B.E. and Béraneck's tuberculin, T.Bk.

The Therapeutic Substances Act, 1925, restricts the term "tuberculin" to the first of these groups, and recommends the name "tubercle vaccine" for any substance obtained directly from the bacterial bodies.

Tuberculins and tubercle-vaccines may be prepared from human or bovine bacilli; if from the latter the letter P. (perlsucht) placed before the letters indicating the variety of tuberculin, signifies its origin, *e.g.* P.T. In administration, some aim at producing reactions and establishing tuberculin tolerance by giving large doses at fairly frequent intervals; others believe in minute doses at longer periods, the chief object being to avoid the production of any reaction. The actual doses are either measured in milligrammes of dried tubercle bacilli, or in cubic centimetres or cubic millimetres of the fluid tuberculin. The usual method is to measure the doses in cubic centimetres or fractions thereof, and to make the necessary dilutions in a series of bottles. Smaller initial doses should be used with a strong tuberculin such as the B.E. than with the weaker ones such as the T. or T.A.F. Thus, if adopting minute doses, $\frac{1}{500,000}$ mgrm. of B.E. would be a suitable initial dose, then for T.R.

$\frac{1}{100,000}$ mgrm. would be used and $\frac{1}{1000}$ mgrm. of T., B.F., or T.A.F. As the different tuberculins are supplied by the makers in varying strengths, 0·001 c.mm. of the original fluid is equivalent to the above doses.

Those who believe in minute doses commence with 0·001 c.mm. and work up to 0·1 c.c., whereas others commence with 0·5 to 1 c.mm. and increase to 1 c.c. The tuberculin should be injected subcutaneously, and a careful observation kept for local, focal and general reactions. Tuberculin, if used injudiciously, can be productive of harm. At Midhurst Sanatorium it was tried for some years, and no better ultimate results were obtained than in the "non-tuberculin" years. It seems wise, therefore, to use tuberculin only in very carefully selected cases, thus T.R. does at times appear beneficial in chronic tuberculosis, promoting the formation of fibrous tissue and leading to the disappearance of tubercle bacilli from the sputum.

Various attempts have been made to remove as far as possible the fatty and waxy constituents from the tubercle bacilli before preparing a vaccine from it. Much and his collaborators have employed partial antigens or partigens derived from tubercle bacilli, singly or in varying combinations. Some good results are on record from both of these methods, but on the whole their use has so far been disappointing.

Grasset has recently recorded success with a preparation described as "tubercle endotoxoid," which he claims is freed from the toxic factor in ordinary tuberculins.

(*b*) *Passive immunisation.*—The various serums such as those prepared by Marmorek and Maragliano have not proved successful, and this applies to the "contra-toxin" of Mehnarto and the "I.K." (immune bodies) of Spengler.

8. Operative Treatment.—(*a*) *Artificial pneumothorax.*—This mode of treatment is now becoming more generally adopted in selected cases. It is increasingly employed in cases of early disease, where there are indications of incipient softening or of recent cavitation. In early cases without softening it is not as a rule used, unless there are indications of rapid spread or of pleural involvement when it is wise to start before adhesions have formed. In extensive bilateral disease it may be dangerous. If old and dense pleural adhesions are present, it is impracticable. If there is much emphysema or cardiac embarrassment, it involves risk. It is also of value in certain cases of repeated severe hæmoptysis. Tuberculous laryngitis or enteritis are not contra-indications, providing that other conditions are suitable. Sterile air is introduced into the pleural cavity, and the lung allowed to collapse. The method of induction of artificial pneumothorax is as follows: A preliminary subcutaneous injection of $\frac{1}{3}$ grain of papaveretum (omnopon) is given half an hour before the start. The patient lies on the sound side with the head low and supported on a pillow. A second pillow is placed under the chest to expand the intercostal spaces. The skin and the tissues down to the pleura are anæsthetised with 2 per cent. procaine hydrochloride solution after the application of iodine. The site usually chosen is in the sixth intercostal space in the mid-axillary region. A special pneumothorax needle, attached by a rubber tube to the pneumothorax apparatus, which is carefully examined to see that it is in proper working order, is then pushed through the intercostal space until the pleural cavity is reached. The apparatus is then adjusted so that the intrapleural pressure can be observed. No air should be introduced until the manometer shows a normal negative

pressure range with inspiration, of 5 to 10 or more cm. of water. This is the test of entry into the pleural space, and when this is established 200 to 300 c.c. of sterile air may be allowed to enter the pleural cavity. The final pressures are then recorded and the needle is withdrawn. A refill is given next day and another after two more days, the quantities of air introduced being determined by the final pressures, which should be kept slightly negative. Subsequent refills are gradually spaced out to a week, then ten days and later to two, three and four weeks' intervals. The usual custom now is to maintain the collapse for three years or even longer. If the condition of the patient is satisfactory, re-expansion may then be permitted cautiously. It should be remembered that after expansion pleural adhesion almost invariably occurs and the treatment by artificial pneumothorax cannot be repeated. In some cases of bilateral disease, which is active but not very extensive in either lung, a cautious use of bilateral artificial pneumothorax has proved practicable and helpful, but very great care is necessary in adjusting the pressures.

There are certain dangers in the procedure. These are now rare, and they can usually be prevented by careful attention to the technique. Death has occurred from pleural shock when the needle has reached the pleura and before any air has been introduced. Adequate anæsthesia of the pleura is the only known method of eliminating or minimising this risk. If the lung is adherent to the chest-wall, owing to pleural adhesions, or if the needle is pushed in too far, it may be inserted into the lung or into a pulmonary cavity; the manometer will then show a swing above and below the zero line instead of entirely below it. Under these circumstances, no air should be allowed to enter. The needle may be inserted into a blood vessel. In this case the manometer pressure will rise above zero, and blood may appear in the glass section inserted in the rubber tube leading from the manometer to the needle. The needle should be withdrawn immediately, lest air should enter the vessel.

If the pleura is found to be adherent at the site of the first puncture, another attempt may be made elsewhere, *e.g.* just below the inferior angle of the scapula. This spot may be selected for the initial puncture in left-sided cases where there is marked cardiac displacement. In cases in which localised band or cord adhesions prevent adequate collapse, it is often possible to cut them by electrocautery or diathermy through an operating thoracoscope, thus ensuring completely effective collapse. This is called internal pneumolysis.

(*b*) *Oleothorax.*—Sterilised olive oil or liquid paraffin with a varying percentage of gomenol is sometimes used to maintain the collapse started by artificial pneumothorax. Paraffin is used when the mediastinum is unduly mobile, since it tends to thicken the pleura. The oil or paraffin is introduced by means of a Dieulafoy syringe, and air is withdrawn at the same time by a reversed artificial pneumothorax apparatus. Whichever is used, it is important to test the sensitiveness of the pleura by small injections of 2 to 5 c.c. to start with. In later injections the amount introduced may be gradually increased to 200 c.c. or more. Oleothorax is now for the most part restricted to cases of therapeutic pneumothorax tending to obliterate from spreading adhesion, and those with mobile mediastinum.

(*c*) *Evulsion or crushing of the phrenic nerve.*—This is now often performed

in order to produce basal collapse, but it helps to produce relaxation at the apex and may aid in the contraction and closure of a cavity. Division alone is not sufficient; it is desirable to remove as long a stretch of the nerve as possible. In recent years temporary paralysis has been induced by crushing the nerve, the effects lasting about 6 months. This is often carried out instead of evulsion, since it does not prejudice further surgical treatment subsequently.

(*d*) *Thoracoplasty.*—If owing to adhesions it is impossible to collapse the lung temporarily by an artificial pneumothorax, permanent collapse by thoracoplasty may be considered. In the Sauerbruch operation, the posterior 3 or 4 inches of the ribs from the first downwards are removed, even to the tenth or eleventh, the lower level being determined by the extent of the compression of the lung it is desired to produce and therefore by the amount and situation of the diseased area. This operation is now performed in two or three stages, and generally under local anæsthesia. Good lateral collapse is usually obtained by this operation, but antero-posterior compression is less complete. Semb's operation is more satisfactory and is now more frequently employed. The first, second and third ribs are completely removed and the fascial supports of the apex of the lung are divided, which is thus allowed to sink down, producing a concentric collapse. The second and if necessary a third stage are similar to those in the Sauerbruch operation.

(*e*) *Apicolysis* (*extrapleural pneumolysis*).—Successful local collapse can sometimes be attained by introducing some extraneous material like paraffin between the chest wall and the parietal pleura over a local area of disease, or a cavity which is not too near the pleura.

(*f*) *Extrapleural pneumothorax.*—In some cases where artificial pneumothorax fails owing to extensive apical adhesions, an extrapleural pneumothorax may be induced. A portion of the fourth rib is removed near the spine and the parietal pleura with the adherent lung is stripped away from the chest wall through the endothoracic fascia. The separation is carried down to the hilum on the mediastinal aspect, to the eighth rib posteriorly and to the fourth costal cartilage in front. The wound is then carefully closed and sutured. The extrapleural space thus produced is maintained by repeated refills of air, at first very frequent, subsequently at longer intervals. After about a month high positive pressures up to +18 and +24 must be maintained, otherwise the space obliterates. This procedure, though sometimes successful, seems less generally satisfactory than apical thoracoplasty. On the other hand it involves less shock than the operation of thoracoplasty, and is therefore practicable in some cases where thoracoplasty cannot be considered. The existence of an intrapleural pneumothorax below where it is necessary to keep the lower lobe under control does not contra-indicate it.

9. Symptomatic Treatment.—When cough is ineffective it may be relieved by a sedative lozenge or linctus containing diamorphine or codeine, or by the well-known liquorice lozenge. If there is difficulty in bringing up the sputum, a simple saline mixture is of value, such as sodii bicarb. grs. 10, sodii chlorid. grs. 3, sp. chlorof. min. 10, and aq. anisi ad fl. oz. 1.

Pain in the chest is usually alleviated by local application of pigmentum iodi, liniments, mustard leaves or other counter-irritants.

Night sweats.—The windows should be widely opened at night. A pill containing zinc. oxid. grs. 3 and ext. belladonn. sicc. gr. ½ is often of value.

Picrotoxin, agaricin and strychnine have also been used. A rush mattress as used in the tropics has been recommended.

Fever.—Rest in bed up to the extent of "absolute rest" is the best means of lowering the temperature. Antipyretic drugs have no effect upon the course of the disease, but may alleviate malaise. Amongst these may be mentioned aspirin and cryogenin.

Slight hæmoptysis, in which the sputum is only streaked, calls for no special treatment. Moderate hæmoptysis, with expectoration of 3 or 4 ounces of blood, requires more active measures. The patient should be put to bed, a saline aperient administered, and if there is anxiety or alarm a sedative drug should be given, such as heroin or morphine. In profuse or persistent hæmoptysis the patient should be confined strictly to bed, and if it is known from which side the bleeding has occurred, it is best to lie on this side. If the cough is troublesome, or if the patient is alarmed, morphine gr. $\frac{1}{8}$ to $\frac{1}{4}$, or diamorphine, hydrochloride gr. $\frac{1}{25}$ to $\frac{1}{12}$ should be injected subcutaneously. The food is best given cold, and may be iced; no alcohol must be taken. A course of calcium lactate grs. 10, t.d.s., may be commenced; but its action is somewhat uncertain. If the bleeding persists, various other remedies should be tried, these include the inhalation of amyl nitrite, or the injection of hæmoplastin, coagulen ciba, horse serum, or emetine hydrochloride subcutaneously. Congo red, given intravenously, has proved of value in some cases. Ergot and adrenaline are both contra-indicated. If the hæmorrhage is still unchecked, or is frequently repeated, the advisability of establishing an artificial pneumothorax must be considered.

Gastro-intestinal symptoms.—Anorexia or dyspepsia can often be relieved by changes in diet, or by the administration of suitable drugs. Alkalis and gentian are especially valuable, and when hypochlorhydria is present, dilute hydrochloric acid (min. 10–30) should be given well diluted after meals. Digestive ferments, such as taka-diastase or papain, may be required at times. All tendency to constipation should be checked by laxatives, and if diarrhœa develops, avoidance of diet leaving bulky or irritating residues should first be tried, before administering drugs containing lead, opium, bismuth or tannic acid.

Insomnia is often a troublesome symptom, and every endeavour should be made to obtain a good night's rest by administration of mild hypnotics, and by relieving distressing cough and pain.

The treatment of the complications of pulmonary tuberculosis is described under their respective headings. The after-care of patients discharged from sanatoria is an important subject, to which considerable attention is being devoted, and involves a consideration of the advisability of establishing training centres or industrial colonies for consumptives. These are proving of very great value.

THE PULMONARY MYCOSES (PNEUMONOMYCOSES)

A number of fungi produce pulmonary lesions. Considerable confusion exists in regard to their nomenclatures, and at the present time it is difficult to give accurate accounts of them. The pulmonary mycoses have one feature in common, in that they produce chronic pulmonary lesions

practically indistinguishable clinically from those of the chronic forms of pulmonary tuberculosis.

Among the varieties of mycotic infection at present separated clinically may be mentioned—(1) Actinomycosis and other streptothrix infections; (2) Aspergillosis; (3) Blastomycosis; (4) Sporotrichosis; (5) Moniliasis; (6) Mucormycosis.

Streptotrichosis (Actinomycosis)

Ætiology.—The general characters of the streptothrix group of organisms are described in the section on Actinomycosis. It is now recognised that more than one of these may be pathogenic for man, and some authors give separate descriptions of the forms due to the various streptothrix organisms. At the present time there seems little advantage in so doing, since the important point in regard to treatment is to recognise that the morbid process is due to some form of streptothrix infection, the identification of the variety being a pathological refinement. The manner of infection is at present obscure. The organism is now believed to be present not infrequently in the alimentary tract, but the conditions favouring its invasion of the tissues are not known. A large proportion of cases show the first lesions in the head and neck regions, but primary pulmonary cases occur, and are probably more frequent than is generally recognised.

Pathology.—The streptothrix group of organisms produces an inflammatory reaction which leads to the formation of granulomatous tissue. This, like the granuloma of tubercle, is very liable to undergo secondary changes producing small areas of pus formation or leading to fibrosis. Unlike tuberculosis, however, streptotrichosis tends frequently to transgress anatomical limitations and spreads by contiguity. In the primary pulmonary cases the distribution of the lesions is at first very similar to that of tuberculosis, and the disease may extend in an identical manner. In the forms due to spread from other organs such as the liver, the base of the lung may be first involved, while in cases extending down from the neck the path of the infection is apparent.

Owing to the tendency of the lesions to spread by contiguity, subcutaneous abscesses may form and simulate caries of the ribs. Pleural adhesion is the rule, but occasionally empyema results. When a subcutaneous abscess ruptures or is opened, the characteristic "sulphur granules" may be found, although this is not invariable. The skin around the sinuses which result is often puckered in a somewhat characteristic fashion.

Symptoms.—These are in general identical with those of the chronic forms of pulmonary tuberculosis, such as cough, expectoration, which may be offensive, dyspnœa, fever and night sweats. The occurrence of local abscesses under the skin or the presence of the organism elsewhere may give rise to special features; but these are late developments in primary pulmonary cases.

Complications and Sequelæ.—These are usually due to the other localisations of the organism; but, in addition, empyema and bronchiectasis may be mentioned.

Course.—This is progressive, and leads eventually to asthenia, emaciation and death.

Diagnosis.—This can only be established by the discovery and identification of the organism in the sputum and the discharge. The characteristic "sulphur grains" are not invariably present, and may escape notice unless looked for carefully. In any obscure case of pulmonary disease in which tubercle bacilli are not found after repeated search, the possibility of streptotrichosis should be considered, and direct films should be specially examined.

Prognosis.—This is serious, although some cases respond well to treatment.

Treatment.—Large doses of potassium iodide should be administered, commencing with 5 or 10 grains three times a day, and increasing until the dose reaches a drachm or even more thrice daily. In addition, collosol iodine (Crookes) may be given intravenously in doses of 5 c.c. at least once a week. If the organism grows well in culture, a vaccine may be prepared and employed cautiously, especially if the iodides do not act satisfactorily. A stock vaccine may be helpful in other cases. Surgical treatment of local abscesses or of empyema may be required. External application of a radium pack is sometimes useful.

Pulmonary Aspergillosis

Ætiology.—Infection of the bronchi and lungs sometimes occurs by the *Aspergillus fumigatus*, more rarely by the *A. nidulans*. The disease has been most frequently observed in France. It occurs among pigeon breeders and hair sorters and combers. The former acquire the disease from the process of artificial feeding, from grains in the mouth to the beak of the bird; the latter from the use of rye flour in cleaning the hair. Millers and farm labourers have also been the subjects of the disease.

Pathology.—The fungus induces nodular formations in the lung tissue somewhat resembling aggregated tubercles. Bronchitis, patchy lobular consolidation and fibrosis result. Emphysema, bronchiectasis and cavity formation may follow. A secondary aspergillosis may occur in chronic cases of bronchitis or lung disease, but is of little clinical importance.

Symptoms.—Primary aspergillosis produces symptoms similar to those of bronchitis, broncho-pneumonia or pulmonary tuberculosis, according to the localisation and degree of the lesions. The sputum may be blood-stained, or definite hæmoptysis may occur. There is generally wasting with irregular fever.

Course.—Acute broncho-pneumonic forms may be fatal in a few weeks or months. The chronic lesions may extend to years, and arrest with fibrosis is not uncommon.

Diagnosis.—The condition has to be differentiated from pulmonary tuberculosis, and from other varieties of pneumonomycosis. This depends upon the recognition of the fungus by microscopical and cultural examination of the sputum.

Treatment.—This consists in avoiding further infection, and giving large doses of potassium iodide as in streptotrichosis. Open-air measures and general tonic treatment are also to be recommended.

Other Mycotic Infections

Fungi of the genera *Blastomyces* (*Oidium*, *Coccidioides*) and *Sporotrichum* are well known to produce cutaneous affections simulating chronic gummatous or tuberculous lesions. They may also give rise to pulmonary disease producing symptoms like those of tuberculosis.

Castellani has described various broncho-pulmonary conditions due to species of the genus *Monilia*, including the "tea-tasters' cough" and "tea-factory cough." Another fungus, *Mucor mucedo*, has been found in the sputum, and is regarded as pathogenic to man.

All these moulds produce bronchitic symptoms and mild infections, while more severe forms simulate pulmonary tuberculosis. The diagnosis in each case depends upon the recognition of the fungus, and the treatment recommended is large doses of potassium iodide.

SYPHILIS OF THE LUNGS

Ætiology.—Clinically recognisable pulmonary syphilis is a rarity; but syphilitic lesions occur in the lungs in both the congenital and acquired forms of the disease.

Pathology.—Even post mortem it is often difficult to establish the syphilitic nature of the pulmonary lesions found in cases of syphilis, owing to the fact that they tend to the formation of scars presenting no characteristic features.

Congenital syphilis.—The essential changes are—(1) Round-celled infiltration with eventual fibrosis, starting round the bronchi and spreading to the inter-alveolar framework; (2) periarteritis of the smaller arteries; and (3) desquamation and degeneration of the epithelium of the alveoli and bronchi. Gummata may be present, but are rare. Spirochætes can be demonstrated in the lesions by Levaditi's method. The microscopic appearances comprise the "white pneumonia" of Virchow and an interstitial pneumonia, which is commoner, although both conditions are frequently associated. White pneumonia is found in premature or still-born infants, and in those dying soon after birth. The condition may be widespread or localised. The affected areas are firm, consolidated, smooth and greyish-white in colour. There are no interstitial changes, and the consolidation is due to the filling of the alveoli with desquamated, degenerating epithelial cells.

In the commoner interstitial form the lung is firmer, harder and darker grey in colour, and the connective tissue is mainly involved. To this condition the term "pancreatisation of the lung" has been applied by Rogers.

Acquired syphilis.—Syphilitic lesions of the bronchi have already been described in the section on diseases of the bronchi. Gummata may occur in or around the intra-pulmonary bronchi or in the lung tissue. They may be single or multiple, and vary in size from that of miliary granules to a hen's egg. They are said to be more common in the deeper parts of the lung near the roots and in the lower lobe. They undergo changes similar to those occurring in gummata elsewhere, but tend more to fibrosis and contraction than to softening. Owing to these secondary changes, the following

conditions may result: broncho-pneumonic processes, widespread fibrosis and contraction with pleural adhesion, bronchiectasis and occasionally excavation.

Symptoms.—Small gummata may be latent and give rise to no symptoms or signs. When fibrosis occurs, they are similar to those of pulmonary fibrosis from other causes. It is generally recognised that in rare cases a destructive process occurs, formerly called "syphilitic phthisis," and almost exactly similar in its clinical manifestations to those of caseous or fibro-caseous tuberculosis.

Complications and Sequelæ.—Syphilitic lesions in the larynx, trachea or bronchi may complicate the course. Bronchiectasis has already been mentioned, and tuberculosis may occur as a complication.

Diagnosis.—This is often difficult and sometimes inconclusive. Obscure pulmonary signs in a syphilitic subject should arouse suspicion. The Wassermann reaction should be determined, and other indications of syphilis looked for in all fibrosing and destructive lung conditions when no tubercle bacilli are found in the sputum. The difficulty of diagnosis is increased by the association of syphilis and tuberculosis mentioned above.

Course and Prognosis.—Where the lesions are localised and can be recognised early, the course is favourable if anti-syphilitic treatment is applied. Where fibrotic changes occur, leading to bronchiectasis, the course is less favourable, and in the destructive form it is serious. An inter-current tuberculous infection increases the gravity of pulmonary syphilis.

Treatment.—When a diagnosis of pulmonary syphilis has been established, vigorous anti-syphilitic treatment should be carried out. Its beneficial effect is undoubtedly promoted by open-air treatment. In cases where tuberculosis coexists with syphilis, anti-syphilitic treatment is strongly recommended, especially by French physicians.

NEW-GROWTHS IN THE LUNGS

Both simple and malignant tumours may occur in the lungs, the latter being the more common.

Ætiology.—Malignant tumours occur more frequently in the male sex in the ratio of five to one; carcinoma is rare before the age of 40, but sarcoma may develop in earlier years. Simple tumours may arise at any age, but are found chiefly in adult life. The exciting cause is unknown. In some cases of malignant growth there is a history of thoracic trauma or disease.

Pathology.—Simple tumours found in the lungs usually arise in the bronchial mucous glands or in the bronchi. They include adenoma, fibroma, lipoma and chondroma (see p. 1141).

Malignant tumours may be primary or secondary. The primary growths are carcinoma, sarcoma or endothelioma. Carcinoma arises in the bronchi, usually as a columnar-celled growth. A variety of bronchial new-growth formerly regarded as a lympho-sarcoma is now called an oat-celled tumour. It is probably derived from the basal cells of the bronchial mucous membrane. Squamous-celled growths of the bronchi are rare and are now said to be derived from basal cells. Round-celled and spindle-celled sarcomata growing from the pulmonary connective tissue are met with, while endotheliomata are

usually derived from the endothelium of blood vessels and lymphatics, or from the pleura. A primary carcinoma of the breast, œsophagus or mediastinum may directly invade the lungs. Secondary carcinoma may have its primary focus in the breast, stomach, intestines, liver, pancreas or prostate, whereas a secondary sarcoma most often results from metastasis of a primary bony growth. Chorion-epithelioma and hypernephroma also give rise to secondary deposits in the lungs.

Primary malignant rumours are unilateral; but secondary growths are often multiple and diffuse. Dissemination in the lungs may occur by spread along the bronchi or vessels, and a condition of miliary carcinomatosis is at times produced. The pleura is often affected by direct extension. Infiltration of, or pressure upon, the mediastinal structures frequently occurs.

Symptoms.—Simple tumours except adenomata are pathological curiosities and, as a rule, only produce symptoms when they cause obstruction of a bronchus or press on mediastinal structures (see pp. 1046 and 1280).

The early symptoms of malignant growths are slight, and consist of malaise with, perhaps, cough and expectoration. Later, when the growth becomes more extensive and exerts pressure on, or involves the larger bronchi, mediastinum or pleura, they are more noticeable. Pain, dyspnœa and loss of weight with cachexia usually develop, and the cough and expectoration are more marked. The latter is often of the typical "currant jelly" or "prune juice" appearance due to altered blood. Microscopically, groups of large fatty cells, or irregular epithelial cells may be seen. Malignant cells may be found in 60 per cent. of cases by Dudgeon's wet method. There are usually no definite physical signs until the tumour causes pressure upon the bronchi, mediastinum or deep thoracic veins or nerves. The chest-wall may bulge locally, owing to the presence of a growth near the surface, or it may be retracted if a main bronchus is obstructed. An actual subcutaneous swelling caused by the tumour eroding through the chest-wall may be visible. Enlarged veins often run across the chest, and one or other arm may be swollen or œdematous if there is mediastinal obstruction. Vocal fremitus is often unaffected; but is increased when the growth is near the surface, and diminished if pleural effusion has occurred. The percussion note over a moderate-sized tumour is impaired and may be extremely dull; more often the dullness is due to collapse of the lung. The breath-sounds vary with the size and position of the growth, and with the displacement or pressure effects produced. They may be weak, or loud and stridorous. The stridor is usually unilateral. Adventitious sounds depend upon the presence of complications such as bronchitis. Some degree of fever often occurs. The supra-clavicular and axillary glands are not infrequently enlarged, and evidence of malignant disease may be present in other parts of the body such as the abdomen.

One special variety of apical carcinoma is the superior pulmonary sulcus or Pancoast tumour, which gives rise to a somewhat characteristic or suggestive clinical picture. The chief symptoms are pain in the shoulder, inner side of the arm and forearm together with weakness and wasting of the small muscles of the hand. Paralysis of the cervical sympathetic on the same side develops. There is usually localised dullness at the extreme apex. Radiological investigation reveals a sharply defined apical shadow with destruction

of the posterior part of the first three ribs and sometimes localised vertebral erosion. Pancoast suggests that these tumours may arise from remnants of the fifth branchial cleft.

Complications and Sequelæ.—Bronchitis is nearly always present in some degree. Pulmonary collapse, fibrosis, bronchiectasis, emphysema, gangrene, hæmoptysis, pleural effusion, abscess and empyema are sometimes observed. The effusion is frequently bloodstained. In cases of primary malignant disease of the lungs, secondary deposits may occur in other parts of the body such as glands, brain, suprarenals, heart and bones.

Course.—This is progressive, the patient gradually losing strength and dying from cachexia or some intercurrent affection.

Diagnosis.—This is difficult in early cases, and not easy in some advanced ones. It not infrequently happens that metastases, especially in brain or bone, afford the earliest manifestations to be recognised. Difficulties may arise in connection with pulmonary tuberculosis, fibrosis and gumma of lung, aneurysm, pericardial and pleural effusion and enlargement of the mediastinal glands due to Hodgkin's disease or tuberculosis. The whole body should be searched for evidence of malignant disease elsewhere. The sputum should be examined repeatedly for tubercle bacilli and for cellular elements, and an X-ray examination made of the chest. By the stereoscopic method excellent evidence of pulmonary neoplasms is often obtainable. Lipiodol injection and X-ray examination or tomography may demonstrate the obstruction of a bronchus by the growth which often presents a tapering or "rat-tail" appearance. Bronchoscopy may also serve to establish the diagnosis especially in bronchial carcinoma. Temporary artificial pneumothorax may be helpful in diagnosis, particularly in differentiating simple tumours in the periphery of the lung, growths in the mediastinum and in the chest-wall.

The Pancoast tumour may give rise to special difficulty. It has to be differentiated from syringomyelia, cervical rib, apical pulmonary tuberculosis and secondary sarcoma.

Prognosis.—Apart from those cases in which early recognition may in suitable conditions render lobectomy, with removal of the growth, possible, this is hopeless, death occurring in a few weeks, or being delayed for two or three years.

Treatment.—Simple tumours are often capable of complete removal with gratifying success.

In malignant growths lobectomy or dissection pneumonectomy with complete removal of the growth is only practicable for cases recognised early in which there are no secondary deposits.

Radon seeds are sometimes used; when practicable they are inserted into the growth through a bronchoscope. In other cases they may be introduced directly into the growth by thoracotomy. Treatment by deep X-ray application may be useful by diminishing local pressure and relieving symptoms chiefly in sarcoma or oat-celled carcinoma. Cure by these methods is rare.

In cases unsuitable for lobectomy and radiation treatment this can only be palliative and symptomatic. Useless cough should be checked by sedative lozenges or a linctus. Dyspnœa due to pleural effusion may be relieved by tapping with or without air replacement; but the fluid often reaccumulates

rapidly. Pain should be relieved by analgesic drugs, and in the later stages those containing opium or its alkaloids may be required.

PARAGONIMIASIS

Synonyms.—Pulmonary Distomatosis; Lung Fluke Disease; Endemic Hæmoptysis; Parasitic Hæmoptysis.

Ætiology.—(See p. 306).

Pathology.—The flukes settle down in the lungs and form burrows. These burrows may coalesce and give rise to cystic swellings, varying from ½ to 1½ inches in diameter. These in turn develop fibrous sheaths and may give rise to abscess formation or pleurisy. The adult fluke is hermaphrodite, and lays numerous eggs which measure 100 × 70 μ. These are coughed up in the sputum, and are easily recognisable owing to their large size. The adult parasites are also occasionally found in the brain, liver, lymph glands and peritoneal cavity.

Symptoms and Complications.—The onset of symptoms, after infection has taken place, is insidious, with cough and expectoration. The latter is very constantly blood-stained, and there may be profuse hæmoptysis. Secondary pleurisy occurs when the cysts reach the surface of the lungs, causing pain. Examination may reveal no abnormal signs, at most there are a few scattered râles, together with signs of dry pleurisy at one point. Later in the disease the characteristic signs of the various complications may appear.

For general, abdominal and cerebral symptoms and complications, see pp. 306, 307.

Course.—This is chronic: the disease often persists for years, without giving rise to any acute disturbance apart from periodic hæmoptysis.

Diagnosis.—Distinction from other forms of hæmoptysis is accomplished by discovering the ova in the sputum. To facilitate the examination a little 0·1 per cent. sulphuric acid should be added to it.

Prognosis.—The immediate prognosis is good, the ultimate unfavourable, as there is considerable difficulty in eliminating the parasites, and permanent damage is wrought in the lungs.

Treatment.—Prophylaxis is important where the disease is endemic. No bathing should be allowed in infected rivers, and all water used for drinking or washing should be boiled or filtered. Crabs should not be eaten. When the disease has developed the patient should move from the infected area. Potassium iodide (grs. 10–20, t.d.s.) is recommended, but other treatment is symptomatic.

CONGENITAL CYSTIC DISEASE OF THE LUNG

Ætiology.—Congenital cysts of the lung may be met with in infants, children or adults. There is no infective or parasitic cause, and as in some instances cysts have been found in the fœtus they are considered to be due to developmental errors.

Pathology.—The following varietes are described: 1. The large balloon

cyst. This may completely compress a lung in an infant or young child. 2. The solitary cyst. This may occupy half the lung-field. 3. Multiple medium-sized cysts, often situated near the root of a lung. 4. Multiple small cysts. These cause a honeycomb appearance of the lung resembling bronchiectasis.

It is probable that in all cases the cysts are of bronchial origin. The lining membrane of the cyst is uniform, the cells having the characters of bronchial epithelium. Microscopically, the irregular distribution of the cartilage, muscle, elastic tissue and mucous glands in the supporting tissues differentiates congenital cysts from bronchiectatic cavities. The cysts may contain air only, or the contents may be watery, mucoid, or purulent if they become infected.

Symptoms.—These vary with the variety of cyst present. The large balloon cyst, met with in infants or young children, may result in severe respiratory and cardiac distress. In such cases there is cyanosis, dyspnœa and displacement of the trachea, mediastinum and heart to the opposite side of the chest. The percussion note over the cyst is hyper-resonant and the breath-sounds are absent. Solitary cysts often give rise to no symptoms and are only discovered on routine X-ray examination. When infected the clinical features may resemble those of lung abscess or bronchiectasis. With multiple medium-sized or small cysts no symptoms usually appear until infection occurs, though hæmoptysis may occur early. When infected, toxæmic symptoms develop, such as loss of weight, irregular fever, cough and expectoration which is sometimes offensive. Clubbing of the fingers may then soon be noted. On examination scattered areas of slight dullness, weak air entry with a few persistent râles may be detected.

Course, Complications and Sequelæ.—The onset of complications usually leads to the development of symptoms which call for investigation. Thus spontaneous pneumothorax may result from rupture of a cyst. In other cases suppuration occurs in the cyst with the formation of lung abscess, bronchiectasis or empyema. Cerebral abscess may be a late sequel.

Diagnosis.—This is suggested by X-ray and by lipiodol or neo-hydriol examinations and possibly tomography. If the space in the cyst is free from fluid the X-ray appearances must be differentiated from those of pneumothorax, an emphysematous bulla, a thin-walled tuberculous cavity or, in some cases, a diaphragmatic hernia. If the cyst contains fluid, further investigations are required to exclude the presence of such conditions as lung abscess, encysted pleural effusion or empyema, hydatid cyst, dermoid cyst or a blood cyst. A definite diagnosis can sometimes only be made after operation by microscopical examination of a portion of the cyst.

Prognosis.—This varies with the type of cyst present, the development of complications, and the treatment adopted. In many cases the prognosis is good, apart from rupture or infection. In the large balloon cyst there is risk of sudden death during an attack of distension.

Treatment.—The large balloon cysts which are causing respiratory and cardiac embarrassment call for immediate treatment by the insertion of a needle. Subsequently the only hope of recovery lies in pneumonectomy.

When the cysts are infected, treatment by postural drainage should first be adopted. Failure usually follows attempts at surgical drainage or collapse operations. If the cysts are unilateral and infected, the only hope of cure lies

in radical removal of the portion of lung involved, either by lobectomy or by pneumonectomy; and so in bilateral cases it necessarily follows that no radical cure is possible.

HYDATID DISEASE OF THE LUNG

Hydatid cysts may develop in the lung in patients infected by the ova of the *Tænia echinococcus*.

Ætiology.—Man is the intermediate host of this parasite, and becomes infected directly or indirectly from the dog. The modes of infection and the life-history of the parasite are elsewhere considered (p. 314). Males are more often affected, and the condition is commoner among the poor than the well-to-do. It is rarely seen in this country except in patients from abroad, especially from Australia.

Pathology.—Hydatid cysts have been described in the lungs in from 5·6 to 16·8 per cent. of cases of hydatid disease in different parts of the world. The right lung is more often the site of the disease than the left, and the cyst is usually basic, though it may occur in the upper parts of the lung. It is generally supposed that infection of the lung is usually secondary to the liver, the ova reaching the lung through the diaphragm; but the occurrence of primary lung hydatid suggests the possibility of the embryo gaining access to the general blood stream, and thus reaching the lung by the pulmonary artery. There is, as a rule, a single cyst in the lung, but multiple or multilocular cysts are occasionally observed. The cyst may become as large as a cricket ball, but usually ruptures before it reaches this size. It has the same structure as hydatid cysts of other organs, with ectocyst and endocyst. It may develop brood capsules and daughter cysts, but is often sterile in this situation.

The reactive changes in the lungs are at first irritative and congestive, but eventually some fibroid changes occur, producing a more or less definite fibroid capsule around the ectocyst. The overlying pleura may become inflamed, thickened and adherent when the cyst grows near the surface. Rupture may occur into a bronchus, into the pleura, pericardium or peritoneum, or occasionally into the aorta or pulmonary vein. Rarely the contents of a small cyst may become inspissated, thus producing spontaneous cure.

Symptoms.—Until the cyst becomes large enough to cause irritation, there may be no symptoms, but sooner or later cough and expectoration develop. The latter is generally mucoid, and frequently bloodstained. Dyspnœa becomes apparent and pain results if the pleura is involved. The signs may be: diminished vocal fremitus, localised dullness and weak or absent breath-sounds and voice-sounds over a limited area, generally in the lower lobe. A few râles may be audible round the dull area. Occasionally with a large cyst there may be some bulging on the affected side, and "hydatid fremitus" has been described. The heart may be displaced in rare cases. Examination by the X-rays generally shows a suggestive rounded shadow with very little change in the surrounding lung, except in chronic cases where some fibrosis may be observed.

Some degree of eosinophilia is common but not invariable. When rupture into a bronchus occurs, there is usually sudden copious expectoration of watery

fluid containing hooklets. Daughter cysts and parts of the ectocyst may be coughed up and lead to dyspnœa and even suffocation from laryngeal obstruction.

After rupture, spontaneous cure may result if the ectocyst is expectorated. More commonly the cavity becomes infected and the symptoms and signs become those of chronic abscess (see p. 1179). Rupture into the pleural cavity produces great pain, dyspnœa, cyanosis and shock, similar to the condition induced by pneumothorax. Rupture into the pericardium or into a vein is usually quickly fatal. When rupture occurs into a serous cavity, urticaria and severe toxic symptoms sometimes develop.

Course.—This is generally progressive, though occasionally spontaneous cure occurs either before or after rupture. More commonly the cyst causes increasing pressure or irritative symptoms, and eventually rupture or suppuration produces acute manifestations.

Diagnosis.—The clinical features of pulmonary hydatid may be suggestive of pulmonary tuberculosis, pleural effusion or new-growth. Diagnosis may be difficult before rupture occurs; after this the discovery of hydatid hooklets or pieces of cyst-wall may establish the diagnosis. In suspicious cases the X-ray findings may be of great assistance, and confirmatory evidence may be obtained from cytological and serological examination. The former frequently shows eosinophilia, and the latter gives complement deviation when a suitable antigen, such as extract of hydatid cyst-wall, is used. A precipitin reaction may also be obtained with the fluid from another cyst. The Casoni intradermal test with the appropriate antigen has established itself as having special diagnostic value.

Prognosis.—The prognosis is serious owing to the risks of rupture and suppuration. Spontaneous cure is rare, but can occur. After rupture into a bronchus, recovery may ensue, but more commonly abscess formation results. Rupture into a serous cavity is frequently fatal. Early surgical treatment either before or after rupture improves the outlook.

Treatment.—Aspiration of the cyst, either exploratory or therapeutic, is to be avoided. If the cyst can be diagnosed or localised before rupture, the lung should be exposed by thoracotomy, the pleura stitched together and the cyst incised, the endocyst removed, and the cavity drained. Suppuration of a pulmonary hydatid must be treated as a pulmonary abscess.

THE PNEUMONIAS

The term pneumonia has been somewhat loosely applied to any inflammatory condition of the lung producing consolidation. When the consolidation affects large areas of lung uniformly it is described as lobar pneumonia, and when it is patchy or lobular in distribution it is called lobular or broncho-pneumonia.

1. LOBAR PNEUMONIA

Synonyms.—Croupous or Pleuro-Pneumonia.

Definition.—This is an acute infectious disease characterised by an inflammatory lobar consolidation.

Ætiology.—*Predisposing causes.*—Pneumonia may occur at any age. It is common in children up to the sixth year, the incidence being about equal in the two sexes. It is commonest between the ages of 15 and 40, when there is a preponderance in the male sex of two or three to one. It is also a frequent terminal malady in the aged of both sexes. It may be doubted whether race has much influence, although in America and in the Rand mines the incidence and mortality among the black races are both high. Pneumonia is met with all over the world, but it is more rife in localities with changeable climate and cold winds. Its seasonal incidence is well marked; it is uncommon in the summer and autumn, and is most prevalent om November to March in this country. Although pneumonia is as a fr le endemic and sporadic in its incidence, it is generally admitted that localised epidemics occur. Urban conditions, defective sanitation, overcrowding and insufficient ventilation all conduce to the incidence of pneumonia. It is not uncommon to obtain a history of several previous attacks. Although the disease often attacks those in normal robust health, there can be no doubt that debilitating conditions and diseases predispose to it, among them being chronic nephritis, diabetes, over-fatigue, exposure and alcoholic excess.

Exciting causes.—The exciting cause in most cases is the presence of the pneumococcus of Fränkel. It may be the only pathogenic organism found in the lung lesions and in the sputum, but not infrequently others, such as streptococci, staphylococci or Pfeiffer's bacillus are also present. Occasionally these organisms, and others, such as Friedländer's pneumobacillus, the *Bacillus typhosus*, the gonococcus and the *B. pertussis*, cause lobar consolidation; but these conditions should be regarded as varieties of secondary pneumonia, and differentiated from the acute primary condition now under consideration.

The pneumococcus.—The pathogenicity of the pneumococcus has been the subject of an interesting study by Cole, Dochez, Avery and Gillespie and more recently by Georgia Cooper and her co-workers. Originally three types were described; Types I., II., III., which together account for more than 50 per cent. of all cases. The remainder were included in a group referred to as Group IV. This has now been separated into 29 other types, making 32 in all, by means of serological reactions.

The American observers have shown that 40 per cent. of contacts with cases of pneumonia due to types I. and II. may harbour the corresponding organism for an average period of 23 days, and that they may develop pneumonia from it. They have further demonstrated that a convalescent patient may carry pathogenic pneumococci in his mouth for as long as 90 days from the onset of the disease. They have also found pathogenic pneumococci in the dust of rooms in which patients suffering from pneumonia have been nursed. The significance of this work is obvious. It confirms the view that pneumonia is an infectious disease, capable of being spread by carriers, by the convalescent patient, and by the dust of rooms.

Although the pneumococcus is the specific exciting cause, its activities are often determined by some other factor, such as chill, exposure, overexertion or injury. The presumption is that these conditions lower the general resistance of the individual, and thus impair the defensive mechanisms. Post-operative pneumonia may be a further instance of this, but doubtless some supposed cases are in reality due to lobar collapse.

Pathology.—The pneumococcus is found in the pulmonary lesions and elsewhere when complications occur. In some patients it is found in the blood. These are referred to as bacteriæmic cases and are usually more severe and often associated with complications. Experimental investigations on animals indicate that the avenue of infection is to the lungs by way of the trachea and bronchi, the blood infection being secondary to the pulmonary lesion. Four stages are commonly described in the process by which the lung becomes consolidated and returns to normal, namely, engorgement, red hepatisation, grey hepatisation and resolution.

In the stage of engorgement the affected part of the lung is slightly enlarged, deep red in colour, and heavier than normal, although it still crepitates and floats in water. The pleura over it may be injected and lustreless and may even show early fibrinous exudate. On section, the hyperemia is obvious and there may be some œdema. On squeezing, frothy, bloodstained fluid exudes. Microscopically, the engorgement of the capillaries, the swelling and partial desquamation of the alveolar epithelium are the chief changes to be noted. In the stage of red hepatisation the affected area becomes completely consolidated, the general aspect on section being remotely similar to liver, hence the name hepatisation. The pleura is now notably inflamed and may be obscured by yellow fibrinous exudate. The hepatised area of lung is larger and much heavier than normal and bears the impress of the ribs upon it. On section, it is seen to be red in colour, solid and completely airless. It does not crepitate and it sinks in water. The lung tissue is found to be more friable than normal. On scraping the cut surface, which has a granular appearance, a reddish fluid is collected, containing small fibrinous plugs, which are practically alveolar casts. Microscopically, the alveoli are occupied by a coagulated exudate rich in fibrin and red blood corpuscles, with scanty leucocytes and a few larger cells derived from the alveolar epithelium. In the stage of grey hepatisation the lung tissue, although still solid, airless and non-crepitant, is greyish in colour, softer in consistence and still more friable. The surface of the section is less granular, and on scraping, a pale yellowish, almost puriform fluid is obtained. Microscopically, the blood vessels are found to be relatively empty, the alveoli are now incompletely filled, the fibrin and red corpuscles have largely disappeared, and the alveoli are occupied by leucocytes and desquamated alveolar cells. In the stage of resolution, the exudate becomes more liquid and its cellular constituents undergo fatty degeneration. The liquefied exudate is largely absorbed, although expectoration may possibly assist in its removal. The lung returns to its normal spongy state and the alveolar epithelium is replaced. Some pleural thickening or adhesion may, however, result. In very severe and fatal cases, the stage of resolution may be replaced by one of purulent infiltration, in which the lung becomes paler, softer and in places almost diffluent. The scrapings are practically purulent.

Although these four stages are described, it should be remembered that they are not sharply defined from one another, and that they only represent special appearances in a continuous process. Consequently, although the major part of the affected area of lung may be characteristic of any one of them, all four stages may be recognisable, especially in cases of a spreading type. The base is more often affected than other parts, and the right side more than the left, in the ratio of 3 to 2. The unaffected parts of the lung

may show some catarrhal bronchitis, or some degree of collateral hyperæmia or œdema. Pleurisy is an integral part of the affection, but it may proceed to serous or purulent effusion. Pericarditis and less frequently acute endocarditis may be found in fatal cases. Pneumococcal meningitis, arthritis and otitis are very occasionally observed. The liver and kidneys may show cloudy swelling, and the spleen is often slightly enlarged and soft. Jaundice may be observed, especially in right-sided cases. The right side of the heart may be engorged and dilated.

Symptoms.—The exact incubation period is not yet established, but it is short, being probably from 1 or 2 days up to a week. The onset is sudden and acute, with chill, shivering or rigor in the majority of cases. In children convulsions take the place of rigors. Vomiting at the onset is not infrequent, occurring in about one-third of the cases. Less commonly the onset is insidious, or is preceded by malaise and catarrhal symptoms. The temperature rises with the rigor, and as a rule a short, dry, irritating cough develops quickly, accompanied by a severe cutting pain on the affected side. The pain often becomes intense, and coughing may cause the patient great distress. The cough is frequently restrained as much as possible, and the breathing is rapid and shallow. By the second or third day the pain becomes less and the cough easier and more effective. Sputum, which at first is scanty, extremely viscid, tenacious and difficult to expectorate, now becomes more abundant, although remaining viscid. In typical cases it is characteristically rusty at this stage, containing mucus, altered red blood corpuscles, alveolar epithelium and large numbers of pneumococci. In a few instances a small but definite hæmoptysis occurs. Occasionally the sputum is thinner and of "prune juice" type.

Sleeplessness is often a distressing symptom, especially in the early and late stages. In some cases there are marked cerebral symptoms. Headache at the onset is common. Delirium is frequent, particularly in the asthenic type, in apical cases, and in alcoholics. In the latter it may be violent and is often like delirium tremens. The temperature is usually of high continuous type throughout, reaching 103°, 104° and even 105° F. or more on occasions, especially in the sthenic type. In the asthenic it is often of lower range. Defervescence is by crisis in about 60 per cent. of the cases. Crisis is commoner in sthenic patients in types I., IV. and VII., and occurs more often on the odd than on the even-numbered days of the disease. The most common day for the crisis is the seventh. It is rare before the third or after the ninth day. At the crisis the temperature falls to normal or subnormal in about 12 hours. The patient often sleeps soundly at this time and may sweat profusely; respiration is slower and easier and the pulse-rate falls. On waking, a dramatic change in the condition is usually noticeable. Pain and distress are ameliorated, cough is loose and easy, and the patient feels better, although weak. Looseness of the bowels and free diuresis are not infrequent, constituting the "critical evacuations." The crisis is sometimes preceded by a pseudo-crisis, in which a considerable fall of temperature occurs, with little or no improvement in the general condition. A slight post-critical rise of temperature of 1° or 2° F. is sometimes seen, but as a rule the temperature remains subnormal for a few days and slowly returns to normal. The pulse-rate may be slow for a time. Convalescence is generally rapid, although in cases which have had marked delirium, some mental confusion may be present for a day

or two. Defervescence by lysis is more common in asthenic patients. The temperature remits and may take from 2 to 4 days to reach normal or subnormal levels.

The physical signs vary with the stage of the disease. At first there is some restlessness, but soon the patient assumes a dorsal decubitus, or lies more on the affected side. The cheeks are flushed, often markedly so on the side of the lesion. The eyes are bright, but the expression is one of pain or anxiety. A crop of herpes on the lips is very common. The tongue is thickly coated and white, becoming dry and cracked in bad cases at a later stage. The skin feels dry and pungently hot. The alæ nasi are in action, and in children a puff or grunt accompanies each expiration, while the pause follows inspiration, instead of expiration. The respiration and pulse-rate are increased, the former disproportionately, so that the pulse respiration ratio becomes 3 or even 2 to 1, instead of the normal 4 or 5 to 1.

In the early stage the pulmonary signs are slight. At the most there is lessened movement and diminished vocal fremitus over the affected area, with dubious impairment of note, weak air entry and possibly a few crepitations (indux), or pleural friction sounds, vocal resonance being unaltered. Of these, lessened air entry is probably the most common. Slight hyperresonance of the opposite lung, with harsh breathing, may lead to error in diagnosis as to the side affected.

The signs of consolidation (hepatisation) are generally apparent on the second or third day, except in cases where the disease starts deeply (central pneumonia). There is definite limitation of movement on the affected side, which is, however, slightly increased in size, as can be demonstrated by mensuration. Vocal fremitus is markedly accentuated over the affected area, except in massive pneumonia, and friction fremitus may be palpable. The note on percussion is dull, but has not the resistant stony character of that over an effusion. The note above or below the consolidated area is sometimes skodaic. The breath-sounds are tubular, and a few crepitations may be heard, but frequently adventitious sounds are absent. In some cases a friction rub is audible. Bronchophony and pectoriloquy are usually very marked over the consolidated area. The breath-sounds in other parts may be vesicular or harsh, and a few rhonchi may be present. The heart is usually in its normal situation, but is sometimes slightly displaced away from the affected side. In later stages the signs of dilatation of the right heart may become apparent.

During resolution, which begins after the crisis or during lysis, the tubular character of the breath-sounds disappears, and they become at first bronchial and later harsh or vesicular. Coarse moist sounds, known as redux crepitations, are heard both with inspiration and with expiration. The dullness gradually diminishes, and the voice-sounds return to normal. In basal cases, in which the diaphragmatic pleura is involved early, there may be pain, tenderness and abdominal rigidity simulating peritonitis, perforation or appendicitis. Graham Hodgson has shown by X-ray examination that the diaphragm rises in pneumonia, and in types I. and II. the consolidation begins near the hilum and spreads peripherally. In type III. the appearances are less characteristic, and may begin peripherally and spread centrally. Resolution reverses the order of appearance. It is rare for the spleen to be sufficiently enlarged to be palpable. The blood shows a leucocytosis up to

20,000, occasionally up to 50,000 in young or sthenic patients. Blood culture may yield pneumococci, although this was successful in only 30 per cent. of cases at the Rockefeller Institute. The urine is diminished in quantity, and there is a great reduction in the sodium chloride excretion until the crisis. Albumin and albumose are frequently found in small quantities in the urine during the febrile stage, and a few granular casts may be present. The uric acid excretion is increased to two or three times the normal, commencing the day before the crisis and generally falling to normal during the ensuing week. This is probably due to disintegration of the exudate in the alveoli, and so forms a measure of resolution, although some authorities maintain that it runs parallel with leucocytosis and not with cell destruction. Pneumococci can sometimes be obtained from the urine at the height of the disease. The blood pressure usually falls during the course of pneumonia, and according to G. A. Gibson a sudden rise indicates the imminence of some complication, such as delirium, whereas a sudden fall suggests the onset of cardio-vascular paralysis.

The disease does not always follow the typical clinical course, and certain varieties are described :

Apical pneumonia.—The consolidation may be limited to the apex or upper lobe of one lung. This is more common in children, the aged and alcoholics, and is often associated with marked cerebral symptoms.

Creeping pneumonia (*Migratory or wandering pneumonia*).—The consolidation spreads irregularly in one or both lungs. Partial resolution occurs, but there is no true crisis, and as successive portions of the lungs become involved the temperature exacerbates, eventually falling by lysis in cases that recover.

Central pneumonia.—The symptoms and appearance of the patient may suggest lobar pneumonia, and yet no abnormal signs can be detected in the lungs. In some of these cases there may be a deep-seated consolidation, which can usually be revealed by X-rays. A typical crisis may occur.

Massive pneumonia.—The bronchi, as well as the alveoli, may be filled with a fibrinous exudate. It is a rare condition and leads to difficulty in diagnosis, as the physical signs resemble those of pleurisy with effusion, vocal fremitus being diminished and breath-sounds weak or absent. The heart, however, is not displaced, or only slightly so.

Post-operative pneumonia.—It is probable that some cases that were formerly described as post-operative pneumonia were in reality instances of massive lobar collapse (see p. 1166). At times a pneumococcal pneumonia follows the administration of a general anæsthetic, but it does not present any peculiar features.

Traumatic pneumonia.—The fact that an injury to the chest may be followed after a short interval by a pneumonic process in the lungs has long been recognised. The condition was called "contusional pneumonia" by Litten in 1881. Külbs showed later that the changes in the lungs in dogs following local trauma were mainly hæmorrhagic, and that the lung opposite to the side injured may be affected by "contre-coup." In the recorded cases of traumatic pneumonia two types can be differentiated—(1) those with hæmorrhagic lesions only, and (2) those showing hæmorrhagic foci with a superimposed bacterial infection. The former recover rapidly, the latter often lead to a fatal issue.

Pneumonia in children.—This often presents certain characteristic features. There is rarely any sputum, the expectoration being swallowed. Convulsions at the onset are common. The lesion is often at the apex of the lung. Cerebral symptoms are frequent, and empyema or otitis media often occurs as a complication.

Pneumonia in the aged.—This occurs frequently as a terminal infection, often leading to a rapid and comparatively painless death. The onset may be insidious and the physical signs slight.

In *pneumonia in the insane*, lobar consolidation is often observed, without marked constitutional disturbance other than fever.

Secondary pneumonia.—Lobar pneumonia may develop during the course of certain acute specific fevers, notably enteric, typhus and plague. It is doubtful whether a true lobar pneumonia occurs in influenza, the condition to which the name influenzal pneumonia is applied being due to coalescing lobular pneumonia with hæmorrhagic extravasations.

Complications.—Delayed resolution not infrequently occurs, the signs of consolidation persisting for weeks instead of days. Frequent careful examinations should be made and possible errors in diagnosis considered, such as the presence of tuberculosis or empyema. Gangrene and abscess are rare but recognised complications.

Dry pleurisy is an invariable accompaniment when the consolidation reaches the surface, and in a considerable proportion of cases slight serous effusion occurs. This occasionally becomes frankly purulent and an empyema results. Bronchitis is common and may be due to a complicating secondary infection. Cardiac failure is a grave occurrence and can be recognised by increasing cyanosis, lividity and dyspnœa, with signs of enlargement of the right heart and with enfeeblement of the heart-sounds. Pericarditis is not very uncommon and is a serious complication. It may be dry or proceed to serous or purulent effusion. Acute endocarditis, sometimes of infective type, occurs. Abdominal complications are comparatively rare. They include pneumococcal peritonitis, colitis and nephritis. Acute dilatation of the stomach occurs in rare cases, and is usually rapidly fatal. Meteorism is more common and, although serious, is more amenable to treatment. Jaundice, due to catarrh of the bile-ducts, or to hæmolysis, is sometimes present.

Pneumococcal meningitis supervenes in rare cases, and is invariably fatal. Delirium has already been referred to, and is especially serious when occurring in alcoholics. Peripheral neuritis has been described, but is very uncommon. Otitis media and arthritis, proceeding sometimes to suppuration, occur as complications, both being commoner in children. A parotitis, sometimes going on to suppuration, is an occasional and serious complication, especially in old people. During convalescence, thrombosis of the veins of the legs may occur in rare instances.

Sequelæ of lobar pneumonia are uncommon. Perhaps the most remarkable is the liability to subsequent attacks possibly due to infection by different types of pneumococcus. Some permanent pleural thickening or adhesion may occur, and after an empyema the usual sequelæ may result. Pulmonary fibrosis (chronic interstitial pneumonia) is rare, especially in comparison with its frequency after broncho-pneumonia; this may lead to bronchiectasis.

Course.—The course depends on the type and virulence of the infection and on the resistance of the patient. In a typical sthenic case, consolidation

is well established by the second or third day, defervescence by crisis occurs usually on the seventh day, signs of resolution become apparent a day later, and all signs clear up within 14 days of the onset. In asthenic cases the course is less typical and often prolonged to 9 or 10 days, defervescence occurring by lysis. In fatal cases, death commonly occurs between the fourth and tenth days, although severe cases may prove fatal as early as the first or second day. After the tenth day a fatal result is generally due to complications. An abortive course is described, in which typical symptoms occur with slight or indefinite signs, the temperature falling by crisis within 36 hours, followed by rapid recovery. This group includes the "maladie de Woilles." It is difficult in many instances to establish the true causation of such cases.

Diagnosis.—When the disease is well established and the history is available, diagnosis is as a rule easy. To prove the pneumococcal origin, sputum examination, lung puncture, or blood or urine culture is necessary. The investigation of serum reactions is necessary to establish the type of pneumococcus concerned if specific treatment is employed.

At the onset, especially before the signs of consolidation develop, difficulties in diagnosis often occur. The initial rigor or convulsion with vomiting may suggest scarlet fever. In children, especially those with early apical pneumonia, headache, vomiting, convulsions, head retraction, squint and even slight Kernig's sign may lead to an erroneous diagnosis of meningitis. Pain in the side and cough, the altered pulse respiration ratio, and the presence even of slight abnormal physical signs in the chest, usually suffice in both instances to suggest the correct explanation.

Occasionally the onset of pneumonia may simulate an acute abdominal condition, such as appendicitis or perforation of a gastric ulcer, owing to referred abdominal pain, sometimes with rigidity. The diagnosis may be very difficult, and laparotomy has not infrequently been carried out in error. The history, the pulse respiration ratio, the absence of tenderness on rectal examination, and the presence of pulmonary signs usually enable a correct decision to be made.

Influenza may start acutely and simulate pneumonia, but the distribution of the signs and the examination of the sputum generally serve to distinguish between them. Typhoid fever less often gives rise to difficulty, but some cases of pneumonia pass quickly into a typhoid state, while some cases of typhoid fever develop consolidation in the first week.

When consolidation is well established, the chief conditions to be differentiated are—(1) Broncho-pneumonia. The slower onset, the more prolonged course, the bilateral patchy physical signs, and the marked predominance of the bronchitic manifestations usually suffice to differentiate this group of conditions. (2) Secondary pneumonias, such as those in plague, typhoid fever, and influenza, can be diagnosed only from the history, the associated symptoms and signs, and from the bacteriological examinations. (3) Friedländer's pneumonia is rare. Its course is short, its prognosis grave, and it can only be recognised by bacteriological investigation. (4) Massive collapse. The diagnosis of this condition and its differentiation from pneumonia are discussed on p. 1167. (5) Acute pneumonic tuberculosis. The onset and early signs may be identical with those of pneumonia. The persistence of the fever, its tendency to become remittent or intermittent, and the

occurrence of night sweats should suggest looking for tubercle bacilli in the sputum. (6) Pleural effusion and empyema. Differentiation is generally easy, except in cases of massive pneumonia. Investigation of the position of the cardiac impulse, and of vocal fremitus and resonance, affords the most valuable aid. Grocco's triangle may also assist. In some cases the diagnosis can only be established by the exploring needle. (7) Infarction of the lung in cardiac disease, causing pain, cough, blood-stained expectoration, and dyspnœa, may simulate pneumonia. The absence of fever, the presence of the cardiac condition and the localised physical signs are generally characteristic. (8) Acute œdema of the lung, especially in mitral stenosis, may suggest pneumonia. Fever is generally absent, the sputum is typical, and the primary cause may be apparent. An attack of paroxysmal tachycardia may give rise to difficulty, when it leads to dullness and crepitations at the bases, but careful examination should establish the very rapid action of the heart and the evidence of venous engorgement in other parts.

Prognosis.—Lobar pneumonia is a serious disease, with a high mortality rate. This is profoundly influenced by age and by recent methods of treatment. It is but little fatal in childhood, except in the first years of life. After the age of 60, the mortality until the new chemo-therapeutic measures were employed was from 60–80 per cent. The New York investigations at the Rockefeller Institute demonstrated the importance of the type of pneumococcus in prognosis; thus, it was found that the mortality of cases with types I. and II. was about 25 to 30 per cent., of those with type III. 50 per cent., and of other types collectively only 12 per cent. With M. and B. 693 (Dagenan, sulphapyridine) the average mortality of all types has been reduced to about 8 per cent.

The previous habits and history of the patient influence prognosis considerably; chronic alcoholism doubles the risk of a fatal issue, and the outlook is grave in patients who are the subjects of diabetes, chronic cardio-vascular disease, nephritis, marked debility or obesity. Unfavourable indications during the course of the disease are profound toxæmia, a pulse-rate persistently 130 or more, a blood pressure in millimetres of mercury lower than the pulse-rate, and a temperature remaining at 105° F. or over for several days. Absence of the usual leucocytosis is generally of sinister import. Dilatation of the right heart, with cyanosis progressing to lividity, is most grave. Modern statistics confirm the traditional view that labial herpes is a favourable prognostic sign.

Of complications, meningitis is invariably fatal, unless it responds to treatment by sulphapyridine while septic endocarditis is extremely grave. Cases with abscess or gangrene, although serious, sometimes recover, especially if operative treatment is practicable. The prognosis of those with pericarditis is serious, but not uniformly unfavourable. Cases with bilateral empyemata show a high mortality. Late delirium is a very serious indication.

Treatment.—PROPHYLACTIC.—Prophylactic vaccination has been used with success by Lister in South Africa. He employed a triple vaccine, made from three types, and gave 6000 millions of each. Three injections were made at weekly intervals.

When a case has occurred, all contacts should have a throat examination, and if virulent pneumococci are found a suitable antiseptic mouth wash

should be used. The room in which the patient has developed the disease should be disinfected afterwards. If possible, no case of pneumonia should be nursed in a general ward of a hospital, and the doctor and nurse in attendance should wear gauze masks. All sputum should be disinfected. The patient should lie in a narrow bed away from a wall to facilitate nursing. The room should be well ventilated, and the temperature maintained at 60° to 65° F. Treatment in the open air is not advisable except in very mild weather. Two important factors are rest and sleep. The patient should, therefore, be disturbed as little as possible by the examination of the physician and by the attentions of the nurse. He should not, however, be allowed to lie flat all the time, to avoid basal congestion. The diet should be restricted to fluids and semi-solids, eggs, milk, meat extracts and the various invalid foods being given up to 2 or 3 pints in the 24 hours. Dextrose, in the proportion of 2 to 4 ounces to the pint of lemonade or orangeade, is useful. Too much milk should be avoided, as it is liable to cause indigestion and flatulence. The irritating cough, which induces such intense pain, should be checked by a sedative linctus, or by lozenges, but it may be necessary to inject $\frac{1}{12}$th grain diamorphine hydrochloride (heroin), or even $\frac{1}{8}$th grain morphine to relieve pain and to induce sleep in the early stage. Local applications to the chest help to relieve pain. Hot linseed poultices to the back and side may be employed, but cataplasma kaolini or antiphlogistine applied on lint does not require such frequent changing and disturbs the patient less. Care should be taken to avoid too hot application, which may injure the skin. A pneumonia jacket is preferred by some, by others the ice poultice or ice-bag is found very soothing. A dose of calomel should be given at the onset, and the bowels should be opened daily, either by a laxative or by a small soap enema unless at any stage the patient is profoundly exhausted.

Sulphapyridine (Dagenan, M. & B. 693) has proved of great value in the treatment of lobar pneumonia due to all types of pneumococcus. It is put up in tablets containing 0·5 grm. for adults, and 0·125 grm. for infants and young children. The usual dosage for adults is 4 tablets repeated in 4 hours, followed by 2 tablets every 4 hours for 2½ days. Subsequently 1 tablet is given every 4 hours for 24 hours, then 1 tablet every 8 hours for 36 hours, making a total of 23 grms. in 5 days. In infants 0·125 to 0·25 grm. is given four-hourly. The dose for children is based on the body weight, but they require proportionately up to 50 per cent. bigger doses than adults, *e.g.* up to the age of 3 years 0·375 grm., and at 5 years 0·5 grm. is given four-hourly, until the temperature falls to normal, when a smaller dose may be given eight-hourly for two further days. Children tolerate the drug well. The tablets are best administered crushed and suspended in water, milk or fruit juices. The patient should not be given sulphur-containing substances such as eggs, onions, Epsom salts or Glauber salts during the course of the treatment. A sufficient quantity of fluid should be taken to result in the passage of at least 50 ounces of urine in the 24 hours. At whatever stage in the illness the treatment is instituted the temperature usually falls to normal by lysis in 24 to 36 hours when the drug is effective, although the actual process of resolution in the lung is not accelerated. In some cases vomiting prevents an adequate concentration of the drug in the blood and the treatment has to be abandoned, but frequently the difficulty can be overcome by varying the method of administration. The most important toxic effects

which may occur include nausea and vomiting probably central in origin, headache, cyanosis due to methæmoglobinæmia, and hæmaturia. The latter may occur if the urine is too concentrated and is thought to be due to the formation of crystals of acetylated sulphapyridine. If the drug is administered for longer than 5 days there is a possibility of further complications ensuing, such as drug fever and granulocytopenia. In the former the temperature may rise to 104° or 105° F. and morbilliform, scarlatiniform or urticarial rashes appear. A preparation of soluble sulphapyridine (Dagenan—sodium) may also be given intramuscularly or intravenously if the patient cannot tolerate the drug by mouth. It is put up in ampoules containing 1 grm. in 3 c.c. The intramuscular injections are given undiluted and are painful. For intravenous injection the contents of the ampoule are diluted to 10 c.c. with normal saline. The usual dose is 1 grm. every 4 hours. In the early stage, a simple saline diaphoretic mixture may give comfort by promoting the action of the skin and by rendering the sputum less viscid. For this purpose liq. ammon. acetat. min. 120, potass. citrat. grs. 20, syrup. aurantii min. 60 and water to the ounce, may be given every 4 to 6 hours. The use of depressant drugs, such as tartar emetic, aconite, or pilocarpine, although formerly recommended, is now generally discarded. Expectorants such as ammonium carbonate or iodide of potassium in doses of 3 to 5 grains are often recommended after the second day, but are of doubtful utility.

Cardiac embarrassment and failure are the conditions requiring the most active treatment in this disease. A careful watch should be kept upon the colour of the patient, the condition of the pulse and the size of the heart. Digitalis, in doses of 5 to 15 minims of the tincture, may be added to the mixture, or given with brandy. Nikethamide (coramine), either by the mouth or hypodermically, is often of value and has largely replaced the use of camphor, though the latter dissolved in sterile oil may be given in 3-grain doses twice daily. If signs of acute heart failure occur, strophanthin gr. $\frac{1}{200}$ may be given intravenously, or digitalin gr. $\frac{1}{100}$ with strychnine sulphate or hydrochloride gr. $\frac{1}{60}$ to $\frac{1}{30}$ hypodermically The latter may be repeated in from 4 to 6 hours if necessary. Strychnine alone may be given in doses of gr. $\frac{1}{60}$ every 4 hours, and is often very useful. Other circulatory tonics which may be employed hypodermically are pituitary (posterior lobe) extract $\frac{1}{2}$ to 1 c.c., or adrenaline 5 to 10 minims of 1 in 1000 solution. Alcohol is often useful; it should not be given too early in the attack, but where there are indications of incipient cardiac weakness 4 to 6 ounces daily may be given, and this even to alcoholics.

Oxygen inhalations may be helpful in any case where there is distress or cyanosis. It should be warmed, and may be bubbled through alcohol. It may be administered continuously by means of a double nasal catheter with flow-meter and humidifier if available, or the B.L.B. mask by which with various adjustments an alveolar concentration of oxygen of more than 90 per cent. can be obtained. An oxygen tent is now rarely used except for infants and children. These methods may prove of the greatest value where there is marked anoxæmia. Venesection to the extent of 10 or 12 ounces is of some value if there is lividity from right-sided engorgement, especially in sthenic cases. As a rule it is best not to interfere with the temperature by antipyretic drugs and measures unless it remains over 104° F., when sponging, either tepid or cold, should be tried.

Sleeplessness is a frequent and distressing symptom and requires treatment. In the early stages 10 grs. of Dover's powder or an injection of morphine or diamorphine hydrochloride (heroin) are usually effective. In the later stages, morphine should only be given with care, and then in association with atropine gr. $\frac{1}{200}$ to $\frac{1}{100}$ and strychnine gr. $\frac{1}{60}$ to $\frac{1}{30}$. Paraldehyde min. 120 with syrup of orange in 2 ounces of water, is safe and often effective. Chloralamide grs. 20 to 30, with bromides may be tried. In cases with delirium an ice-cap should be applied to the head, and the patient sponged with tepid water. Morphine may be necessary, and in severe cases hyoscine, gr. $\frac{1}{100}$, may be injected; but the latter is a dangerous drug and the patient's condition should be watched, and strychnine administered if necessary. Tympanites, when present, is distressing and exhausting, and should be treated by passing a rectal tube or by the administration of an enema of asafœtida or a turpentine wash-out. If these measures fail, carbachol (doryl) or acetylcholine may be employed cautiously.

Specific.—Specific antiserums are now available for many of the types, and have been used with some success. Horse serums, highly concentrated and refined by Felton's method, are now available for types I., II., IV., V., VII. and VIII. Rabbit antipneumococcus serum is available for type III., and many others. It has the advantage of ease of preparation and of considerable concentration. If it is proposed to employ serum treatment it is necessary first to determine the type of pneumococcus concerned by serological tests. A rapid method involving the testing of the organisms in the fresh sputum against test serums has been introduced by Armstrong and simplified by Neufeld. The specific serum causes swelling of the capsules in the corresponding type. The patient's sensitiveness to the serum must then be determined by an intradermic injection of 0·02 c.c. of diluted serum (diluted $\frac{1}{10}$ with saline), and if he shows a reaction he must be desensitised by small injections to prevent anaphylaxis. The serum is then diluted with an equal volume of warm sterile saline and 10 to 15 c.c. injected intravenously at the rate of 1 c.c. a minute, followed by 90 c.c. more during the next quarter of an hour. This dose is repeated every 8 hours until improvement occurs. Felton's serum (2000 units in 1 c.c.) is administered intravenously undiluted, after being warmed to body temperature and after careful preliminary tests as to sensitiveness. The initial dose is 10,000 units, slowly injected intravenously. Amounts up to 40,000 or 50,000 units are given in the first 24 hours, though as much as 100,000 units may be necessary in severe cases. The earlier it is given, the greater is the likelihood of success. It is as a rule unnecessary in young children and adolescents, and contra-indicated in advanced age and in patients known to be allergic. Rabbit serums are given undiluted intravenously after being warmed to body temperature. At least 5 minutes should be taken to inject each dose. If anaphylactic manifestions occur adrenaline should be given subcutaneously at once.

Vaccine treatment is recommended by some, but the results are generally disappointing during the acute stage. A common method is to give 20 millions of a stock pneumococcus vaccine, and then to use an autogenous one as soon as it can be made. Sensitised and detoxicated vaccines have also been prepared. Vaccines seem to be more valuable in cases of delayed resolution.

Artificial pneumothorax has been suggested as a method of treatment.

There is as yet no convincing evidence of its value, but in cases with severe pain, the introduction of sufficient air to separate the inflamed surfaces of the parietal and visceral pleura is worth considering.

2. BRONCHO-PNEUMONIA

Synonyms.—Lobular Pneumonia; Catarrhal Pneumonia; Capillary Bronchitis.

Pulmonary consolidation of lobular distribution occurs in a variety of conditions which have little else in common. A satisfactory classification is at present difficult. The term capillary bronchitis is misleading and should be regarded as obsolete, since any inflammatory condition affecting the finer bronchi is invariably associated with alveolar changes. For convenience the following varieties of broncho-pneumonia may be described: (1) Primary. (2) Secondary. (3) Aspiration or deglutition. (4) Tuberculous.

a. Primary Broncho-pneumonia

Ætiology.—This form almost invariably affects infants under 2 years of age, in whom a lobular pneumonia seems sometimes to occur under conditions which would induce lobar pneumonia in older children or adults. It occurs equally in the two sexes, and is commoner in the winter and the spring. Rickets, malnutrition and debility are predisposing conditions, but it sometimes develops in healthy robust infants after exposure or chill. The pneumococcus is the organism usually found, either alone or in association with others, such as streptococci, staphylococci, the *Micrococcus catarrhalis* or Friedländer's pneumo-bacillus.

Pathology.—Widely scattered patches of consolidation are found in one or both lungs. These may be small and separated by areas of collapse or emphysema. Occasionally they are almost confluent, and at first sight appear like lobar pneumonia, constituting the pseudo-lobar form; but careful observation shows that the distribution is lobular and that zones of incomplete consolidation or of normal lung tissue separate the solid areas. If the process reaches the surface some degree of pleurisy is present, although this is less than in lobar pneumonia.

Microscopically, the appearances approximate to those of the lobar form; the alveoli are found to be filled with exudate, in which leucocytes and desquamated epithelial cells are present, together with some fibrin and red blood corpuscles. Catarrhal changes are also present in the bronchi.

Symptoms.—The onset is acute, with vomiting and chill, or convulsion, as in lobar pneumonia, but may be more gradual. Cough, cyanosis and dyspnœa develop rapidly. There is no expectoration, since infants and young children swallow the sputum. Cerebral symptoms simulating meningitis are common. The temperature rises quickly to 103°, 104° F., or higher, and the range is of the same character as in lobar pneumonia. Defervescence by lysis is the rule.

The physical signs are variable. In cases with widespread consolidation they are very similar to those of lobar pneumonia, with dullness, tubular breathing, increased voice-sounds and crepitations. In other cases, although

the aspect of the infant appears characteristic of pneumonia, with rapid breathing, cyanosis, reversed rhythm of inspiration and expiration, sucking in of the lower ribs and dilation of the alæ nasi, the signs are more scattered. Tubular breathing and increased voice-sounds may only be heard in localised patches, especially in the lower lobes. Crepitations are commonly present, and rhonchi may be audible over both lungs.

Complications and Sequelæ.—These are similar to those of lobar pneumonia.

Course.—This is usually short, the temperature falling in from 3 to 7 days, but it may be more prolonged and be suggestive of tuberculosis, or some other form of secondary bronchitis.

Diagnosis.—Primary broncho-pneumonia has to be distinguished from the lobar form to which ætiologically and pathologically it is so closely related. The acute onset without previous respiratory symptoms will suggest its primary character, while the patchy distribution of the signs generally suffices to establish its lobular distribution. In pseudo-lobar forms, this differentiation may be almost impossible during life. The cerebral symptoms at the onset, and the early absence of pulmonary signs may give rise to difficulty, as in the first stage of lobar pneumonia.

Prognosis.—The prognosis of primary broncho-pneumonia is generally unfavourable, especially in very young or debilitated infants.

Treatment.—This is practically identical with that of secondary broncho-pneumonia in children.

b. Secondary Broncho-pneumonia

In this condition there is inflammation of the bronchi, spreading down to and involving the alveoli. It is generally a catarrhal process, but may go on to septic or suppurative manifestations.

Ætiology.—A secondary broncho-pneumonia may occur at any age, but is much more common in early and advanced life. It is equal in its incidence in the two sexes. It frequently occurs as a complication of measles, whooping-cough, psittacosis and influenza, less commonly in cases of diphtheria, scarlet fever, plague and the enteric group. A bronchitis starting in the larger tubes may spread downwards to the alveoli. Broncho-pneumonia may develop during the course of acute gastro-enteritis. A secondary broncho-pneumonia occurs as a terminal infection in many old and debilitated persons and in those with chronic wasting or cachectic diseases, and also in chronic cardio-vascular conditions, chronic renal disease and in many progressive nerve degenerations. Any septic process may produce a metastatic broncho-pneumonia. This occurs in association with otitis media, suppurative processes about the appendix or Fallopian tubes, and cerebral abscess.

Bacteriology.—This is, as might be expected, very varied. Streptococci are frequently present, especially the hæmolytic variety, generally associated with other organisms, such as the pneumococcus, Pfeiffer's *H. influenzæ*, staphylococci and those found in catarrhal conditions of the upper air-passages. The *B. pertussis* may be found in cases associated with whooping-cough, the *B. pestis* in plague, and occasionally the *B. diphtheriæ* in diphtheritic broncho-pneumonia. The importance of Friedländer's *B. pneumoniæ* was formerly overestimated in this connection.

Pathology.—When, from any of the above-mentioned causes, an inflammatory process reaches the finer bronchi, the alveoli become affected in three different ways. Owing to the blocking of the bronchi by secretion or exudate, small areas of collapse of lobular distribution are produced. The inflammatory process extends into some or all of these, and areas of lobular consolidation result. Not infrequently the adjacent groups of alveoli become distended and are thus in a condition of acute emphysema. The lungs are normal in size or slightly enlarged. The surface presents a somewhat uneven, mottled appearance. There are small projecting patches of firmer consistence and reddish-grey colour, due to the consolidated lobules. Adjacent areas may be depressed and slaty blue, from lobular collapse, while the intervening lung tissue is normal or pinkish and emphysematous. There may be dimness or slight roughening of the pleura where the consolidated areas reach the surface, but serous or purulent effusion is uncommon. On section, the lung is found to be congested and sometimes œdematous, especially at the bases, while the bronchi exude pus or muco-pus from their cut ends. The reddish-grey areas of consolidation are found to vary in size from a pin's head to a hazel nut. They are generally more abundant in the lower lobes, especially posteriorly. The consolidated and collapsed areas both sink in water, and do not crepitate. There is often some peribronchitis, and the bronchial glands are usually enlarged. Microscopically, the finer bronchi and the consolidated alveoli are found to be filled with an exudate containing large numbers of leucocytes and desquamated, proliferating epithelial cells, but in which few red blood corpuscles and little or no fibrin are found.

In the very acute condition to which the name capillary bronchitis was formerly applied, consolidation may not be apparent, but microscopical examination invariably demonstrates the involvement of the alveoli. In influenzal broncho-pneumonia the pathological changes probably commence as an exudative bronchiolitis, associated with capillary hæmorrhages. Secondary infections are probably responsible for the consecutive broncho-pneumonic process, which results in flooding of the alveoli with an exudate containing red cells, but little or no fibrin.

Symptoms.—In the cases ensuing on bronchitis in infants or old people (formerly called capillary bronchitis), initial symptoms may be slight, and simply those of ordinary bronchitis, namely, malaise, slight fever and cough, with or without expectoration. The implication of the finer tubes and alveoli is usually marked by a rapid rise of temperature, great prostration, quick breathing and an irritating, persistent and often ineffective cough. In children, the alæ nasi work, the lower ribs are sucked in, and the pneumonic type of breathing develops. The patient becomes cyanosed, the pulse is rapid, 120 or more, and the respirations 50 or 60 per minute. The physical signs are in general indistinguishable from those of primary broncho-pneumonia, but breath sounds are often harsh and puerile, while tubular breathing is not heard, or only in very localised areas. In old people, cyanosis, restlessness and delirium may occur, and later the cough become less frequent, the patient being drowsy and tending to sink down in the bed, whereas previously there was orthopnœa. These symptoms are ominous and indicate failure of the respiratory centre.

The physical signs are often those of bronchitis, harsh or weak inspira-

tion and prolonged expiration, sibilant and sonorous rhonchi and crepitations or crepitant râles, especially at the bases. Patches of tubular breathing with increased voice sounds may develop but are not always present.

In other forms of secondary broncho-pneumonia similar symptoms and signs develop more insidiously in the course of the primary disease. Broncho-pneumonia should be suspected when cough, expectoration and dyspnœa, together with a remittent type of temperature, develop in the course of an acute specific fever or other severe illness. In all forms, anorexia is common, the mouth and tongue become dry, and thirst is complained of. The urine presents the usual high-coloured, concentrated character of febrile conditions. It is often diminished in quantity, may contain a small quantity of albumin, and not infrequently deposits urates.

Complications and Sequelæ.—These are relatively infrequent. Pleurisy may proceed to effusion, and when this occurs it is often purulent. Abscess and gangrene are rare, but develop rather more frequently than after lobar pneumonia. Other complications, such as pericarditis, endocarditis, meningitis and nephritis, are probably due to blood-borne metastasis.

The most important sequel is pulmonary fibrosis, which is often the origin of bronchiectasis later in life. Pulmonary tuberculosis is frequently described as a sequel, especially after measles, and may be due to inflammatory changes in the bronchial glands activating a quiescent tuberculous deposit there. In many cases of tuberculosis described as following on broncho-pneumonia, it is more probable that the original lung affection was tuberculous.

Course.—Secondary broncho-pneumonia generally has a longer course than either the primary form or the lobar variety of pneumonia. The fever often persists in remittent type for two or three weeks, and sometimes even for two or three months, although in this case tuberculosis should be suspected. The decline is almost always by lysis. Convalescence is often slow, the patient being left thin, weak, anæmic and debilitated.

Diagnosis.—The development of pulmonary symptoms, and of more or less characteristic physical signs in the course of measles, whooping-cough or one of the other diseases mentioned above, usually renders the diagnosis easy. Difficulty may arise in regard to tuberculosis, which in one form produces lobular pneumonic lesions with symptoms and signs indistinguishable from other varieties of secondary broncho-pneumonia. In any case where the fever lasts more than three weeks, or where the signs show no tendency to resolve or are chiefly apical, tuberculosis should be suspected. Unfortunately in children sputum is rarely available. An attempt is sometimes made to obtain it on gauze held in forceps, after exciting cough by touching the fauces. The mucus in the fauces may also be examined for tubercle bacilli. The diagnosis may, however, remain doubtful, until signs of softening become established.

Bronchitis rarely gives rise to difficulty. The fever is usually less high, and of shorter duration, while the physical signs are different, signs of consolidation being entirely absent. Hypostatic pneumonia may have to be considered. There is usually some obvious cause for this, such as cardiac disease and failure, or prolonged confinement to bed. The temperature is generally lower and the distribution is lobar.

Pleural effusion and empyema can generally be differentiated by the alteration of vocal fremitus and the displacement of the cardiac impulse.

In case of difficulty the exploring syringe enables a distinction to be made.

Prognosis.—The prognosis in secondary pneumonia is serious. Many deaths occur from this complication in the acute specific fevers, particularly with measles and influenza. Even the form following on severe bronchitis is frequently fatal, especially in old people and in wrongly fed or debilitated infants. The development of delirium, of a pulse-rate over 150, of marked cyanosis and dyspnœa is unfavourable. In old people, drowsiness, sinking down in the bed, and cessation of cough are very grave indications.

Treatment.—The treatment is very similar to that of lobar pneumonia, except that stimulant and expectorant drugs may be necessary from the first. At the present time there is practically no difference in the methods of treatment applicable to the primary and secondary forms. In cases due to pneumococcal infection sulphapyridine should be employed (see p. 1234). If streptococci are established as the infecting agent, one of the sulphanilimide preparations should be given at once.

The patient must be in bed, and the position should often be changed so as to prevent hypostatic congestion. The room should be well ventilated, but without draughts, and the temperature kept at 65° F. both night and day. In the early stages the air may be moistened by a steam kettle, but the use of a tent is generally to be avoided. Poultices are now less generally employed than formerly, especially for children, and a light pneumonia jacket of Gamgee tissue is usually preferred. The diet should be restricted to fluids and semi-solids, as in pneumonia. Stimulants may be given early if the pulse becomes weak, in doses of 10 drops of brandy every 2 hours to infants, and quantities up to 4 or 6 ounces in the 24 hours to old people. The dry, distressing cough at the onset may be loosened by giving a simple alkaline febrifuge mixture, such as liq. ammon. acetat. min. 120, pot. citrat. grs. 10, sod. bicarb. grs. 10, with flavouring agents, such as syrup of tolu and chloroform water. Later, ammon. carb. and tinct. ipecac. may be given, but large doses of expectorants are to be avoided because of their irritant effect on the stomach. Opiates should not be administered except as tinct. opii camphorata or possibly Dover's powder in the early stages. In infants they should not be given at all.

When in infants or children, the bronchi are becoming blocked by the secretion within them, as evidenced by increasing dyspnœa, an emetic should be given. For this purpose tinct. ipecac. or ammon. carb. in emetic doses is the most effective. In old people, ammon. carb. may be given in milk in doses of grs. 10 two or three times a day, and energetic counter-irritation applied to the bases by means of turpentine stupes, dry cupping or strong liniments.

Strychnine either by the mouth or hypodermically is strongly recommended in cases in which the respiratory centre shows signs of failure. It may be pushed, if necessary, to the point of producing slight muscular twitchings. Nikethamide (coramine) or camphor injections and cardiac tonics may be given under the same conditions as in lobar pneumonia. The administration of warmed oxygen may give relief to dyspnœa and distress.

In cases in which resolution is delayed the question of vaccine therapy may be considered. It seems sometimes to be of distinct value.

c. Inhalation, Aspiration and Deglutition Broncho-pneumonia

Acute broncho-pneumonic processes may be caused by the inhalation or aspiration of fluid or solid particles, derived from the upper air-passages or from other parts of the lung. To this form the name of aspiration, or inhalation pneumonia is applied. When from any cause food particles are drawn into the bronchi and broncho-pneumonia results, the condition is referred to as deglutition pneumonia. The resultant processes are similar, and are in effect analogous to those caused by other septic or infected foreign bodies inhaled into the bronchi.

Ætiology.—These conditions may occur at any age, but are more common in adult life. They result from septic processes in the mouth, naso-pharynx, larynx or trachea, and from any morbid state leading to anæsthesia of the pharynx, or to difficulty in deglutition. They occur in association with ulcerating growths of the mouth, tongue, tonsil, pharynx or larynx, and after operations for these conditions or upon the nose and throat, including tracheotomy. Aspiration broncho-pneumonia may also result from vomiting during or after the administration of an anæsthetic. Carcinoma of the œsophagus eroding the trachea may be a cause. Diphtheritic or other forms of paralysis, coma from any cause, especially cerebral vascular lesions and uræmia, may lead to the passage of food particles into the air-passages. Other cerebral lesions, such as abscess or tumour and bulbar paralysis, can also produce the same condition. Infected material may be aspirated from diseased to healthy parts of the lung, as in hæmoptysis, abscess, gangrene and bronchiectasis, or after rupture of an empyema into a bronchus.

Pathology.—Any material reaching the air-passages in this manner is certain to be laden with infective micro-organisms, which may induce bronchitis and broncho-pneumonia. Since pyogenic organisms are often present, suppuration is frequent and single or multiple abscesses result, or even gangrene. If the pleura becomes involved, empyema may develop.

Symptoms.—These are in general similar to those of secondary broncho-pneumonia and are superadded to those of the primary condition. There is generally high temperature, sometimes with rigors, cough and expectoration which is occasionally offensive. It may be mixed with food material and with blood. The physical signs are those of bronchitis and widespread broncho-pneumonia.

Complications and Sequelæ.—These are somewhat similar to those of other inhaled foreign bodies, and comprise abscess, gangrene and empyema.

Course.—The course is generally short, owing to the severity of the process and the gravity of the primary cause. In the comparatively rare cases that recover the course may be severe and protracted.

Prognosis.—From the nature of the primary condition and the intensity of the resulting broncho-pneumonia, this is usually grave.

Treatment.—Prophylactic.—The utmost care should be paid to the toilet of the mouth and pharynx in disease of, or operations upon, these parts. In paralysed or unconscious patients it may be necessary to resort to nasal feeding. In hæmoptysis or bronchiectasis the patient should lie rather on the affected side.

The treatment of the developed condition can be only palliative or

symptomatic in many cases. In most instances the general treatment is similar to that of secondary broncho-pneumonia.

d. Tuberculous Broncho-pneumonia

This constitutes one form of pulmonary tuberculosis (see Acute Caseous Tuberculosis, p. 1191).

PNEUMONITIS

Definition.—A localised or disseminated inflammatory process involving the whole texture of the lung and bronchial structures in the areas affected.

Ætiology.—Any severe septic infection of the bronchi or lungs may proceed to pneumonitis. The commonest infecting agents are streptococci, especially the hæmolytic and anærobic varieties. The fusi-spirochætal organisms may also cause it. Pneumococci alone seldom lead to pneumonitis, though they may be found in association with other organisms. Pneumonitis is chiefly met with in later adult life, and more in the male sex. It may be produced by the aspiration of foreign bodies. It sometimes occurs in association with bronchiectasis and may be one of the conditions associated with the febrile attacks occurring in that condition.

Pathology.—The affected area is deeply congested, solid and airless. The bronchi may exude pus. Softening is frequent, leading to the formation of one or more abscesses. Empyema may occur as a sequel or complication.

Symptoms.—The onset is usually acute and the general clinical features are identical with those of severe broncho-pneumonia. There is usually troublesome cough, with more or less copious mucopurulent expectoration. Dyspnœa and cyanosis may be marked. There is marked prostration and the patient is almost always gravely ill. The physical signs are usually those of localised pneumonia or broncho-pneumonia. The blood picture is similar to that of abscess of the lung—a leucocytosis with polymorphonuclear preponderance.

Diagnosis is generally established by X-ray examination, showing diffuse dense areas of consolidation, often progressing to abscess formation. The areas may be multiple and the process may spread widely.

Prognosis.—The prognosis is in the main serious, and depends to some extent upon the cause. Many cases, however, recover under treatment either with or without abscess formation.

Treatment is in the first instance that of broncho-pneumonia. When abscess formation occurs, postural drainage, adapted to the situation of the abscess or abscesses, should at once be adopted.

A *simple pneumonitis* has been described in children by Gill. The symptoms are cough, anorexia and loss of weight. On physical examination one or more areas of impaired percussion note with a few râles are found. Radiological examination reveals opacities in the corresponding situations. These symptoms and signs usually clear up in a few days without treatment.

R. A. Young.
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DISEASES OF THE PLEURA

PLEURISY

Pleurisy or pleuritis is an inflammation of the pleural membrane covering the lung, or of its parietal reflexions.

An ætiological classification, based on the bacteriological findings, would be the most satisfactory one, but is at present impracticable, chiefly owing to the difficulty of establishing the bacteria concerned in many cases. The classification usually adopted depends upon the effects produced. If the process leads only to fibrinous deposit it is described as *dry pleurisy*. If, in addition, much serous fluid is poured out, the condition of *pleurisy with effusion* results, while if pus-formation occurs, the affection is described as *purulent pleurisy* or *empyema*.

It is, however, important to recognise that, although such a classification is convenient from a clinical standpoint, the three conditions are in reality only stages or degrees in the pleural response to irritative or noxious agents. The form occurring in any given case depends upon the nature of the cause, the extent of the infection and the degree of resistance possessed by the individual affected. Further, pleural inflammations may be primary or secondary to local disease or to blood infection, and they may be acute or chronic in course.

A.—ACUTE DRY PLEURISY (ACUTE FIBRINOUS OR PLASTIC PLEURISY)

Ætiology.—This affection may be primary or secondary, the latter being much more common. Even in many cases of so-called idiopathic or primary pleurisy, the condition is in reality secondary to latent or unrecognised disease of the lung or adjacent structures.

Primary dry pleurisy.—Predisposing causes include occupation and climate. Exposure to sudden changes of weather or cold winds, and the necessity of remaining in wet or damp clothing, favour its onset. It is commoner in men, particularly in those of poor physique. It may occur at any age, but is most frequently seen between the ages of 20 and 40 years. Chill seems to be common as a determining cause. It is now certain that the great majority of cases are due to the tubercle bacillus, and that chill or injury is simply concerned in lowering resistance and thus promoting activity of the bacillus It is possible that some cases may be due to acute rheumatism.

Secondary dry pleurisy.—Dry pleurisy is a frequent complication or concomitant of many diseases of the lungs, notably of pulmonary tuberculosis in any form. It is almost invariably present in lobar pneumonia. It occurs in association with pulmonary collapse, interstitial pulmonary fibrosis, bronchiectasis, abscess, gangrene, infarcts and new growths of the lung. Injuries of the chest-wall, disease of the ribs, chronic nephritis, septicæmia or pyæmia may all be complicated by acute dry pleurisy.

Pathology.—The inflamed area is often localised, but the process may be

widespread or even involve the whole pleural surface. Either the visceral or parietal layer may be first affected, but as a rule both become involved. There is at first hyperæmia with exudation of serum into the subpleural connective tissue. The pleura then appears slightly dull or matt, instead of shiny. Further exudation leads to the deposit of fibrin on the roughened pleural surfaces in the form of a thin false membrane, which often presents a rough or even shaggy appearance. This membrane consists of fibrin entangling leucocytes, a few red blood corpuscles and desquamated epithelial cells.

During the process of resolution, localised adhesions commonly form, but this is not invariable, and a patch of thickening without adhesion may be the ultimate result.

Symptoms.—The onset is usually sudden with acute pain in the side, often described by the patient as a "stitch." Occasionally a sense of malaise may precede the development of the pain by a few hours or even days, but this is not the rule. The pain is aggravated by deep inspiration, by coughing or even by movement. Cough is generally an early symptom, and it is characteristically short, dry, ineffective and distressing. The temperature is usually raised, but, as a rule, only to 100° or 101° F., and some cases are practically apyrexial. In secondary pleurisy these symptoms are added to those of the primary condition.

The decubitus is variable. The patient may lie on the affected side, but in some cases this aggravates the pain, and it is more comfortable to lie on the back or slightly turned towards the sound side. There is diminished movement on the affected side, and breathing may be rapid, although not dyspnœic. On palpation, vocal fremitus is unaffected, but local tenderness is sometimes elicited, and occasionally a friction fremitus may be felt. The breath-sounds are generally unaltered, but they may be short or jerky in the neighbourhood of the lesion. The characteristic sign of dry pleurisy is the friction rub. This is typically a creaking, rubbing or leathery sound heard towards the end of inspiration and sometimes at the beginning of expiration. In the early stages there may be fine crepitant friction sounds only at the end of inspiration. These are very similar in character to intrapulmonary crepitations and can only be distinguished by their association with local pain, and by being unaltered by cough. Pleural friction sounds may be localised to a small area, and may not be present with every respiration. They may sometimes be brought out again after disappearance by moving the arm, or by taking a deep breath. The voice-sounds are not altered.

Complications and Sequelæ.—Dry pleurisy may proceed to effusion, or may lead to pleural adhesion, and this in turn may result in interstitial pulmonary fibrosis. The most common sequel is pulmonary tuberculosis, sometimes after an interval of years, the explanation being that the original pleurisy is frequently tuberculous. Aching pain in the side with some dyspnœa may be a temporary sequel of dry pleurisy.

Course.—The temperature usually subsides in 2 or 3 days, the pain in the side and cough disappear, and convalescence is rapid, unless effusion occurs.

Diagnosis.—The differentiation of dry pleurisy from the other causes of pain produced in, or referred to, the chest-wall is not always easy and

requires careful observation of the case. The distinction is important, since an erroneous diagnosis of pleurisy may arouse a suspicion of tuberculosis in subsequent febrile diseases. In the conditions comprised in the term pleurodynia, which include fibrositis of the intercostal muscles and membranes, the pain is increased by deep inspiration, by other muscular movements, and by local pressure, but there is no rise of temperature and pleural friction is not present. In intercostal neuralgia, the pain follows the course of the nerve and is often periodic in character. It may be influenced by movement, but is less affected by respiration than that of pleurisy. There may be tenderness and hyperalgesia over the points of exit of the posterior primary, lateral or anterior cutaneous branches of the nerve affected. Similar manifestations may occur at the onset of acute posterior ganglionitis or herpes zoster. Other conditions inducing pain referred to the chest-wall are tumours or aneurysm pressing on the intercostal nerves, malignant disease of the spinal cord or of its membranes, and caries of the vertebræ. Where the pain lasts more than a few days, and no friction is heard, these conditions should be borne in mind.

Occasionally adventitious sounds of extra-pleural origin may give rise to some difficulty. Contraction of the muscles of the chest may cause a muscular "susurrus"; grating sounds may be produced in the shoulder-joint or in the fascial planes of the back muscles. The origin of these sounds can usually be determined by causing the patient to cease breathing while carrying out movements of the shoulder or back muscles. Occasionally true friction sounds may have a cardiac rhythm as well as a respiratory one, when the area of pleura involved is near the pericardium. It is then referred to as pleuro-pericardial friction.

Having established the evidence of dry pleurisy, a careful search should be made for some primary condition before regarding the case as one of simple primary dry pleurisy. Pulmonary tuberculosis, pneumonia, bronchiectasis and the other causes mentioned above should be considered and excluded.

Prognosis.—The immediate prognosis is good, but as has been mentioned already, the condition may be of tuberculous origin, and eventually be followed by active disease of the lung.

Treatment.—The patient should be kept in bed, no matter how mild the attack. The diet should be fluid or semi-fluid, especially if more than a moderate degree of fever occurs. The pain can often be relieved by strapping the affected side. Strips of adhesive plaster are applied from the sternum to the vertebræ, beginning from below and working upwards. Occasionally this fails to afford relief and may even induce dyspnœa. As alternatives, a local application of tincture or ointment of iodine, a mustard leaf, capsicum ointment or small flying blisters may be employed. Leeches may also give relief in severe cases. Sometimes the pain is so intense that a small injection of heroin or morphine is necessary. A small artificial pneumothorax has been suggested as a means of separating the inflamed surfaces and giving relief to the pain in severe cases. A dose of Dover's powder is useful in the early stage to ensure a night's rest. The irritative cough is often relieved by strapping, and a sedative linctus or lozenge may be a comfort to the patient. An aperient is usually advisable. As a rule no other drugs are necessary, but in cases suspected to be due to rheumatism, salicylates and alkalis should

be administered. Convalescence is usually rapid, but the patient should not be allowed to resume work until fully restored to health, and if a tuberculous origin is suspected prolonged treatment on sanatorium lines should be advised.

Certain localisations of dry pleurisy require separate notice. These are the diaphragmatic and interlobar forms.

Diaphragmatic Acute Dry Pleurisy

Ætiology.—This affection may occur primarily under conditions similar to those causing dry pleurisy in other parts; not infrequently it is secondary to pathological changes in the abdomen. Thus hepatic cirrhosis, perihepatitis, perisplenitis, perinephric suppuration or peritonitis may lead to a spread of infection through the diaphragm to the adjacent pleura. It may also occur as a localised variety of secondary dry pleurisy, when the primary lesion is situated near the base of the lungs.

Symptoms.—Pain is usually very severe and may be referred to the shoulder or to the abdomen. The former is caused by nociceptive impulses ascending the phrenic nerve to its origin in the third to the fifth cervical segments of the spinal cord, leading to pain and hyperæsthesia referred to the cutaneous area of distribution of the fourth cervical root, at the summit of the shoulder. The abdominal pain is in the epigastric and hypochondriac regions, and in addition there is a localised tender spot, known as the "bouton diaphragmatique" of Guéneau de Mussy. This is situated in the subcostal plane, about 2 inches from the mid-line. The diaphragm is nearly motionless on the affected side, and there is often some rigidity of the corresponding upper abdominal muscles. Hiccough may be a noticeable and troublesome symptom. The diaphragm, being nearly fixed in the inspiratory position, may cause a slight downward displacement of the liver if the pleurisy is on the right side. A pleural friction rub is rarely heard, the only abnormal signs commonly present being diminution of air entry, and possibly slight dullness over the corresponding lower lobe of the lung.

Diagnosis.—This is often difficult, owing to the fact that the severity of the symptoms and their localisation frequently suggest the occurrence of some acute abdominal catastrophe such as perforation of a hollow viscus. The abdomen should be most carefully examined in every case. The history, the collapsed state of the patient and the evidence of free gas in the peritoneal cavity in perforation may assist in distinguishing between these conditions.

Treatment.—This is similar to that of simple dry pleurisy elsewhere, save that morphine should be withheld until the diagnosis is conclusively established.

Interlobar Dry Pleurisy

Just as inflammation may be limited to the diaphragmatic portion of the pleura, so the membrane in the cleft between two lobes of the lung may be alone affected. This does not give rise to definite symptoms and signs by which it can be diagnosed during life, though its effects are not infrequently seen in X-ray films. It is frequently discovered on autopsy, but is generally secondary to pulmonary tuberculosis or pneumonia, and there is usually

evidence of pleurisy elsewhere. It only assumes clinical importance when followed by effusion, and this condition is considered later.

B.—CHRONIC DRY PLEURISY

Under this heading a variety of conditions are included. Strictly it should be restricted to those rare cases, probably usually tuberculous in origin, in which the signs of dry pleurisy persist for long periods, or recur at frequent intervals. In such cases coarse dry friction may be heard over large areas of one lung, often with little or no accompanying pain.

Pleural adhesion and thickening are usually included in the group of chronic dry pleurisies. There may be no symptoms, or at most slight dyspnœa on exertion, with aching or pain on straining, or on lifting weights. Signs suggesting adhesion are local flattening and limitation of movement of the chest-wall. Litten's sign is also absent or diminished when the adhesion is basic, that is, the shadow cast by the movement of the diaphragm, best seen in the region of the seventh and eighth ribs in the anterior and mid-axillary lines, is not present or is much restricted. The vocal fremitus may be diminished and the percussion note impaired. The breath-sounds are often slightly weaker, and the voice-sounds may be diminished over the area where the thickening or adhesion exists.

Chronic diaphragmatic pleurisy or adhesion may give rise to a group of symptoms simulating chronic gastric ulcer. There is pain in the hypochondrium extending through to the back and aggravated by food. Radiographic examination may be of value in demonstrating limitation of movement of one cupola of the diaphragm, together with an angularity due to alteration of its normal contour. Investigation of the gastric functions may also prove of value in diagnosis.

The treatment of chronic dry pleurisy is mainly symptomatic.

C.—PLEURISY WITH EFFUSION

Many cases of pleurisy, possibly the majority, proceed to effusion. The effusion is usually serous in character, but may be hæmorrhagic. Inflammatory effusions must be distinguished from passive transudates, which will be considered separately under the heading of hydrothorax.

Sero-fibrinous Pleurisy

Ætiology.—This is in the main identical with that of dry pleurisy, of which it is, in effect, a later stage. It has now been established that the majority of cases of sero-fibrinous pleurisy are due to the tubercle bacillus. The evidence on which this conclusion has been arrived at is—(1) the subsequent history of the cases shows that a considerable proportion develop active lung signs within 5 years; (2) the cytological and bacteriological examination of the exudate; (3) post-mortem examination of fatal cases; (4) the results of tuberculin reactions.

Other conditions which may give rise to serous effusions are lobar and lobular pneumonia, pulmonary infarcts and new growth. It may also occur

in the course of generalised infections such as the enteric group, acute rheumatism, and septicæmia due to streptococci or staphylococci. In most of these conditions the exudate often becomes purulent. Inflammatory serous effusion may also occur as a complication of severe anæmias, leukæmia, chronic nephritis, injury to the chest-wall and inflammatory conditions below the diaphragm or in the pericardium. It is also a common feature of polyorrhomenitis.

Pathology.—The affection commences with dry pleurisy, spreading over the visceral and parietal pleura, the fibrinous exudate soon forming a thick rough layer on the surface. Further exudation of fluid occurs and accumulates in the pleural cavity, the lung collapsing *pari passu* to accommodate it. Owing to the hilar attachment of the lung, it retracts upwards and inwards, allowing the fluid to accumulate at the bases and in the axillary region, where it reaches its highest level, unless previously existing adhesions prevent it. The lung retracts in this way owing to its elasticity, until the pleural negative pressure is completely abolished. In like manner the mediastinal contents, including the heart, are displaced away from the affected side. If fluid continues to be effused after the lung has retracted to the full extent, and after the negative pressure has become abolished, a positive pressure is produced. The lung is now compressed, and the diaphragm with the liver and spleen are pushed down, while the mediastinal structures are now displaced further towards the sound side. In long-standing cases, the lung may undergo the change known as carnification, as the result of the compression apneumatosis. The lung appears dark red or slaty grey in colour, is firm, airless and heavier than water. If old adhesions are present, the effused fluid may be loculated and the collapse of the lung may be only partial.

If there is much positive pressure collateral hyperæmia of the sound lung may result and progress to œdema. The fluid in the pleural cavity is pale and clear; it often coagulates after withdrawal. Its characters are further described on page 1252. The quantity may amount to as much as 5 or 6 pints.

Symptoms.—The onset is usually similar to that of dry pleurisy, but the constitutional symptoms are often more marked. There may be an initial rigor, but as a rule pain and dry cough are the earliest symptoms. The fever is of moderate degree, although it may reach 103° F. or more. When effusion develops the pain is often relieved owing to the separation of the inflamed pleural surfaces. If a large quantity of fluid is poured out rapidly, distress of another kind becomes apparent, namely dyspnœa caused by the mechanical effects of the fluid, collapsing the lung and dislocating the mediastinum. In more slowly developing effusions there may be little or no dyspnœa, except on exertion. Expectoration is not common, unless there is co-existent pulmonary disease, or unless œdema of the sound lung develops.

The patient often lies on the affected side or may be propped up in bed. Cyanosis is not a marked feature even in large effusions, unless there is collateral hyperæmia of the sound side. There is generally some prominence on the side of the effusion, but the intercostal spaces are rarely bulged. Movement is restricted or absent in the lower part of the chest on the affected side, although with a moderate effusion the apical region may still expand. The cardiac pulsations may be seen in an abnormal position, the impulse being displaced away from the side of the fluid. In left-sided effusions, the

absent, but the position of the cardiac impulse is generally of decisive importance. In malignant disease and aneurysm, careful observation should afford diagnostic indications, such as glandular enlargement or abnormal pulsation, and in both instances the X-rays may establish the diagnosis. Malignant disease of the pleura may first show itself as a pleural effusion; the tendency to recur after tapping, the presence of blood in the effusion, and the onset of emaciation may help to suggest the cause. In massive collapse there is, as a rule, but little difficulty, owing to the displacement of the cardiac impulse to the affected side. In pericardial effusion the shape of the cardiac dullness may be suggestive, and the dislocation of the impulse may indicate the real condition; moreover, the dullness over the lung behind is rarely of extreme degree unless pleural effusion coexists. In any doubtful case, examination by the X-rays is desirable, since it may give valuable aid in diagnosis. The shadow of serous fluid is generally dense, but does not obscure the rib shadows completely. The upper level is curved and shifts to some extent with the position of the patient. It merges into the shadow of the collapsed lung above. The diaphragm is immobile on the affected side. A further aid to diagnosis consists in exploratory puncture, which has the advantage of establishing the nature of the fluid as well as its presence. The technique of puncture is similar to that of paracentesis described on pages 1253, 1254, save that a 5 or 10 c.c. syringe with a needle long enough to enter the pleura is used instead of an aspirator. The preliminary local anæsthesia by novocain or some similar preparation, with or without adrenaline, should be employed in every case, not only to avoid pain but also to obviate the risk, remote though it be, of pleural shock. Serous pleural fluid of inflammatory origin varies in colour from pale greenish yellow to brown. The specific gravity is usually 1018 or over. Protein is present as serum albumin, serum globulin and fibrinogen, the total quantity being, as a rule, over 4 per cent. The fluid generally clots spontaneously after withdrawal. The cytology of the fluid is varied, showing lymphocytes, polymorphonuclear cells, erythrocytes and altered endothelial cells in varying proportions. A marked preponderance of lymphocytes is very suggestive of a tuberculous origin, while the presence of large numbers of polymorphonuclear cells is usually an indication of some other infection, generally by a pyogenic organism. In rare cases large numbers of eosinophils have been found. The origin of these cases of so-called "eosinophil pleurisy" is at present doubtful. Cultural examination of tuberculous fluid usually proves sterile unless Loewenstein's medium is used, but in fluid from other causes the infecting organism can often be grown. To establish the tuberculous nature of a pleural fluid, inoculation of 15 c.c. of the fluid into a guinea-pig may be tried. Other methods formerly employed were examination of the centrifugate from the fluid, and Jousset's "inoscopy," which consists in examination of the clots derived from the fluid after they have been submitted to artificial gastric digestion. These two methods, however, fail in many cases. The methods of differentiation of an inflammatory exudate from a passive transudate are given on page 1259.

Prognosis.—The immediate prognosis is good, although with large effusions of 4 pints or more, sudden death sometimes occurs from acute œdema of the lungs, cardiac failure or embolism. The ultimate result depends on the cause. In non-tuberculous effusions, recovery may be complete, save for

pleural adhesion, or they may progress to empyema. In tuberculous effusions arrest may remain complete, but, as already stated, a considerable proportion of the cases develop active pulmonary disease in after years.

Treatment.—The patient should be kept in bed in an airy and well-ventilated room until the temperature is normal. Fluid should be restricted, and the diet may be salt-free with advantage. The administration of diuretics, diaphoretics and saline or mercurial aperients may assist in the disappearance of the exudate. The use of iodide of potassium has been recommended, but it is of doubtful value in these cases. The application of counter-irritants to the chest-wall in the form of iodine or of fly blisters is often helpful. A sedative lozenge or linctus may be given for the irritating cough present in the early stage. Exploratory puncture is generally advisable to permit the examination of the fluid. Opinions differ somewhat as to the indications for paracentesis, which, however, is nowadays performed earlier and more frequently than was formerly the case. It is unnecessary in cases in which absorption of the fluid is apparent within 10 days. The following conditions may be considered to suggest its employment: (1) if the effusion is large and causing positive pressure, as shown by dullness up to the clavicle, marked dyspnœa, downward displacement of the liver or spleen, and collateral hyperæmia of the sound lung; (2) if absorption is slow, the fluid remaining at the same level for a fortnight or more; (3) if acute œdema with albuminous expectoration occurs; (4) in cases of bilateral effusion with increasing dyspnœa, the side with the larger effusion may be aspirated. Paracentesis can be performed in various ways. The simplest method is that of siphonage; a long rubber tube filled with sterile saline solution is attached to a trocar and cannula, which are passed into the pleural cavity and the fluid is siphoned into a receptacle at a lower level. This method has the great advantages that the degree of suction employed is under control, and the lung expands gradually as the fluid is withdrawn. It is often difficult to remove a large quantity of fluid by this means, and it fails in loculated effusion. Aspiration is more generally effective, and may be carried out either by Dieulafoy's pump and two-way tap, Martin's syringe, or by Potain's apparatus. With these methods it is impossible to withdraw all the fluid, and removal with air replacement is now often practised with advantage. For this purpose an aspirator and an apparatus like that used in the induction of artificial pneumothorax are required. This method permits of almost complete removal of the fluid, prevents cough and discomfort, lessens the tendency to recurrence of the effusion and promotes expansion of the lung. In performing aspiration the patient should sit up in bed, or lie slightly turned on the unaffected side, and the area for operation should be painted with iodine. The skin and muscles down to the pleura should be anæsthetised with procaine (novocain) or other local anæsthetic, and a small incision made through the skin, though this is not essential in the case of a small instrument. The trocar and cannula are then pushed carefully into the pleural cavity just above a rib to avoid puncturing the intercostal artery. The sites chosen depend on the situation of the fluid, but the most convenient are in the sixth space in the mid-axilla, the seventh space in the posterior axillary line, or the eighth space just below the angle of the scapula. Aspiration should be stopped if cough occurs, if pain is severe, or if albuminous expectoration with signs of œdema supervenes. In rare cases sudden death from pleural

shock has occurred. The risk of this may be obviated by careful local anæsthesia down to the pleural level. Other risks are due to faulty technique, and comprise entrance of air into the pleural cavity from wrong connection of the apparatus or from wounding the lung, and infection of the pleural cavity from failure in the aseptic preparations leading to empyema. Air replacement seems preferable, since it allows of almost complete removal of the fluid.

After absorption or removal of the fluid, re-expansion of the lung may be promoted by the use of Wolff's bottles, or by appropriate breathing exercises. With the former, fluid is forced from one bottle to another by blowing. In the latter, the patient takes deep inspirations while seated in a chair with the sound side partly fixed. In all cases in which a tuberculous origin is proved or suspected, prolonged convalescent treatment on sanatorium principles is advisable.

Anomalous Pleural Effusions

Two unusual forms of pleural effusion require brief mention—they are encysted interlobar and encysted diaphragmatic sero-fibrinous pleurisy. The former of these can only be recognised by X-ray examination followed by exploratory puncture. Encysted diaphragmatic sero-fibrinous pleurisy is rare, but a case has been erroneously recorded as acute serous mediastinitis. This condition is simply one of pleural effusion localised to the space between the mediastinal pleura, the diaphragm and the lung. Both of these conditions, if diagnosed, should be treated on general principles. The effusion may absorb spontaneously, but if not, aspiration may be necessary.

Purulent Pleurisy (Empyema)

In this condition the pleural exudate becomes purulent. The fluid may be turbid and the presence of pus be apparent only on microscopical examination, or it may consist of typical pus.

Ætiology.—Predisposing Causes.—Empyema is common in children under 10 years of age, and the younger the child the greater the probability that any effusion will be purulent. In adults it is commonest between the ages of 20 and 40 years, probably owing to the heavy incidence of pneumonia in this age period. Debility, exposure and alcoholism may promote its occurrence. Purulent pleurisy is but rarely primary, except in the form due to the pneumococcus. It is most commonly due to extension from the lungs, especially from lobar pneumonia and from broncho-pneumonia. Other pulmonary causes are tuberculosis, bronchiectasis, abscess, gangrene, new-growth, or septic infarcts in infective endocarditis. It may develop in association with mediastinal lesions, such as suppurating glands, ulcerating carcinoma of the œsophagus, or from suppuration in the neck tracking downwards. Infection of the pleura may occur through the chest-wall as a result of gunshot wounds, stabs, fractured ribs, and faulty technique in aspiration of a serous effusion. The primary source of pleural infection may be in the abdomen, the organisms passing through the diaphragm from a perinephric, subphrenic, or hepatic abscess, or from localised or generalised peritonitis consequent on rupture of a gastric or duodenal ulcer. The involve-

ment of the pleura may take place through the blood in septicæmia, suppurating gunshot wounds, compound fracture of the femur, and in otitis media with lateral sinus thrombosis.

Empyema may develop during the course of many of the acute specific fevers, such as scarlet fever, variola, measles and the enteric group; but since in these conditions it is usually secondary to broncho-pneumonia, it belongs strictly to the pulmonary group.

Exciting Causes.—The organisms most frequently found in purulent effusions are the pneumococcus and the streptococcus, the former accounting for more than half of the cases. Occasionally the pus proves to be sterile on culture; such cases are generally the result of the tubercle bacillus or of a pneumococcus which has died out. Other organisms less commonly found are staphylococci, Pfeiffer's *H. influenzæ*, the *B. typhosus*, and Friedländer's pneumo-bacillus. Streptothrix organisms are occasionally found (see Actinomycosis), also various saprophytes and anaerobic organisms, especially in fetid empyema.

Pathology.—The initial stages are similar to those of dry and sero-fibrinous pleurisy, but when the effusion occurs, it proves to be rich in leucocytes undergoing disintegration and to contain the infecting organism. It varies from a slightly turbid semi-translucent fluid to typical thick, opaque, creamy pus. Its colour ranges from pale amber to green or greenish grey. It may be odourless or extremely offensive. In cases secondary to gangrene, it may be thin and horribly fetid, while in pneumococcal cases it may be curdy and of slightly sweetish odour. The pleura is covered with a more or less thick layer of sodden fibrinous exudate. In cases due to the pneumococcus this false membrane may be very thick. Adhesions form quickly, leading to encystment or loculation of the pus. Such adhesions also prevent the lung from expanding after evacuation of the pus, with the result that the lung becomes carnified and interstitial fibrosis results. There is usually some enlargement of the bronchial glands. In long-standing cases there may be lardaceous disease of the liver, spleen, kidneys and intestines.

Symptoms.—Since empyema usually develops in the course of, or as a sequel of, some other disease, its symptoms are often masked by those of the primary disease and may easily be overlooked. In primary cases due to the pneumococcus the onset may be like that of pneumonia; in the more common secondary cases a rise of temperature and increase of signs develop after the crisis. In general it may be stated that the symptoms are similar to those of sero-fibrinous pleurisy, but more severe. There is more malaise, and the patient may appear profoundly ill, with rigors, sweats and dyspnœa. The temperature ranges higher, up to 103° F. or more, and may be of septic type with marked daily remissions, but some cases are almost if not completely apyrexial. The signs are usually exactly similar to those of sero-fibrinous effusion, but in some instances special features may be noticed. In neglected or prolonged cases, wasting, pallor and cachexia become marked. The intercostal spaces may be found to bulge, and œdema of the chest-wall is sometimes apparent. The pus may track through an intercostal space, generally the fifth near the nipple, producing a fluctuating swelling known as a pointing empyema or *empyema necessitatis*. This may infiltrate the skin and simulate a superficial abscess. The swelling so induced may pulsate, especially if it be on the left side—a condition known as pulsating empyema.

Pulsation communicated to the chest-wall may also be observed in some large left-sided purulent effusions without local swelling. The displacement of the liver or spleen may be greater than with serous effusions, probably owing to the higher specific gravity of the pus, which is usually 1030 or more, and to the associated inflammation of the diaphragm. In fetid empyema, the breath and sputum may be offensive, even before rupture into a bronchus occurs. Clubbing of the fingers and toes occurs in empyema of long standing, but may develop in a few weeks. Blood examination reveals a moderate leucocytosis in the majority of cases. Counts of 15,000 leucocytes per cubic millimetre are usual, and in some instances figures up to 100,000 per cubic millimetre are obtained.

Complications and Sequelæ.—In neglected or untreated empyema the pus may track and become discharged in various directions. The commonest is rupture through the visceral pleura into the lung and discharge through a bronchus. This may lead to sudden death from suffocation; on the other hand, in small empyemata spontaneous cure may follow this evacuation of the pus. In other instances pyo-pneumothorax results, and occasionally gangrene of the lung. A second method of discharge is through the chest-wall, as an *empyema necessitatis*. Perforation may occur into the pericardium, or into the œsophagus with the formation of a pleuro-œsophageal fistula. The diaphragm may be perforated with the production of a subphrenic, lumbar or psoas abscess, while in other cases general peritonitis may ensue.

The pericardium or the mediastinum may become infected without perforation; similarly costal periostitis may be induced. After spontaneous or operative evacuation the cavity may fail to close and a chronic empyema or sinus result. This is generally due to the lung being permanently collapsed and adherent, and therefore failing to expand. It subsequently undergoes fibrosis with development of bronchiectasis. Sometimes the failure to close may be due to the nature of the infection, particularly when it is due to tuberculosis or actinomycosis (streptotricosis). In other cases it may be due to a bronchial fistula, or to a foreign body in the pleura. Generalised infection is rare, but cerebral abscess, probably of embolic origin, is not very uncommon, especially in cases due to streptococci. Chronic pulmonary osteo-arthropathy is an occasional complication, and lardaceous disease sometimes occurs in cases of long duration. Diphtheritic infection of the wound, with subsequent paralysis, has been recorded after operation, more especially in cases secondary to influenzal broncho-pneumonia.

The sequelæ in untreated cases may be fistulæ, such as pleuro-bronchial, pleuro-œsophageal or external, and various deformities. The sequelæ after operation may be a small amount of pleural thickening, or if operation were delayed, and re-expansion incomplete, there is falling-in of the chest, with flattening, dropping of the shoulder and secondary scoliosis. In other cases, as mentioned above, a chronic sinus may result.

Course.—Apart from spontaneous cure of small empyemata by inspissation of the pus, or discharge through a bronchus or through the chest-wall, death generally occurs in untreated cases within a month or two. As in sero-fibrinous pleurisy, sudden death may occur. Death may occur after operation, from exhaustion or from cerebral abscess.

Diagnosis.—The diagnosis of empyema involves two distinct problems—one, the recognition of the presence of fluid in the pleura, which is considered

under sero-fibrinous pleurisy; the other, the demonstration of its purulent character. In spite of the more severe symptoms, empyema is frequently overlooked even by physicians of experience. This is partly due to the fact that its development may be insidious, with signs increasing but little from day to day, and partly to its secondary character, its onset being obscured by the clinical features of the primary condition. It is wise, therefore, to suspect its existence in any case of obscure lung signs, especially those with dullness, cardiac displacement and fever, consequent on pneumonia of any variety.

There are a few special difficulties as compared with sero-fibrinous effusion which merit separate mention. The first of these is subphrenic abscess. This may lead to immobilisation of the diaphragm on one side, more commonly the right, and cause collapse of the lung and even pleural effusion. The difficulty is the greater when the subphrenic abscess contains gas as well as pus. The history, the absence of displacement of the heart's impulse, and examination by X-rays may all assist, but the differentiation is often extremely difficult.

Empyema necessitatis may simulate a tuberculous or other abscess about a rib, and empyema should always be suspected in any case of local fluctuating swelling about the chest-wall. Pulsating empyema requires to be distinguished from aortic aneurysm; the pulsation is less forcible and little, if at all, expansile in the former. The cardiac displacement, the X-rays and cautious exploratory puncture, enable the nature of the condition to be recognised.

In any case in which empyema is suspected three examinations may be undertaken—a blood count, radiographic methods, and exploratory puncture. A polymorphonuclear leucocytosis of 15,000 per cubic millimetre and over, a dense shadow in the radiogram obscuring the ribs, together with cardiac displacement may be very suggestive, while puncture may prove the presence of pus. Sometimes, however, puncture may fail, although pus is present. This may be due to the pus being too thick to pass through the needle, to loculation of the pus, or to wrong choice of the site for puncture. In this case, if the other signs indicate pus, repeated punctures with a larger needle under anæsthesia are called for, but it is well to be prepared to proceed to operation if pus is found.

Prognosis.—This depends upon the primary cause, the method of treatment adopted, and the duration of the effusion before the operation. The most favourable forms are those due to the pneumococcus, which are recognised and treated at an early stage. In neglected cases, with profound toxæmia, with gangrene of the lung or lardaceous disease, the outlook is extremely grave. Empyemata due to streptococcal infection are serious, unless recognised early; similarly with cases of fetid empyema due to anaerobic infections. Infected hæmothorax consequent on gunshot wounds of the chest is of grave prognosis. The outlook is serious in cases of bilateral empyema, but recovery may follow successive evacuation of the pus on the two sides.

Treatment.—This consists in the evacuation of the pus by operation as soon as the diagnosis is established in pneumococcal cases. In those of streptococcal origin, operation should not be resorted to while the fluid is of thin sero-purulent character, but should be postponed until it is definitely purulent. Premature operation in streptococcal cases has been shown by

the American Empyema Commission to be a very dangerous procedure, since the fluid is not shut off by adhesions and operation may lead to open pneumothorax, with flapping mediastinum. At this stage, the condition is described as pyothorax. A preliminary aspiration is of advantage in large effusions, and may be repeated in streptococcal effusions until they are ready for operation. The operation consists in drainage by removal of a piece of rib subperiosteally and incision of the parietal pleura. For the operation a general anæsthetic may be given, but it is now almost always carried out under local anæsthesia; but if the patient's condition renders this undesirable, an incision under local anæsthesia may be made through an intercostal space and a drainage tube inserted, a piece of rib being removed later under general or local anæsthesia when improvement has occurred. The wound is dressed at least daily and the drainage tube sterilised, every endeavour being made to prevent secondary infections. To this end the pleural cavity may be irrigated daily by the Carrel-Dakin method, or washed out with some antiseptic such as flavine or brilliant green. To avoid pleural shock, free exit for the wash fluids must be ensured. By some authorities pneumococcal empyemata, particularly in young children, are treated by repeated aspirations or by siphon drainage. If the pus is thick and difficult to evacuate, incision of the pleura with immediate suture is performed, any reaccumulation being treated by aspiration with or without oxygen replacement. If, however, toxic symptoms persist, drainage should be effectively established at once.

In cases of chronic empyema, or of sinus failing to close, the question of some plastic operation must be considered. Various forms of operation have been devised, involving removal of portions of many ribs, and the decortication operation of Fowler and Delorme. The general condition of the patient must be carefully considered before these operations are advised. In some cases an autogenous vaccine seems to be of value, if drainage is satisfactory.

Special varieties of Empyema.—Certain special localisations of purulent pleurisy require separate consideration, notably apical, interlobar and diaphragmatic empyemata.

Apical empyema.—This condition is usually secondary to apical pneumonia, less commonly to pulmonary tuberculosis. It is one variety of encysted empyema, the pus being shut off from the rest of the pleural cavity by adhesions. The symptoms and signs are not characteristic, but may be suggestive. There is very marked dullness below the clavicle, not transgressing the middle line, with weak or absent breath-sounds, and possibly some indications of mediastinal displacement. Diagnosis can, as a rule, be established only by the X-rays and exploratory puncture, the latter being carried out in the second space near the mid-clavicular line. The treatment consists in drainage by incision as near the lower limit of the effusion as possible.

Interlobar empyema.—Pus collecting between two of the lobes may be difficult to differentiate from pulmonary abscess, gangrene and bronchiectasis. It is often not diagnosed until rupture into a bronchus draws attention to it. The signs are generally most marked in the axilla or near the angle of the scapula. They are often slight until rupture occurs, and even then there may be only a small area of dullness in the line of an interlobar fissure, with distant or weak bronchial breathing and a few râles. The pus expectorated may be fetid, and the patient's breath may be offensive a few days

before rupture occurs. The condition simulates abscess of the lung, and may be almost impossible to differentiate from that affection. Examination by the X-rays gives the greatest help in the diagnosis. Recent observations suggest that interlobar empyema is much less common than abscess. The treatment is identical with that for pulmonary abscess.

Diaphragmatic empyema.—The pus is usually encysted, and may be so deeply situated as to give but few signs. The initial symptoms are generally severe, being those of diaphragmatic pleurisy, but hiccough is often a troublesome feature. When pus forms, there may be marked constitutional symptoms, and obscure signs may develop, such as dullness, at a point just above the base behind, with weak or distant bronchial breathing. With such a history and obscure basic signs, especially when they occur after an attack of pneumonia, the use of the X-rays and of the exploring needle should not be neglected. In cases not recognised and treated, rupture into a bronchus or through the diaphragm may occur. The treatment is similar to that for ordinary empyema.

HYDROTHORAX (DROPSY OR HYDROPS OF THE PLEURA)

Hydrothorax is the name applied to a collection of clear fluid in the pleural cavity, the result of passive transudation from the capillaries.

Ætiology.—The commonest cause of hydrothorax is cardiac failure from chronic valvular disease, or from myocardial weakness or degeneration. It occurs in acute and chronic renal disease, under conditions similar to those leading to dropsy in these affections. It is sometimes found in severe anæmias, especially pernicious anæmia. Obstruction to the azygos veins may lead to transudation into one pleural cavity or into both. This obstruction may be induced by pressure from without by a mediastinal or pulmonary new-growth, or by internal causes such as thrombosis.

Pathology.—The pathology of hydrothorax is that of dropsy elsewhere. It is produced by mechanical or chemical conditions affecting the blood flow through the capillaries, and it must be distinguished carefully from inflammatory effusion. There is a difference in the composition as well as in the origin of the two kinds of pleural fluid. The characters of inflammatory effusions have been described under pleurisy with effusion. The fluid in hydrothorax is pale yellow in colour, and the specific gravity is 1015 to 1010 or less. It is clear and does not clot after removal. There is little protein, often not more than 1 per cent., but transudates due to local obstruction may contain as much as 3 per cent. The cellular elements are scanty, although some endothelial cells may be present, often united together in plaques. The fluid may be definitely bloodstained, when it is described as hæmo-hydrothorax.

Hydrothorax is usually bilateral in cases due to cardiac or renal disease, but in the former there is often more fluid on the right side, or the fluid may be confined to that side. The explanation of this is somewhat obscure. It has been suggested that it is due to pressure or traction on the vena azygos major by the enlarged right heart, but according to Fetterolf and Landis, a more likely explanation is pressure of the distended right auricle upon the pulmonary veins. Fluid may also collect in greater quantity on the side

upon which the patient lies most constantly. In cases with unilateral pleural adhesion, œdema of the lung may occur on that side, while hydrothorax occurs upon the other.

Symptoms.—The symptoms of hydrothorax are generally overshadowed by those of the condition causing it, but the occurrence of dyspnœa and cyanosis in any case of cardiac or renal disease should suggest careful examination of the bases of the lungs. In the absence of inflammatory complications the condition is afebrile. The signs are identical with those of sero-fibrinous pleurisy, save that no friction sounds are audible at any stage. It is, however, more difficult to assess the significance of displacement of the cardiac impulse, owing to the increased size of the heart in the cases of cardiac origin.

Diagnosis.—This depends upon the presence of signs of fluid in the pleura in association with cardiac or renal disease, with absence of fever, and also upon the characters of the fluid withdrawn by puncture or aspiration.

Treatment.—Removal of the fluid may give great relief. It may be necessary to repeat the operation, since the fluid often reaccumulates. The treatment of the primary condition should also be carried out.

HÆMORRHAGIC PLEURAL EFFUSIONS

All fluids poured out into the pleura contain a certain number of red blood corpuscles. It is only when a number sufficient to give a definite red colour are present, that the fluid is regarded as hæmorrhagic.

For convenience of description three forms may be differentiated—(1) Hæmorrhagic pleurisy or hæmo-serothorax; (2) hæmo-hydrothorax; and (3) hæmothorax.

1. HÆMORRHAGIC PLEURISY.

This is simply a pleurisy with effusion, in which the exudate is blood-stained.

Ætiology.—The usual causes are malignant disease of the lungs, pleura or mediastinum, and rarely tuberculosis of the lung and pleura. Hæmorrhagic pleurisy may occur in association with hepatic cirrhosis, but in this case it is often the result of a terminal tuberculosis. It occurs less frequently in association with blood diseases, such as purpura, and with the malignant or hæmorrhagic varieties of acute infectious fevers such as scarlet fever and small-pox, and occasionally with lobar pneumonia. Sometimes in tapping a sero-fibrinous effusion for the second-time, it is found that the fluid, which was originally clear, is now blood-stained. This is not necessarily an indication of increase in the severity of the process, but may be due to injury of a blood vessel at the first operation.

Symptoms.—The symptoms and signs are identical with those of serous effusion, and the hæmorrhagic character can only be recognised by withdrawal of the fluid. An interesting point is the frequency of excess of eosinophils in these effusions. Diagnosis and treatment are the same as for sero-fibrinous pleurisy.

2. HÆMO-HYDROTHORAX.

This condition has been referred to under hydrothorax. It consists simply in blood-staining of a passive transudate into the pleura.

3. Hæmothorax.

Hæmorrhage into the pleural cavity is the result of injury or disease of the vessels of the lung, mediastinum or chest-wall.

Ætiology.—The chief causes are injury, such as penetrating chest wounds or fracture of the ribs, rupture of an aneurysm, and erosion by new-growth. Experience of the traumatic group has been largely increased during the War of 1914–1918. Hæmothorax was noted in about 70 per cent. of chest wounds.

Pathology.—The effused blood generally comes from the lung vessels, less commonly from the intercostals. It is "whipped" by the movements of the heart and lungs, with the result that fibrin is deposited in layers upon the diaphragmatic pleura, and the parts of the visceral and parietal pleura in contact with the blood. The fluid remaining in the pleura or withdrawn by aspiration is largely defibrinated and therefore does not clot, unless a secondary pleurisy develops.

The lower lobe of the lung on the affected side becomes collapsed and eventually carnified, unless absorption occurs or unless the blood is aspirated. The upper lobe may show some compensatory emphysema, and adhesions may form in the pleura, separating it from the hæmothorax below. When secondary infections of the bronchi or lungs occur, such as bronchitis or broncho-pneumonia, the collapsed lower lobe is not affected.

Symptoms.—The symptoms of hæmorrhage into the pleura from medical causes, such as rupture of an aneurysm or erosion of a large vessel, are collapse and rapid death. When due to disease or injury of an intercostal vessel, they may be insidious and slowly ingravescent until dyspnœa, restlessness and the other indications of internal hæmorrhage develop. When due to injury, similar symptoms occur, but may be masked or overshadowed by the shock, hæmoptysis and cough, induced by the wound of the lung or chest-wall. The signs are those of pleural effusion, but in traumatic cases certain special features may be mentioned. There is a great tendency to retraction of the chest-wall on the affected side, and the cupola of the diaphragm on this side is displaced upwards. This is thought to be due to an active lobar collapse of the lung, the lung contracting, not as the result of the pressure of the effusion, but in consequence of a nervous protective reflex initiated by the trauma. Vocal fremitus is usually diminished or absent. The breath-sounds over the effusion are frequently bronchial, and well-marked bronchophony and pectoriloquy may be present.

Complications and Sequelæ.—The most serious complication is infection of the effusion. This is generally due to organisms introduced at the time of the wound, either by the missile or by portions of the clothing or skin carried in with it. Aerobic organisms, such as a streptococcus, or anaerobic ones, as the *B. aerogenes encapsulatus* or the *B. sporogenes*, may be present. A hæmo-pneumothorax may develop, the gas entering the pleural cavity from the wound in the lung or through the chest-wall. Gas may also be formed by gas-producing infecting organisms in the effusion. Massive collapse may occur in the contralateral lung, or other complications may arise, such as bronchitis, broncho-pneumonia, lobar pneumonia or œdema of the lungs. If the effusion is small and not infected, there are usually no permanent after-effects. In severe cases sequelæ, similar to those of sero-fibrinous pleurisy and empyema, may result.

Course.—This depends upon the cause and size of the hæmothorax, and upon the mode of treatment adopted. It is profoundly and gravely influenced by infection of the effused blood. A small sterile hæmothorax is generally absorbed spontaneously. Medium-sized and large effusions may not disappear unless aspirated. An infected hæmothorax will inevitably prove fatal, if untreated.

Diagnosis.—Hæmothorax should be suspected when basic dullness develops shortly after a gunshot wound of the chest. The mistake that is most likely to be made in such cases is to confuse hæmothorax with lobar pneumonia. The cardiac displacement and the diminution of vocal fremitus over the dull area are the most valuable diagnostic signs. An active lobar collapse is distinguished by the fact that the heart is displaced towards the affected side. The X-rays afford valuable confirmatory evidence in most cases. When air and blood are present, the upper border of the dark area in the radiogram has a sharply defined edge, while the pleural cavity above is very translucent. The use of the exploring syringe generally settles the diagnosis, except in certain cases in which, although a considerable quantity of blood may be present, none is removed by aspiration owing to the needle entering the clot.

Prognosis.—In a sterile hæmothorax due to a chest wound the prognosis is good. If infection occurs, the prognosis depends upon the promptitude with which this condition is recognised and radically treated, although in very acute infections death may occur in 2 or 3 days despite immediate operation.

Treatment.—A small sterile hæmothorax may be left untouched. In medium and large-sized effusions, recovery is accelerated by aspiration. The possible danger of renewal of the hæmorrhage, as the result of lowering the pleural tension by this operation, is very slight, and negligible if it is delayed until 2 or 3 days after the wound. If the temperature in a case of hæmothorax rises suddenly to 102° or 103° F. in the evening, it is criminal to wait until the next morning to see what will happen. A specimen of fluid should be withdrawn and examined microscopically. Direct films may occasionally reveal the presence of organisms, but the important point to determine is the number of polymorphonuclear leucocytes present. When these are numerous, operation should be performed without awaiting the findings of aerobic and anaerobic cultures. A rib should be resected as in empyema, and the blood and clots should be removed from the pleural cavity and drainage established.

CHYLOUS AND OTHER MILKY EFFUSIONS

A milky fluid is occasionally obtained on exploratory puncture or aspiration of a pleural effusion. It is usual to classify such fluids into three groups —(1) Chylothorax; (2) chyliform fluid; (3) pseudo-chylous fluid.

1. CHYLOTHORAX.

There is an effusion of pure chyle or of serous fluid mixed with chyle.

Ætiology.—Chylothorax is usually the result of injury to, or disease of, the thoracic duct. The traumatic form is, as a rule, secondary to crushing of the chest-wall with fracture of the ribs. In disease, the thoracic duct may be pressed on by a malignant growth or enlarged mediastinal glands,

or the flow may be obstructed by thrombosis of the left subclavian vein. Invasion of the thoracic duct by the *Filaria sanguinis hominis* may also be a cause.

Pathology.—The fluid in true chylothorax is a milky emulsion which remains so on standing, although a cream-like layer may form at the top. With the microscope fat globules can be seen, which stain with the usual fat stains and can be dissolved by ether.

2. CHYLIFORM EFFUSION.

In this condition fat is present, but it is not derived from the thoracic duct.

Ætiology.—Chyliform effusions occur in association with tuberculosis and carcinoma of the pleura or lung.

Pathology.—The fluid is milky and contains fat in emulsion, although in smaller quantities than in true chylothorax. On microscopical examination large fat droplets are seen, and numbers of cells, chiefly leucocytes undergoing fatty degeneration. It is, no doubt, from this process that the fat is derived.

3. PSEUDO-CHYLOUS EFFUSION.

In this condition the milky appearance is not due to fat, but to other particles causing opalescence.

Ætiology.—Pseudo-chylous fluid has been observed in chronic effusions due to heart disease, nephritis, tuberculosis and malignant disease.

Pathology.—The milky appearance is due in some cases to a lecithin globulin complex (Wallis and Schölberg). Other rare causes of milky, opalescent or turbid effusions are the presence of particles of calcium phosphate, cholesterin or filarial embryos. These fluids are distinguished from the above by showing a deposit on standing.

Diagnosis.—This can only be established by microscopical and chemical investigation of the fluid withdrawn.

Prognosis.—The prognosis in most cases of milky effusions is serious, owing to the gravity of the primary condition. Some traumatic cases of true chylothorax recover.

Treatment.—The treatment is for the most part symptomatic and dependent upon the primary condition. In true chylothorax, removal of the fluid is inadvisable, unless it is causing dyspnœa or other symptoms of pressure. The drain of fat caused by it is a serious loss, especially if the tapping has to be repeated frequently. In chyliform effusions there is a marked tendency to recur after removal of the fluid.

PNEUMOTHORAX

In pneumothorax, gas, usually air, collects between the layers of the pleura, which now becomes a real instead of a potential space. When serous fluid is present as well as the gas it is called a hydro-pneumothorax, when pus forms the condition is described as pyo-pneumothorax, and when blood and gas collect the term hæmo-pneumothorax is applied.

Ætiology.—Pneumothorax is more common in men, and the maximum incidence is between the ages of 20 and 40 years, but it may occur at any age. The air may gain access to the pleural cavity in the following ways: (1) Through the visceral pleura from the air in the lungs and bronchi. This

accounts for 95 per cent. or more of the cases. The commonest cause is rupture of a subpleural tuberculous focus. Rupture of an empyema into the lung is the next most frequent antecedent condition. Other pulmonary causes are gangrene, abscess, septic infarct, bronchiectasis, new growths of lung and pleura, and rupture of an emphysematous bulla or vesicle. Puncture of the lung during paracentesis, or rupture of the pleura over a diseased focus, owing to rapid expansion of the lung during the same operation, may lead to pneumothorax. A broken rib perforating the lung can also induce it. It may occur as a complication of artificial pneumothorax treatment, especially when this is bilateral. (2) Through the chest-wall, as a result of penetrating wounds, although pneumothorax is not a common result. An abscess in the chest-wall opening externally and through the pleura, or a discharging *empyema necessitatis*, may be a cause. (3) Through the mediastinum, by ulceration of an œsophageal growth, or of a diseased bronchial gland, into the pleura, or from accidental perforation of the œsophagus during the passage of an œsophageal bougie or œsophagoscope. (4) Through the diaphragm, from some hollow abdominal viscus, *e.g.* an ulcer of the stomach or duodenum may perforate, leading to the formation of a subphrenic abscess, which in turn may break through the diaphragm into the pleura. (5) Gas may accumulate in the pleura owing to infection of a pleural effusion by gas-producing organisms. This is generally the result of wounds.

Sudden spontaneous pneumothorax in apparently healthy persons occurs more commonly than is generally recognised, and is described as simple or benign pneumothorax. The causation is obscure. Rupture of an emphysematous vesicle, or of a latent or healed tuberculous focus, have both been suggested, though the latter is improbable, since there is usually no pleural reaction and the lung rapidly re-expands. In rare cases, however, the collapse of the lung is long-continued and may even be permanent. The condition is often recurrent, and is exceptionally bilateral. Complete recovery is the rule. Very occasionally spontaneous hæmopneumothorax occurs. The symptoms are usually more severe and a fatal result is not uncommon.

The exciting cause of pneumothorax may be physical strain or violent cough, but many cases occur while the patient is at rest or even during sleep.

Pathology.—The entrance of air between the layers of the pleura disturbs the pressure relations in the thorax in a similar way to the effusion of fluid; but whereas with the latter the process is gradual, in pneumothorax it is rapid, and the pressure within the pleura changes from the normal negative figure to that of the atmosphere, often in a few minutes or less. Mediastinal and cardiac displacements like those in pleural effusion, and due to the unopposed traction of the sound side, are also rapidly produced. The subsequent pressure relations depend upon the source of the air. If the opening is in the chest wall, the intrapleural pressure will remain equal to the atmospheric, until the opening becomes closed. If the opening is in the lung, three varieties occur: (1) the opening may remain patent, when the pressure keeps at atmospheric level; (2) the opening may be valvular, permitting the entry of air into the pleura during inspiration, but preventing its escape during expiration. In this case the pressure in the pleura rises above that of the atmosphere, and

the air within it is at a positive pressure, causing further cardiac and mediastinal dislocation with downward displacement of the diaphragm; (3) the opening becomes sealed, and there is a condition of closed pneumothorax in which the pressure may be equal to, greater or less than, that of the atmosphere.

To demonstrate pneumothorax post mortem, the autopsy may be performed under water, or a flap being made of the skin and muscles at the side of the thorax, this may be filled with water before puncturing the intercostal spaces. A third method is to dissect carefully through an intercostal space down to the pleura, when the lung will be found to be retracted. On opening the thorax the appearances vary. If the air entering the pleura is sterile, no inflammatory reaction occurs, the pleura remains shiny and no fluid is formed, the condition being one of simple pneumothorax. More commonly, bacteria gain access to the pleura with the ingoing air, or subsequently through the opening when this remains patent, with the result that either serous fluid or pus collects. In the former case the condition is described as hydro-pneumothorax, in the latter as pyo-pneumothorax. The appearances of the pleural membrane are similar to those found in serofibrinous pleurisy and empyema respectively. The lung is collapsed in every case of pneumothorax, and lies retracted towards the hilum and the spine. In tuberculous disease, a caseous focus or small cavity just under the pleura is the most frequent cause. The perforation may be a large circular rent or a small pin-hole, but multiple apertures may occasionally be present. The opening can usually be found, even if small, by submerging the lung under water while pumping air down the trachea. When extensive adhesions are present, the collapse of the lung is largely prevented and the pneumothorax is only partial. In such cases the perforation is frequently near the adhesions. In cases where fluid is present the diaphragm may be seen to be depressed on the affected side and its curvature lessened or reversed.

Symptoms.—In a considerable proportion of cases the onset is sudden and the condition of the patient becomes alarming at once. On the other hand, pneumothorax may develop insidiously, with surprisingly little pain and dyspnœa, so that its occurrence may be overlooked or only discovered on routine physical and radiographic examination, including a lateral film. This is more likely to be the case when perforation occurs in a lung extensively diseased or when the aperture is small, and the leak of air is slow. In the acute form of onset the patient is seized with severe pain while coughing or engaged in some extra exertion. There is often a feeling of "something having given way," and at once great dyspnœa develops with signs of collapse and severe mental anguish. The patient may appear blue, cold and clammy, breathing is rapid and shallow, the temperature falls to subnormal, the heart beats quickly and the pulse becomes small and weak. The patient is often restless, very alarmed and unable or afraid to speak. Occasionally death occurs in a few minutes. As a rule, the more acute symptoms subside in a few hours, but the temperature rises and the rapid breathing usually persists for some time. On examination the patient will usually be found sitting up, with alæ nasi working and with rapid shallow breathing. The affected side is almost or entirely immobile and is usually bulged. The displacement of the cardiac impulse towards the unaffected side is generally

obvious, and is almost immediate. Palpation confirms the absence of movement, and vocal fremitus is found to be absent, except where the collapsed lung remains in contact with the chest-wall, over which area it may be increased. The exact position of the cardiac impulse should also be determined: in right-sided cases it will be found in the left axillary region; in left-sided cases it may be under or beyond the right nipple. The liver may be felt much depressed in right-sided cases. The note over a pneumothorax is characteristically tympanitic or drum-like, as a rule, but in cases with positive pressure the tympany may be flat and muffled. The tympanitic area should be carefully mapped out; it may be found to extend across the middle line, or to encroach on or obliterate the liver dullness in right-sided cases. On the other hand, in partial pneumothorax, the area may be small and easily escape recognition. In left-sided cases, the cardiac dullness may be completely wanting on that side, and a dull area found to the right of the sternum. This may give a useful hint as to the diagnosis. On auscultation, the breath-sounds are often absent, but they may be present at the apex, although weak. In other instances distant tubular breathing may be audible from the collapsed lung; in cases with a large patent opening hollow cavernous breathing may be heard. The voice sounds have an amphoric or metallic quality, and an amphoric echo may occur with any sound produced near the pneumothorax. Metallic tinkling is an example of this, being the quality conveyed to râles or other adventitious sounds produced in breathing. The bell sound or *bruit d'airain* is a valuable sign, but is not invariably present. It is elicited by listening to the chest, near where a coin is placed flat on it and tapped with another. A similar sound may be heard with the stethoscope on flicking over a pneumothorax with the thumb and finger. The displacement of the heart can be confirmed by auscultation, and the heart sounds may be found to have a metallic character. When air and fluid are present in the pleura the signs are somewhat modified. There is dullness at the base, which shifts its level with the patient's movements, the upper limit being straight, in contrast with the curved line of ordinary effusions. A marked succussion splash may be heard and felt on shaking the patient, or the patient may demonstrate the sign by a sudden shake or jerk.

Complications and Sequelæ.—Cardiac failure and rapid death occur occasionally. The chief complications are due to the entry of infective organisms into the pleura, leading to pleurisy and the effusion of sero-fibrinous fluid or pus. The sequelæ may be pleural adhesions in cases that recover, especially if effusion occurs. There may be also permanent collapse of the lung in long-standing cases, and in pyo-pneumothorax a fistula, either pleuro-pulmonary or external, may remain in spite of treatment.

Diagnosis.—The recognition of a large or of a complete pneumothorax is easy as a rule, the signs being characteristic. When a large quantity of fluid is present in an open pneumothorax, the presence of air may not be recognised until after paracentesis or X-ray examination. The latter gives information of the greatest value and sometimes demonstrates the presence of local pneumothorax where it has not been suspected. The air space between the lung and pleura shows most clearly in radiograms, and if fluid is present as well, the dead level of the upper border of the shadow, varying with position, is most characteristic. Diagnosis is more difficult in cases where

pleural adhesions exist, or where the pneumothorax is small and localised, especially if X-ray examination is not available. The following conditions may give rise to difficulty and should be considered in doubtful cases. (1) Total excavation of a lung, or a large pulmonary cavity, in either of which the note may be boxy or even tympanitic, the breath sounds amphoric and the râles metallic or tinkling, while the coin sound may be obtained. These conditions can usually be distinguished by the flattening and retraction of the chest-wall over them, and the absence of cardiac displacement, or if it exists, the traction of the heart towards the affected side by fibrosis. (2) Advanced emphysema, with complete obliteration of the cardiac dullness, may be confused with pneumothorax. Large bilateral bullæ may be mistaken for bilateral pneumothorax. (3) Massive collapse of one lung, with compensatory emphysema of the opposite side, may also be mistaken for it. In both these conditions careful examination will establish the real nature. (4) A subphrenic abscess containing gas (subphrenic pyo-pneumothorax); in this condition the diaphragm may be displaced upwards, and the note over the lower ribs may be markedly tympanitic. These signs are more suggestive when right-sided. Succussion splash and bell sound may be elicited. The heart, if displaced, is pushed upwards. The history of previous abdominal disease may be helpful, and a radiogram may give conclusive evidence of the subphrenic origin of the condition. (5) A hernia of the stomach or bowel through the diaphragm, or eventration of the diaphragm, all rare conditions, may simulate pneumothorax, but in all there is generally abdominal flattening and little if any cardiac displacement. Examination by X-rays after an opaque meal will, as a rule, establish the nature of the condition.

Course and Prognosis.—The course and prognosis of pneumothorax are profoundly influenced by the cause. In cases due to rupture of an emphysematous vesicle, or of a small localised healed tuberculous focus, where the pleura remains sterile and the aperture of entry closes, the air is usually completely absorbed in a few weeks and recovery is often complete. In tuberculous cases with moderate disease, in which the pleura remains sterile, pneumothorax may exert a favourable influence. In tuberculous cases with extensive disease, the pleura becomes infected and death usually results in a few weeks or months, although with judicious treatment life may be prolonged for years in some cases especially where surgical treatment such as thoracoplasty becomes practicable. In pneumothorax secondary to some grave disease, such as carcinoma or gangrene, the course is brief and the prognosis is grave in the extreme. In cases secondary to empyema, surgical treatment may be followed by complete recovery.

Treatment.—The indications in cases of acute onset are to relieve the patient's pain, distress and anxiety, and to lessen the intrapleural pressure, if this is positive. A hypodermic injection of morphine, gr. $\frac{1}{4}$ for an adult, with oxygen inhalations if necessary, may achieve the first of these. If dyspnœa is extreme and the cardiac displacement marked, a trocar or large hypodermic needle should be inserted through an intercostal space to allow air to escape. An initial pneumothorax needle, with a long rubber tube, the end of which is placed under water, is the safest. This simple manœuvre may be the means of saving the patient's life in valvular pneumothorax, as well as of relieving distress. In less urgent cases, the pressure may be taken with

an artificial pneumothorax apparatus, and if the pressure be positive, as much air as is necessary may be removed by its means. In simple cases no other treatment may be required, although the puncture may need to be repeated. In cases of recurrent spontaneous pneumothorax or of persistent valvular pneumothorax, it is sometimes helpful to induce an aseptic pleurisy by means of various injections into the pleural space. Chandler recommends for this purpose a solution of gomenol in olive oil. At first 2 c.c. of a 2 per cent. solution are used, and this is gradually increased if necessary up to 20 c.c. of a 20 per cent. solution. A strong solution of dextrose is sometimes employed for the same purpose. In valvular pneumothorax Chandler has used a self-retaining catheter with a valvular attachment allowing the escape of air. If serous fluid or pus collect in the pleura, they may be withdrawn, preferably by siphonage, and in this case, as also with removal of air, too much should not be withdrawn in the early stages, as a slight positive pressure may assist in closure of the aperture in the lung, whereas a negative pressure may open it, after it has begun to close.

The question of operation in pneumothorax may be difficult to decide. In cases secondary to empyema, resection of a part of a rib and drainage often lead to satisfactory results. In cases of moderately severe or advanced tuberculosis with pyo-pneumothorax, open operation is generally contra-indicated, and if performed is liable to result in a permanently open pneumothorax. It is preferable to remove fluid from time to time by aspiration, with or without air replacement until thoracoplasty can be considered. Pleural wash-outs with mild antiseptics, such as weak methylene blue, flavine, or eusol, are often useful. This method of aspiration sometimes seems to assist the lung to re-expand. Surgical methods sometimes employed are intercostal tube drainage with slight suction, water-sealed drainage, or thoracoplasty in several stages.

HYDATID DISEASE OF THE PLEURA

Hydatid cysts may be primary in the pleura, or may encroach on the pleura, although originating in adjacent structures such as the lung, liver, spleen or mediastinum (parapleural hydatid).

Ætiology and Pathology.—Primary pleural hydatid is rare, but secondary invasion of the pleura is more common. In this situation the cyst may reach a large size, even 5 or 6 inches in diameter, before rupture occurs. As in other situations, a fibrous capsule is developed around the cyst from the irritative changes set up in the adjacent tissue. Contrary to what might be expected, extensive pleurisy is uncommon until rupture or suppuration of the cyst occurs. The pressure of the cyst may lead to collapse of the contiguous areas of lung and to displacement of the heart and mediastinum.

Symptoms.—These may be absent until the cyst is large enough to produce pressure symptoms, such as dyspnœa, pain and cough. There is little or no expectoration, unless rupture into a bronchus occurs, when cyst wall, daughter cysts and hooklets may be found in it. There is no fever until suppuration occurs. The signs are practically identical with those of encysted pleural effusion.

Complications and Sequelæ.—Rupture and suppuration are the two most important complications. Rupture may take place into the lung, into the pleural cavity, rarely through the chest-wall or through the diaphragm. At the time of rupture an urticarial rash may develop. This is probably an anaphylactic phenomenon associated with the liberation of toxin present in the fluid of the cyst.

Course.—The cyst may be latent for some time, but it usually enlarges and produces increasing symptoms, culminating in rupture or suppuration. Very rarely death of the cyst occurs and its contents become inspissated.

Diagnosis.—The symptoms and signs generally suggest either pleural effusion or new growth, and hydatid disease may not be suspected. Obscure basic signs, in patients coming from countries where hydatid disease is common, should suggest special methods of investigation as to the possibility of its presence. Should it be suspected, aspiration is to be deprecated, unless all preparations for immediate operation are complete, if the diagnosis is confirmed. These methods comprise X-ray examination, an eosinophil blood count, the complement-fixation test, the Casoni intra-dermic test and the precipitin reaction (see page 315).

Prognosis.—If untreated until rupture occurs, a fatal result is most probable. If diagnosed and treated before rupture, the prognosis is not unfavourable.

Treatment.—The former practice of aspiration and injection with formalin or iodine, although sometimes successful, is dangerous and should be discarded. Exposure of the cyst by thoracotomy, and its removal entire, should be the treatment if practicable, or if too large, it may be aspirated and then dissected out.

STREPTOTRICHOSIS (ACTINOMYCOSIS) OF THE PLEURA

The general characters of infection by the streptothrix group of organisms, and the special features of the pulmonary localisations have been described. It is possible, although improbable, that the infection may be primarily pleural, more commonly clinical manifestations may point to a predominating involvement of the pleura, although the primary lesions may be in adjacent structures, such as the lungs, mediastinum or liver.

Symptoms.—The symptoms and signs in such cases are those of empyema, but the following points are noteworthy. The empyema is rarely large, and it commonly extends through the chest-wall, producing a local swelling which soon discharges through the skin if untreated, causing a suggestive infiltration and puckering around. Exploratory puncture of a streptothrical empyema often fails, since the grumous caseous material it contains may be too thick to pass through the needle.

Diagnosis.—The characteristic " sulphur granules " in the pus may draw attention to the real nature of the condition, but they are not always present. Direct films should always be made from the pus obtained from empyemata. The streptothrix may be found in this way, when culture fails. If the lung is involved as well as the pleura, the organism may be found in the expectora-

tion, and the nature of the pleural condition may thus be established before operation.

Prognosis.—Some cases respond to treatment, but prognosis is in general unfavourable, death resulting from exhaustion or toxæmia due to dissemination of the disease.

Treatment.—The pultaceous pleural contents should be removed as far as possible by operation, and large doses of potassium iodide given by the mouth, increasing the quantity until 60 to 90 grains, three times a day, are given. An autogenous vaccine may be tried if the organism can be grown. A radium pack has sometimes given successful results.

SIMPLE TUMOURS OF THE PLEURA

These are very rare and are, as a rule, only discovered after death. They are almost invariably of extrapleural origin and their presence in the pleura is due to the direction taken by the growth. Lipoma of the subpleural or of the mediastinal fat may occur as small pedunculated tumours or very rarely as a large mass. They can be differentiated from tumours of the lung by X-ray examination after a diagnostic pneumothorax.

MALIGNANT TUMOURS OF THE PLEURA

Primary malignant disease of the pleura is rare, and may take the form of endothelioma, carcinoma or sarcoma. Secondary carcinoma and sarcoma are more common.

Ætiology.—Primary endothelioma of the pleura is more common in late adult life and in the male sex. Sarcoma is more likely to occur in children and in young adults. Secondary growths may occur at any age, but more commonly in later life.

Pathology.—Endothelioma of the pleura is a growth of obscure origin. It has not been conclusively established that it is derived from the pleural endothelial cells, and by some writers it is classed as a carcinoma. It is at first unilateral, but it involves the affected pleura over a wide area, sometimes universally. The membrane appears to be overlaid with an irregular, rough hard covering, sometimes nodular. In other cases there is more thickening and the condition may be localised. There is nearly always a large amount of blood-stained serous effusion. The condition may spread to the bronchial or supraclavicular glands, the lung, the spine, the diaphragm and the peritoneum.

Primary carcinoma of the pleura has also been described, but is very rare. Primary sarcoma is also extremely uncommon, but the round-celled and spindle-celled varieties may occur, and angio-sarcoma, fibro-sarcoma, myxo-sarcoma and chondro-sarcoma have all been recorded.

Secondary carcinoma and sarcoma of the pleura are relatively common, and may occur from direct *extension* in growths of the lung, bronchi and mediastinum, by *metastases* of growths in almost any distant part, or by *lymphatic permeation* in mammary carcinoma. In the last-named condition

pleural and pulmonary growths are a not infrequent form of recurrence, sometimes occurring months or years after removal of the primary growth.

Symptoms.—These are not characteristic, and increasing dyspnœa due to an accumulation of fluid may be the first indication. More commonly pain and cough, similar to those of pleurisy, may occur acutely or develop more gradually. Although afebrile as a rule, the occurrence of fever does not exclude malignant disease. Cachexia and wasting are often not marked until the condition is advanced. The signs are generally indistinguishable from those of ordinary pleural effusion, unless secondary growths become manifest in the cervical or axillary glands. Sometimes coarse dry friction may be heard, or there may be signs of pleural thickening without fluid. There is often local pain and tenderness over the chest. Exploratory puncture may demonstrate the hæmorrhagic character of the effusion. The specific gravity is generally 1018 or over, and the cytology of the fluid may be suggestive, especially if excess of endothelial cells, often aggregated into plaques, is found.

Complications.—The growth may spread to the lung and cause cough and expectoration, often blood-stained, or it may involve the chest-wall. Metastases sometimes develop along the course of the needle track after aspiration of the fluid. The secondary growths, especially those in the glands, may exert pressure, *e.g.* the axillary glands may cause œdema and swelling of the arm.

Course.—This is almost invariably progressive, the duration being rarely more than 2 years, and occasionally much less.

Diagnosis.—A chronic pleural effusion in a middle-aged man, not associated with fever, and not due to tuberculosis, should arouse suspicion of malignant disease of the lung and pleura. Evidence of fluid in one pleura, at an interval after excision of the breast for malignant disease, is very suggestive of secondary pleural growth. A hæmorrhagic effusion, not due to tuberculosis or renal disease, should also arouse suspicion of malignancy, especially if reaccumulation after tapping is rapid, and if the subsequent tappings show increasingly hæmorrhagic characters. When aspiration of a considerable quantity of fluid gives little relief to symptoms, or when irregular dull areas remain where resonance might be expected, the probability of growth must be borne in mind. Growth involving the chest-wall, or the presence of cervical or axillary glandular metastases render it certain. Radiological examination after removal of some of the fluid may show characteristic plaques on the pleura.

Prognosis.—Malignant growth of the pleura is invariably fatal unless removal is possible.

Treatment.—From the nature of the condition this can only be palliative. Analgesic drugs may be given freely for the relief of pain, morphine being reserved for the severe forms and later stages, as far as possible. Repeated tappings may be almost compulsory, if there is much distress from the reaccumulation of the fluid, but it must be remembered that in hæmorrhagic effusions the loss of blood by this means is considerable. Air replacement may sometimes give relief for a longer period than simple aspiration. In rare cases, removal by operation may be practicable if the diagnosis is made early and the growth is localised in an accessible position.

INJURY

Injury to the pleura may occur in fracture of the ribs, the fragments piercing or tearing it. Similarly in penetrating wounds of the chest, the pleura may be extensively lacerated. It may also be torn by direct violence without breaking of the ribs, and in rare cases a hernial protrusion of lung may occur, forming a small swelling in an intercostal space, protruding with inspiration and emptying with expiration.

R. A. Young.
G. E. Beaumont.

DISEASES OF THE DIAPHRAGM

SPASM OF THE DIAPHRAGM

Diaphragmatic spasm may be either clonic or tonic, the former being termed *hiccough*.

Clonic spasm.—This may be due to a variety of causes, namely: (*a*) Alimentary: From irritation of the œsophagus or stomach by pungent or irritant substances such as pepper, pickles, or tobacco. It occurs also as a symptom in gastritis, dilatation of the stomach, enteritis, intestinal obstruction, tympanites and peritonitis, and in the late stages of debilitating disease. (*b*) Nervous: as in hysteria, cerebral tumour, meningitis, hydrocephalus, epilepsy and alcoholism. It may also result from peripheral nerve irritation, in such conditions as mediastinal tumour, mediastinitis, enlarged thoracic glands, diaphragmatic pleurisy, or pericardial effusion. *Epidemic hiccough* has been regarded as a form of encephalitis lethargica. There is usually some slight pyrexia, and the condition may persist without intermission for several days. (*c*) Renal: As in chronic nephritis and uræmia.

Tonic spasm.—This may be met with in tetanus, strychnine poisoning, laryngismus stridulus, eclampsia, epilepsy and hydrophobia. If there is associated intercostal or laryngeal spasm, there is grave risk of death from asphyxia.

Treatment.—Simple hiccough may often be relieved by holding the breath, pressure on the chest, or by simple inhalations, such as of ammonia, ether, or spirits of chloroform. Hiccough due to organic disease or to peripheral irritation may only be relieved by removal of the cause. In epidemic hiccough, in obstinate cases of hiccough due to other causes and in the tonic form of spasm, various antispasmodic measures may be tried, such as trinitrin, bromides, or phenobarbitone, by the mouth; adrenaline, or adrenaline and pituitary (posterior lobe) extract, hypodermically; or the inhalation of chloroform.

DIAPHRAGMATIC PLEURISY

This condition is described on page 1247 under the heading of Pleurisy.

PARALYSIS OF THE DIAPHRAGM

Definition.—Paralysis and inactivity of either leaf of the diaphragm, or of both.

Ætiology.—Paralysis of the diaphragm may be caused by disease damaging the centre in the spinal cord, by conditions affecting the phrenic nerve in its course, or by reflex inhibition of the centre. Causes involving the centre include poliomyelitis, hæmorrhage into the spinal cord, and tumours of the spinal cord or its membranes, or of the spine itself. The phrenic nerves may be affected by diphtheritic neuritis. Either or both of the nerves may be compressed by mediastinal tumours, or by inflammatory exudates. They may be severed or injured by wounds in the neck. Evulsion or crushing of the phrenic nerve is now frequently employed therapeutically, in order to promote collapse of the base of one lung and closure of cavities in cases of tuberculosis and in bronchiectasis.

Symptoms.—Diaphragmatic paralysis results in the affected leaf of the diaphragm becoming immobile and remaining at a higher level in the thorax than normal, or showing paradoxical movement, *i.e.* ascending with inspiration. This can easily be seen on X-ray examination. Sometimes this is noted as a reversal of the ordinary abdominal movements during respiration, with the result that there is epigastric recession during inspiration.

Treatment.—This is, in general, that of the condition causing the paralysis.

HERNIA OF THE DIAPHRAGM (see p. 553, 554)

EVENTRATION OF THE DIAPHRAGM (see p. 666)

DISEASES OF THE MEDIASTINUM

The mediastinum is the interpleural space, and occupies the median part of the thorax, from the superior aperture above to the diaphragm below. Strictly speaking, any affection of any of the important structures occupying this space, such as the pericardium, heart, great vessels, air passages and the thymus, might be included under this heading. They are, however, more conveniently grouped under the various systems to which they belong, and diseases of the mediastinum are commonly restricted to conditions arising in, or affecting the connective tissue and glands found in this space.

MEDIASTINITIS

Mediastinitis, or inflammation in the mediastinal connective tissue, may be acute or chronic. In the acute forms there may be an inflammatory serous exudate causing œdema, or the inflammation may progress to abscess formation. The chronic forms are indurative or fibroid in character, although chronic abscess may occur.

Acute Simple Mediastinitis

Ætiology.—Acute mediastinitis without suppuration may result from injuries to the chest-wall or sternum, and from lacerating wounds of the œsophagus or trachea. It is sometimes secondary to inflammatory processes in the lungs, pleuræ, pericardium or peritoneum, and to periostitis of the sternum or vertebræ. Pneumonia is a not uncommon cause.

Pathology.—There is hyperæmia of the mediastinal connective tissue with inflammatory œdema. Mediastinal serous effusions have been described, but these are, without doubt, encysted pleural effusions encroaching on the mediastinum.

Symptoms.—The clinical manifestations of acute mediastinitis are vague and not characteristic. There is a mild pyrexia, the temperature reaching 99° or 100° F. Pain under the sternum may be complained of, and on auscultation over it a few fine crepitations may be heard on deep breathing, or they may occur synchronously with the heart beats.

Course.—The affection may subside or proceed to abscess formation. It may result in fibroid thickening or adhesions.

Diagnosis.—Mediastinitis is often not recognised or suspected, since it is masked or overshadowed by the clinical manifestations of the primary condition.

Treatment.—No special treatment is required, apart from that appropriate to the condition inducing it.

Acute Suppurative Mediastinitis

Ætiology.—Acute suppurative mediastinitis or mediastinal abscess is more common in males, and may occur at any age, although it is more frequently seen in early adult life than at other periods. Some cases are of traumatic origin, and follow perforating wounds or blows on the sternum, not necessarily causing fracture. Perforation or injury of the œsophagus is a comparatively frequent mode of access of pyogenic organisms to the mediastinum. This may occur from ulceration of an œsophageal new-growth, from injury due to a swallowed body such as a tooth-plate, or from the passage of an œsophagoscope or bougie. Perforation of the trachea or main bronchi by an inhaled foreign body is sometimes the cause of mediastinal suppuration. Various pulmonary conditions may lead to pyogenic infection of the mediastinum, such as pulmonary abscess or gangrene, pneumonia and bronchiectasis. Periostitis or osteomyelitis of the sternum, vertebræ or ribs, suppuration in the mediastinal glands, or tracking down of deep cervical abscesses may all lead to mediastinal abscess. Extensions of pyogenic processes from the pericardium, pleura or peritoneum may also be causes. A suppurating hydatid or dermoid cyst may rupture into the mediastinum, and, lastly, the infection is blood-borne in some cases from infective endocarditis, pyæmia, erysipelas or enteric fever. Dieulafoy pointed out that certain cases of empyema, originating near the mediastinum, may, by encroaching on this region, induce predominating mediastinal symptoms, which he described as the "mediastinal syndrome." Such cases, although abscesses in the mediastinum, are not mediastinal abscesses, but are in reality special instances of encysted empyema.

Pathology.—The suppuration may be limited to any part of the anatomical subdivisions of the mediastinum, or may spread from one compartment to another. The pus sometimes tracks in various directions, *e.g.* upwards to the neck, downwards to the abdomen, or it may point in the chest-wall. The abscess may rupture into the œsophagus, trachea, aorta, pleura or pericardium.

Symptoms.—The onset may be insidious or acute. In the latter case it may be ushered in by severe pain under the sternum, radiating to the back and shoulders. The symptoms may be divided into those due to the inflammatory process, and those resulting from the pressure exerted by the collection of pus. The former comprise malaise, fever and sometimes rigors, while blood examination may demonstrate a leucocytosis of 10,000 per c.mm. or over. The pressure symptoms vary according to the amount of pus produced and its situation. They include dyspnœa and paroxysmal or brassy cough, from compression of the vagus nerve or direct pressure on the trachea. There may also be dysphagia from obstruction of the œsophagus, and hoarseness from pressure on the left recurrent laryngeal nerve. Pressure on the spinal nerve roots, intercostal nerves, or brachial plexus may lead to severe neuralgic pains. Partial or complete obstruction of the great veins may be apparent from distension of the superficial thoracic veins or of those in the neck. Œdema of the chest-wall is sometimes seen from this cause, or it may result from the inflammatory process extending to the chest-wall. The signs in severe cases will be those caused by the pressure effects just described. The patient looks ill, distressed, dyspnœic and more or less cyanosed. The respirations may be noisy, as there is sometimes inspiratory dyspnœa with stridor, this being known as the *bruit de cornage*. The dilated veins may be apparent and the direction of the current may help to localise the seat of the obstruction. There is sometimes local redness and œdema from pointing of the abscess, near the sternum, in the neck, or in the interscapular region on either side. Palpation may reveal local tenderness and even fluctuation in any of these areas. There is often dullness over the sternum, sometimes extending to one or other side, or the dullness may be found in the interscapular region. It is said that the dullness may shift with the position of the patient in some cases. Breath sounds are distant, and weak or bronchial over the dull area, except when it is behind the sternum, when they are harsh.

Complications and Sequelæ.—The important complications are those due to rupture of the abscess. If this occurs into the lung or the œsophagus. pus is expectorated, or passes into the stomach. Gangrene of the mediastinum may follow, or death may occur from suffocation or hæmorrhage. Extension of the abscess may lead to purulent pleurisy, pericarditis or peritonitis, or to suppuration in the neck. In cases that recover, chronic mediastinitis with matting together of the mediastinal contents may be a sequel.

Course.—The disease is acute and rapidly progressive, unless relieved by operation or by spontaneous external drainage in a few fortunate cases.

Diagnosis.—The "mediastinal syndrome" of dyspnœa, stridor, paroxysmal cough, hoarseness and dysphagia with signs of pressure on arteries, veins and nerves is common to many conditions causing mediastinal pressure, notably mediastinal new-growth, enlarged mediastinal glands, aneurysm and

pericardial effusion. The differential diagnosis of these is more fully considered under mediastinal new-growth. The occurrence of fevers and rigors, the presence of a pointing swelling, and the demonstration of a leucocytosis may give strong suggestion as to the inflammatory origin of these symptoms and signs. The X-rays may reveal a localised mediastinal shadow, often non-pulsating, although it must be remembered that in rare cases a mediastinal abscess may pulsate.

Prognosis.—This is very grave, and the majority of cases die unless recognised and treated early. If gangrene develops, a fatal result is inevitable. The outlook is more hopeful when the anterior mediastinum alone is involved.

Treatment.—PROPHYLACTIC.—Foreign bodies in the œsophagus and trachea should be removed as soon and as gently as possible. The utmost care should be exercised in the passage of a bougie or the œsophagoscope in cases of œsophageal stricture.

CURATIVE.—As soon as mediastinal suppuration has been diagnosed and localised, surgical measures should be adopted. The mediastinum can be reached by resection of pieces of costal cartilage or by trephining the sternum.

CHRONIC MEDIASTINITIS

This also occurs in two forms, chronic indurative mediastinitis and chronic abscess

CHRONIC INDURATIVE MEDIASTINITIS.—This may occur as a sequel of any form of acute mediastinitis. The best known is that associated with chronic adhesive pericarditis, and usually known as chronic indurative mediastino-pericarditis (pp. 961–963). Other forms include the chronic inflammation and thickening which occur around enlarged, sclerotic and pigmented mediastinal glands, and around the same glands when affected by caseous or calcareous tuberculous lesions.

CHRONIC MEDIASTINAL ABSCESS is generally of tuberculous origin, arising from breaking down caseous bronchial or mediastinal glands, or from tuberculous disease of the spine or ribs. A chronic abscess may, however, be caused by a foreign body, such as a bullet.

Symptoms.—Simple indurative mediastinitis may give rise to practically no symptoms or signs. Chronic abscess may cause symptoms of ill-health and of mediastinal pressure, or may only become apparent when it points superficially.

Treatment.—The treatment of chronic mediastinal abscess is practically the same as that for other "cold" abscesses due to tuberculosis, incision and drainage being avoided if possible in favour of aspiration and injection of antituberculous substances. Other cases may require operation.

EMPHYSEMA OF THE MEDIASTINUM

In performing tracheotomy, the pretracheal layer of deep cervical fascia is of necessity incised. If difficulty arises in inserting the tube into the tracheal incision, air may be drawn deep to this fascia by the vigorous attempts at respiration and thus pass into the superior mediastinum, or superficial to

it into the anterior mediastinum. Rupture of the trachea, bronchi or œsophagus, or rupture of air vesicles or pulmonary lesions where the pleura is adherent, may also cause it. In acute interstitial emphysema of the lungs, the escaped air may track along to the root and reach the mediastinum.

Symptoms.—Emphysema of the mediastinum may give rise to very indefinite indications. A few fine crackling sounds may be heard on listening over the sternum, sometimes varying with respiration or with the heart movements. The percussion note over the præcordium may be hyperresonant, and the heart sounds may be distant and muffled. Small quantities of air escaped into the mediastinum can be rapidly absorbed and may not be of serious import.

Diagnosis.—This is often a matter of speculation, unless the air spreads upwards to the neck and causes superficial surgical emphysema.

Prognosis.—This depends entirely on that of the underlying cause, which is often of serious nature.

Treatment.—No special treatment is required, as a rule, apart from that of the primary condition, except that pain may necessitate the use of analgesic drugs at the onset.

ENLARGED MEDIASTINAL GLANDS

The mediastinal lymphatic glands are arranged in groups. A few small ones are found in the anterior compartment, another group is situated in the posterior mediastinum. The most important of these is the tracheobronchial group, situated around the bifurcation of the trachea and extending along the bronchi. It is enlargement of this group that most often gives clinical manifestations.

Ætiology and Pathology.—A simple inflammatory enlargement of these glands may occur in many acute affections of the bronchi and lungs, and in certain acute specific fevers, notably influenza, pertussis and measles. A more chronic enlargement, associated with indurative changes, results from chronic respiratory diseases, such as chronic bronchitis and the pneumokonioses. In the latter case, considerable pigmentary changes may be found, from deposition of the particles derived from the dusty inspired air. In town-dwellers, these glands are often grey or black in colour from deposited carbon. Tuberculosis is the commonest cause of enlargement of the mediastinal glands, particularly of the tracheo-bronchial group, those about the right bronchus being most affected as a rule. This is a frequent early localisation of tuberculous disease in children. The infection spreads from the lungs in the majority of cases (Ghon), but in some instances the path of infection is from the tonsils through the cervical lymphatics and glands, while in others the mode of entrance is from the intestines through the mesenteric glands. The lesions may be miliary tubercles, or small caseous nodules which calcify subsequently, or which may soften and lead to local spread or generalisation. In other cases a fibroid hyperplasia of the glands results.

In syphilis, mediastinal adenitis may occur in the secondary or tertiary stages. In Hodgkin's disease and in lymphatic leukæmia, the mediastinal glands may share in the general adenopathy, and in the former the condition

may be primary in these glands. Enlargement due to malignant disease is of great importance and receives separate consideration.

Symptoms.—These may be slight and escape notice, unless the enlargement is sufficient to produce pressure or irritation. Cough is the commonest symptom; it is usually dry, irritative, noisy and ineffective. It may occur in paroxysms, somewhat suggestive of those of whooping-cough. Dyspnœa and dysphagia occur only when the enlargement is considerable. Vomiting sometimes develops, probably reflexly from vagal stimulation. Pain behind the sternum or in the upper thoracic region posteriorly may be complained of. In children with tuberculous disease in these glands, there is often languor, anorexia, anæmia and wasting, sometimes with slight irregular fever and night sweats. Such symptoms in a child of 5 to 12 years of age are very suggestive. The signs are also variable and frequently inconclusive. In tuberculous cases, the appearance of the child, pale, delicate looking or sallow, with long eyelashes and fine hairy growth over the back, may also be suggestive. In glandular enlargement from any cause, there may be dilated veins over the front or back of the chest, especially in the upper part, and a " hilum dimple " has been described as appearing in the second intercostal space beside the sternum, on holding the breath at the end of inspiration. One pupil may be larger than the other, owing to sympathetic stimulation. Small areas of dullness may be found at the back, near the upper thoracic spines, or in front close to the manubrium. Breath sounds over these areas may be bronchial or harsh. Occasionally the enlarged glands impede the air entry to a lower lobe, generally the right, in which case breath sounds are notably weakened over this area, while the percussion note may be impaired. Normally, whispering pectoriloquy ceases at the seventh cervical spine; with enlarged mediastinal glands it may be heard along the middle line or close beside it, in the upper thoracic region from the first to the fifth thoracic spines. This is known as d'Espine's sign or tracheophony. It is a confirmatory sign, when other indications are present. Eustace Smith's sign is of little value. It consists in a venous hum, audible over the manubrium sterni, when the child's head is thrown back as far as possible. Occasionally pressure on the recurrent laryngeal nerve may lead to an abductor paralysis of one vocal cord. In cases of tuberculosis, syphilis, Hodgkin's disease or leukæmia, enlarged glands may be present in other parts of the body, and may thus assist in diagnosis.

Complications.—A caseous gland may ulcerate into a bronchus or into the trachea, and death has resulted from glottic impaction of a portion of the gland. Ulceration into the œsophagus has been described. Rupture into the mediastinum may lead to mediastinal abscess. Invasion of the pleura, lung or pericardium may occur, or generalisation causing widespread miliary tuberculosis.

Diagnosis.—Whenever the condition of mediastinal glandular enlargement is suspected, an X-ray examination should be made if possible. It may help to distinguish between other conditions causing mediastinal pressure, such as aneurysm, abscess and malignant growth. Unfortunately in regard to tuberculous disease, it shows best the condition of least importance, namely, the old healed calcified glands. " Soft " or " woolly " shadows are regarded as indicative of active disease, but in doubtful cases it is wise to act upon the clinical indications.

Prognosis.—This varies with the cause, being serious in Hodgkin's disease and leukæmia. In tuberculous cases, the prognosis is as a rule good, apart from complications, provided treatment is prompt and adequate.

Treatment.—In tuberculous adenitis, the general condition should be improved by every possible means. The child should be taken from school, rest and exercise are to be carefully graduated, and a liberal diet supplied, with extra milk, cream and butter. In England, the Isle of Thanet seems especially valuable in the climatic treatment of glandular tuberculosis. Cod-liver oil, malt extracts and the syrup of the iodide or phosphate of iron are useful. In afebrile cases, tuberculin cautiously given may be of value in children of 8 years or over, but it is not necessary, as a rule. If given, the initial dose should be small, $\frac{1}{500,000}$ mgrm. B.E., and the dosage gradually increased. In glandular enlargements due to syphilis, Hodgkin's disease and leukæmia, the treatment appropriate to these diseases should be employed, and symptoms due to pressure relieved as far as possible.

MEDIASTINAL TUMOURS OR NEW-GROWTHS

The mediastinum may be the seat of either simple or malignant new growths, the latter being much more common.

Simple Tumours of the Mediastinum.—These, except retrosternal goitre, rarely give rise to symptoms, and the recorded cases have, as a rule, only been discovered in the course of a routine X-ray or post-mortem examination. The chief varieties found are retrosternal goitre and persistent thymus, lipoma, fibroma, chondroma, osteo-chondroma and myoma.

Malignant Tumours of the Mediastinum.—Although it is certain that some malignant growths arise primarily in the mediastinal tissues, while others invade the mediastinum secondarily by extension or metastasis, it is often impossible, even at autopsy, to determine whether a mediastinal growth originated in the mediastinal tissues or in one of the adjacent organs, particularly the lungs and bronchi. The differentiation between primary and secondary growths is therefore less sharp than in other situations.

Sarcoma of the Mediastinum.—Recent research has proved that the majority of primary mediastinal growths are sarcomatous, but these are less common than was formerly supposed. A primary sarcoma may arise in the lymphatic glands, connective tissue, periosteum of the sternum or vertebræ, or in the remains of the thymus gland. The commonest variety is the lympho-sarcoma, but spindle-celled and chondro-sarcomata may occur. Mediastinal sarcoma is commoner in males than females; it may occur in early life, and the majority of cases occur before the age of 40 years. Oat-celled tumours invading the mediastinum and formerly regarded as lympho-sarcomata are now believed to be of bronchial origin and carcinomatous nature.

Carcinoma of the Mediastinum.—This is rare as a primary tumour. It occurs in older people. It may originate from the trachea, bronchi or œsophagus, in the remains of the thymus or in a retrosternal goitre.

Secondary Malignant Growths of the Mediastinum.—These usually result from direct extension of primary growths of the lung, bronchi, trachea, œsophagus, chest-wall or breast, but true metastases may occur from

mammary growths or from more distant primary tumours. Endothelioma has been described in the mediastinum, but is probably generally secondary to endothelioma of the pleura.

Pathology.—The morbid appearance depends upon the situation of origin, the directions of growth, and the nature of the tumour. Sarcomata are generally soft, pinkish in colour and vascular, while carcinomata are paler and firmer. There may be one large mass weighing several pounds, or there may be multiple growths. When the tumour reaches a considerable size it may infiltrate, surround, compress or displace contiguous structures. This is particularly the case in the lympho-sarcomata. The trachea, œsophagus, and large vessels may be surrounded, the pericardium and heart may be extensively infiltrated, and the nerve trunks may be enclosed and compressed. Secondary deposits are common in other glands, but not infrequently the pigmented bronchial glands may be seen entirely enclosed in growth without being infiltrated.

Symptoms.—The onset is often insidious, and the condition may not be suspected until cachexia and pressure signs develop. Malaise, weakness, shortness of breath, cough and pain are often early symptoms, which become more pronounced as the case progresses. The pressure symptoms and signs constituting the " mediastinal syndrome " comprise—

1. *Pressure on the air passages*, giving rise to dyspnœa, cough and expectoration. The dyspnœa may be inspiratory and associated with stridor, or expiratory and paroxysmal. The cough is harsh and may be " brassy " ; it is often associated with mucoid, blood-stained, or even " prune juice " sputum. Bronchiectasis may result in some cases.

2. *Pressure on or infiltration of the lung*, leading to collapse and sometimes breaking down of lung tissue. If the pleura is reached or invaded, pleural effusion, often blood-stained, may result.

3. *Pressure on arteries.*—Compression of branches of the pulmonary artery may lead to local gangrene, or in other cases the growth may ulcerate into a larger vessel and cause fatal hæmorrhage. Pressure on the subclavian artery may cause inequality of the radial pulses, and, according to Ekgren, this may only be present when the patient is lying and not when he is standing.

4. *Pressure on veins.*—Dilated tortuous veins may be seen over the front of the chest and abdomen, or in the neck. The flow of blood in these superficial veins may be reversed in direction, owing to the obstruction of the superior vena cava or its main radicles. The current then runs from above downwards, instead of from below upwards, as normally. There may be œdema of the chest-wall or of the face and neck from the same cause.

5. *Pressure on nerves.*—The vagus may be compressed, causing paroxysmal dyspnœa and cough. Laryngeal paralysis or spasm may result from involvement of the recurrent laryngeal nerve. Dilatation of the pupil, followed later by constriction, drooping of the upper lid and enophthalmos, occurs when the sympathetic is involved. Paralysis of the diaphragm on one side from compression of the phrenic nerve, and pain from involvement of the intercostal nerves, may be present.

6. *Pressure on the œsophagus* may lead to dysphagia of increasing degree.

In addition to the signs afforded by these various conditions, there may be glandular enlargements in the neck, the suprasternal notch, or in the axillæ.

The growth may invade the chest-wall at any spot, and in rare cases it may cause visible or palpable pulsation. The pulmonary physical signs are dyspnœa, sometimes orthopnœa and cyanosis. In some instances the patient prefers to lean forward; this is said to be due to the fact that in this position the antero-posterior diameter of the mediastinum is increased, and the tension caused by the growth is thereby lessened. There may be dullness over the sternum or over the upper thoracic spines, and over any part of the lung invaded or compressed by the growth. The breath sounds heard over the dull area may be harsh, bronchial, tubular, weak or absent. The signs due to any secondary condition, such as bronchitis, bronchiectasis or a pleural effusion may be found in addition.

Complications.—These include the secondary conditions just mentioned. Others are due to ulceration of the growth through the chest-wall, or into the trachea, bronchi, œsophagus or aorta. Pericarditis may occur if the growth invades the pericardium, and hæmopericardium may result from ulceration of a vessel.

Course.—The growth enlarges progressively and the course is often rapid, particularly in lympho-sarcoma. Fulminating cases lasting only a few weeks occur; more commonly the patients live from 6 months to 2 years from the onset, rarely more.

Diagnosis.—When signs of mediastinal pressure become apparent, new-growth should be suspected, in common with aneurysm, mediastinal abscess or cyst, enlarged mediastinal glands and pericardial effusion. The history, the general condition of the patient, the physical signs, blood examination, and the X-rays may all help in distinguishing between these conditions. The evidence afforded by the X-ray may be of the utmost value. The pulsating shadow of an aneurysm, the large area of a pericardial effusion, the indefinite edge of an infiltrating growth extending into the lung, may be shown clearly, but the appearance should always be interpreted in the light of the other clinical features, and a diagnosis should not be made on X-ray findings alone, since a growth may pulsate, or may give rise to an effusion, while a mediastinal abscess or a cyst may give a sharp shadow. An œsophageal new-growth can sometimes be differentiated by the œsophagoscope, but this should only be employed when aneurysm can be excluded. Diagnosis from pulmonary or bronchial new-growths may be almost impossible. Before the onset of pressure symptoms, growth may be suspected from the cough and emaciation, and here again the X-rays may give valuable indications. Chronic tuberculous disease should always be excluded by repeated sputum examinations. The diagnosis of mediastinal growth may sometimes be obscured by some of the complications it induces, notably pleural effusion and bronchiectasis. The rapid onset and progress of these conditions and the bloodstained character of an effusion may all suggest the possibility of a malignant cause. The presence of enlarged glands in the neck or axillæ, or of nodular growth in the chest-wall or episternal notch, may afford almost conclusive evidence of malignancy.

Prognosis.—This is practically hopeless and death occurs from exhaustion, starvation, toxæmia, asphyxia or hæmorrhage.

Treatment.—The treatment of simple tumours is surgical if they are capable of removal. The treatment of malignant tumours is that of inoperable malignant disease elsewhere. X-ray applications, or radium treatment in some

form may be tried. Otherwise treatment is symptomatic and palliative. Pain may be relieved by aspirin, codeine or morphine. Sleep may be induced, if there is insomnia, by chloral hydrate, papaveretum (alopon, opoidine, omnopon) or other hypnotics. If effusion is causing dyspnœa it may be tapped, but the fluid usually collects again rapidly. Air replacement is sometimes useful.

CYSTS OF THE MEDIASTINUM

SIMPLE CYSTS.—These are usually small and of no clinical importance.

DERMOID CYSTS AND TERATOMATA.—These are rare and become apparent generally in young adult life. They may enlarge, giving rise to symptoms and signs similar to those of a mediastinal tumour, or they may lead to empyema. They usually contain pultaceous material, and sometimes hairs, muscle, cartilage, bone and teeth. Such cases are almost certainly teratomatous in nature and derived from included embryos. This condition may sometimes be diagnosed during life by the expectoration of hair, teeth, bone or cartilage. The prognosis is, as a rule, serious, but some cases recover under appropriate surgical treatment.

HYDATID CYSTS.—A hydatid cyst may be primary in the mediastinum and may give rise to signs of mediastinal pressure, but the condition is extremely rare. Its presence may be shown by X-rays and its nature demonstrated by the blood and skin reactions. Such cysts have been successfully treated surgically.

Other rare mediastinal conditions are hernia of the stomach or colon through the diaphragm into the mediastinum. A retrosternal goitre may also form a mediastinal swelling.

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SECTION XVI

DISEASES OF THE KIDNEYS

THE CHARACTERS OF NORMAL URINE

THE amount of urine normally secreted in 24 hours is 50 ounces or 1500 c.c. The specific gravity of the total should lie between 1015 and 1025, though individual specimens will vary considerably more, according to the amount of fluid imbibed or the quantity excreted by the skin and bowels. The reaction is generally acid, due to the presence of acid sodium phosphate, NaH_2PO_4. The total acidity is such that about 650 c.c. of decinormal caustic soda will neutralise the daily output. This is equivalent to 82 grains of $NaHCO_3$, but it requires a rather larger quantity (120 grains according to Spriggs) of bicarbonate of soda by the mouth to effect this neutralisation. Expressed in terms of H-ion concentration, the *p*H varies between 4·7 and 10. The total acidity of the urine rises very considerably in acidæmia, and may be more than doubled despite large doses of alkalis. Normally, urine is more acid during fasting than during absorption of food, the acid and alkaline tides being thus produced. The alkaline tide may be partly due to the absorption of organic vegetable salts, as it is more marked in herbivora, but the increased activity of the respiratory centre after getting up in the morning, is chiefly responsible for an increase in the *p*H of the urine (diminished H-ion concentration), by removal of excess of CO_2 from the body; in fact, it alone may be responsible for a morning alkaline tide. On decomposition, either in the bladder or after excretion, the urine becomes alkaline, from the conversion of urea into ammonium carbonate.

The constituents of urine are partly derived from the food (exogenous) and partly from the katabolism of the tissues (endogenous). We may briefly consider the source and significance of the principal constituents.

Nitrogenous constituents.—The total nitrogen excreted each day on an ordinary mixed diet is about 18 grammes or 270 grains. Of the various nitrogenous constituents urea is by far the most abundant, its output being 33 g., which contains 15·4 g. of nitrogen, or 85 per cent. of the urea total. As so much of the urea comes directly from the food, the amount of urea falls both absolutely and relatively in starvation; the total nitrogen drops to 5 g. or even less, of which urea nitrogen forms about 60 per cent. On a diet rich in carbohydrates and fat, but containing hardly any nitrogen, these figures may fall still lower, as the assimilation of other foodstuffs reduces the waste of tissue nitrogen to a minimum. This is often forgotten, and in nephritis undue importance is attached to a drop in the output of urea, which is simply due to the diet prescribed being poor in nitrogen, whereas the urea excreted depends mainly on the quantity of protein ingested.

Next in importance come the purin bodies. Purins contain the group C_5N_4, and the best known is tri-oxy-purin or uric acid $C_5N_4H_4O_3$. A small quantity of the less oxidised purins, xanthin and hypoxanthin is also excreted. Exogenous purins come mainly from meat juices, from the nuclei of cellular organs (such as liver and sweetbread), and from tea, coffee or cocoa. Only from one-tenth to one-half of the ingested purins are excreted as such, the remainder being destroyed by the liver, ultimately appearing as urea. The alkaloids of tea, coffee and cocoa give rise chiefly to xanthin and hypoxanthin, the rest to uric acid. On a diet rich in meat the daily output of purins amounts to 0·34 g. of nitrogen, and on a purin-free diet to 0·202 g. This endogenous purin, which forms the larger part, comes mainly from the disintegration of the nuclei of maturing red blood corpuscles, and also the leucocytes and muscles. Anything increasing the leucocytes in the circulation increases the output of endogenous purins, and in leukæmia the excretion of uric acid may rise to 5 g. a day. Unaccustomed exercise diminishes the output of uric acid, while increasing that of the less oxidised xanthin and hypoxanthin, the total purin excretion remaining the same. Uric acid is only excreted as such when the urine is highly acid; normally it appears as acid sodium urate. (See also Urinary Deposits.)

Creatinin is, according to Folin, the most constant of the nitrogenous constituents on a meat-free diet, and serves as a measure of endogenous nitrogenous metabolism. In a healthy young man on a diet consisting entirely of bread, about 0·9 g. is excreted daily, while on a diet containing meat extracts more than 2 g. may be passed. During muscular wasting its output is increased, while in a subject already wasted it is diminished. All this suggests that it is derived from the creatin of muscle—both of the body and of the food. It may be recognised in urine by Weyl's test; with sodium nitroprusside and caustic soda it gives a ruby-red colour, which, unlike that given by acetone, is at once destroyed by glacial acetic acid. Jaffe's test depends upon the deep orange colour, given by even dilute solutions of creatinin on the addition of a saturated solution of picric acid and some 10 per cent. solution of caustic soda; this has been utilised for the colorimetric estimation of creatinin by Folin. Creatinin can be obtained from creatin by dilute boiling mineral acids. Creatin, which is abundantly present in muscles, is not normally present in the urine.

Ammonia is normally excreted to the extent of about 1 g. a day. An increase in this amount is not, as was formerly thought, a sign of incapacity on the part of the liver to form urea, but a sign of acidæmia. The body protects itself against acids in the circulation by forming ammonia from the proteins of the tissues. The increased excretion of ammonia is, therefore, a measure of the degree of acidæmia, and it is estimated by the amount of acid set free from the urine on the addition of formalin, which combines with the ammonia to form hexamine. In the acidæmia of diabetes, the output of ammonia may rise to 4 g. a day, or even more.

Hippuric acid is not an important nitrogenous constituent of urine, but it is of interest as being made by the kidney itself by the combination of benzoic acid with glycocoll. It is, therefore, increased by a diet of green vegetables, and is diminished when there is conspicuous degeneration of the renal tubules.

The pigments of urine are nitrogenous. The principal one, urochrome, to which urine normally owes its colour, though closely related to urobilin, has an independent origin from hæmoglobin. Even when all the bile escapes from the body through a biliary fistula the excretion of urochrome is unaltered. Urobilin, on the other hand, is a reduction product of bile pigment. The reduction is effected by bacterial action in the bowel, whence it is reabsorbed by the blood and excreted by the kidney. Normally it is not excreted as such, but as a colourless chromogen. The appearance of preformed urobilin is evidence either of increased hæmolysis or of septic infections of the gall-bladder or bile-ducts, or of increased intestinal putrefaction, or of increased time for reabsorption, as in intestinal obstruction. It can be recognised with the spectroscope by the absorption band it gives in the blue, or by the green fluorescence it shows on the addition of zinc chloride and ammonia. Very little is known of uroerythrin; it is an unstable body and is readily carried down by urates, to which it imparts the characteristic pink colour. A trace of hæmatoporphyrin is also normally present in the urine; but an obvious amount is an abnormality, which will be considered later.

Non-nitrogenous constituents.—These are principally salts. Chlorides are the most abundant, averaging about 10 to 13 g. of sodium chloride a day. Chlorides are retained whenever the body retains excess of fluid. This explains the reduced output of chlorides in such diverse conditions as œdema, serous exudates, pneumonia and acute dilatation of the stomach. Reduced chloride intake or loss through excessive vomiting are other causes. On the other hand the output is much increased in Addison's disease. The phosphates are partly excreted as acid phosphates of sodium and potassium, partly as earthy phosphates of calcium and magnesium. The former are not precipitated on neutralisation, while the latter are. A phosphatic deposit, as stellar crystals of calcium phosphate or tables of magnesium phosphate, is no proof of a real increase in the output of phosphates, but is usually merely an indication of diminished acidity. Ammonio-magnesium phosphate, on the other hand, is evidence of ammoniacal decomposition. It forms a deposit of "coffin-lid" or "knife-rest" crystals. The amount of phosphoric acid excreted daily amounts to about 2·5 to 3·5 g., of which the earthy phosphates form half. Sulphates are present in the urine to the extent of 1·5 to 3 g. of SO_3 a day. Very little sulphate is taken in the food, and most of that which is taken either as food or medicine is excreted by the bowel, so that the urinary sulphates come almost entirely from the oxidation of the sulphur in the protein molecule. About nine-tenths are excreted as sulphates of the alkalis, and the remaining one-tenth as ethereal sulphates, formed by conjugation with putrefactive products from the tyrosin and tryptophan of the protein molecule. Of these, the most striking is indican, or indoxyl-sulphate of potash. It is best detected by adding an equal quantity of strong hydrochloric acid to some urine, then a few drops of hydrogen peroxide, and shaking up the mixture with some chloroform to which it imparts a blue colour. Its presence in excessive amount is some evidence of excessive intestinal putrefaction, especially when due to obstruction of the small intestine. Not so much importance, however, is attached to indicanuria as formerly. All the sulphur in the urine is not excreted as sulphates; some 6 per cent. appears as neutral sulphur, derived from the

sulphocyanide of the saliva, the taurine of the bile salts and substances allied to cystin. The neutral sulphur is diminished in insanity.

Many other substances are normally present in traces in the urine, but except diastase, they are of little clinical importance. Ten to 30 units of diastase are normally present, but less will be found in some forms of impaired renal capacity and a great deal more in most pancreatic diseases. The presence of 50 units suggests a pancreatic lesion, while 100 or more make this certain. In severe pancreatitis 300 to 500 may be found.

THE ESTIMATION OF RENAL FUNCTION

It may be necessary to determine (1) the total renal capacity, or (2) the adequacy of either kidney separately. Generally speaking, the first is more the concern of the physician, and the second that of the surgeon. Estimation of the latter is of vital importance before nephrectomy is considered, lest the remaining kidney should prove inadequate to maintain life. Estimation of the former is an assistance both to diagnosis and prognosis. Some of the tests under the first heading have for their object the determination of the part of the kidney involved. These will be considered first.

A.—ESTIMATION OF CAPACITY OF BOTH KIDNEYS

1. Examination of the Blood.—The damaged kidney will fail to excrete substances which it should, and examination of the blood may reveal their presence in undue amount. The quantity of urea in the blood throws important light on renal capacity; normally this ranges from 15 to 40 mgm. per cent. in health, but after middle age figures up to 50 mgm. per cent. (urease method) may be within normal limits. The urea content of the blood, as well as that of the cerebro-spinal fluid, is raised in various kidney diseases, and also in alkalosis. A blood urea figure of 200 mgm. per cent. and over is of serious clinical significance. It may rise higher than this, even to 280 mgm. per cent., in acute nephritis, and gradually fall to normal with complete recovery. In chronic nephritis such figures generally indicate a terminal phase of few months' duration, but a patient may live for a year or more with a blood urea of 190 mgm. per cent. The amount of sodium chloride in the blood may be raised from the normal 0·45 to 0·5 g. per cent. to 0·6 or higher. When there is extreme renal failure there may be an increase in the H-ion concentration, the uric acid and the indican of the blood, while the calcium content may fall from the normal 10 mgm. per cent. to 6.

2. The Urea Concentration Test.—Although ordinary estimation of the percentage of urea in urine gives no information of value, the response of the kidney to a given dose of urea does. On this MacLean and de Wesselow based their useful urea concentration test. Fifteen grammes of urea dissolved in 100 c.c. of water, and flavoured with a little tincture of orange, are given to a patient just after he has emptied his bladder. The urea in the urine passed one, two and three hours afterwards is estimated by the hypobromite method. If this amounts to 2 per cent. or over in one or more of the three specimens the kidney is efficient according to the test. A concentration of 2·5 per cent. or over is more satisfactory. The volume of urine should not exceed 120 c.c. in the first hour, or 100 c.c. in each of the second and third hours. Excessive

diuresis may be due to release of water previously retained in the tissues, and the test should be repeated. This test is of less value if the patient is taking a low nitrogen diet.

3. The Blood Urea Clearance Test.—This test was introduced by Möller, McIntosh and Van Slyke as a simple and reliable method of estimating the urea-excreting function of the kidneys. In principle it is based on the relation of the blood-urea concentration to the urea excretion in the urine. The result is expressed as cubic centimetres of blood cleared of urea per minute. For details a textbook of clinical pathology should be consulted. It is claimed that this test is more sensitive and will reveal minor defects not revealed by other tests.

4. Volhard's Tests as Modified by Rosenberg.—On the first day the patient, after passing urine, drinks 1500 c.c. of water within half an hour. Urine is passed at half-hourly intervals for the next 4 hours, each specimen being saved separately and tested for volume and specific gravity. Normally the whole 1500 c.c., often more, is excreted within the 4 hours, and the specific gravity falls to 1002, or less. The second day, ordinary meals are given, but the amount of fluid is limited to 500 c.c. for the whole 24 hours, taken in four roughly equal portions. Fruit should not be given, or should be reckoned as fluid. Urine is passed as and when the patient wishes, and each specimen is again collected separately and tested for volume and specific gravity. The total urine for the day should not exceed 750 c.c., and the specific gravity should rise to at least 1027. These are known as the dilution and concentration tests respectively.

In cases of renal insufficiency the volume of urine on the first day is too little, while that on the second day is too much, as excretion tends to continue at the same rate irrespective of variations in the requirements of the body. The limits of variation in specific gravity become more and more narrowed as the disease progresses, until at length a fixed point of about 1009 is reached. Often the dilution test will show a minimum of about 1005, and the concentration test a maximum of about 1015, long before the patient complains of any symptoms or the blood shows any evidence of uræmia.

In our opinion the concentration test is more reliable than the dilution test, but both of them set up too rigid a standard of what constitutes normal function.

5. Fixation of Specific Gravity.—This is a simpler method. The patient takes no fluid drinks or liquid foods or fruit from after breakfast one day until breakfast-time the next day. The urine passed in the first 12 hours need not be kept, but that secreted in the second 12 hours is collected and pooled. If the renal function is satisfactory the specific gravity of this urine should be at least 1024, and the concentration of urea should be more than 2 per cent.

B.—ESTIMATION OF CAPACITY OF EACH KIDNEY

Catheterisation of each ureter under the direct view of the cy is the only reliable method of obtaining the required information. It is usual to encourage secretion during examination by giving some tea or simple diuretic. Additional information is gained by the intramuscular injection of 15 minims of a 5 per cent. aqueous sterilised solution of methylene-blue. It is first excreted as a colourless chromogen and, later, as methylene-blue itself.

The chromogen turns blue when boiled with acetic acid, and should appear in the urine in from 15 to 20 minutes, after which the excretion of unaltered methylene-blue should begin. It should reach its maximum in from 4 to 5 hours, and should have disappeared in from 40 to 50 hours. Obviously, catheterisation of the ureters cannot be continued all this time, so that observation is directed towards a marked delay in the appearance of blue on one side as compared with the other. Afterwards, hexamine should be given as a precautionary measure, and the patient kept in bed for 36 hours. As in acute or subacute nephritis the rate of methylene-blue excretion is entirely unaffected, the utility of this test is confined to unilateral chronic disease.

Indigo-carmine may be used for a similar purpose; 10 c.c. of a 0·4 per cent. solution is injected intravenously or intramuscularly. The urine should be coloured in about 10 minutes, first appearing green and then blue. Excretion reaches its maximum in about an hour, so that this test has advantages over the methylene-blue method. Delay in the appearance of the dye and a feeble staining of the urine may be taken as evidence of disease.

Pyelography is a valuable means of determining the position of the kidneys and their relation to shadows in or in the neighbourhood of the urinary tract. By this means the position of renal or ureteric calculi may be defined, and such shadows as those caused by calcareous tuberculous glands, gall-stones, and fæcal calculi may be recognised as outside the urinary tract. It is an invaluable means of demonstrating the presence of a hydronephrosis, especially when small. It will show dilatation or irregularities in the course of the ureter. By the absence of the shadow caused by the dye, a failure in function of one kidney or its absence may be indicated. Renal growths and tumours of the renal pelvis may be diagnosed by abnormalities in the pyelogram, and calculi not evident in a plain radiogram may be shown by this means. The intravenous method is now commonly adopted in the first approach to a urinary case, but instrumental pyelography is often required to confirm the findings obtained.

A drug, opaque to X-rays, which is eliminated by the kidneys, is introduced intravenously, and radiograms are taken at short intervals after its injection. Uroselectan B (a non-toxic iodine-containing substance) is the best preparation for this purpose. For instrumental pyelography a 12 to 20 per cent. solution of sodium iodide or sodium bromide is used. Before iodine is given for the purpose of pyelography, the patient's tolerance of the drug should be tested by giving five or ten grains by mouth, in order to exclude an idiosyncrasy.

ABNORMALITIES OF THE URINARY SECRETION

1.—POLYURIA

Polyuria may be due to—

1. Increase in the quantity of fluid imbibed.

2. Increase in the molecular concentration of the urine as in diabetes mellitus, or after saline diuretics. More water is thereby attracted into the blood stream by osmotic pressure.

3. Incapacity of the kidney to excrete a concentrated urine, as in chronic interstitial nephritis.

4. Dilatation of the kidney vessels, as produced by stimulating diuretics of the caffeine group. These diuretics have been shown by Curtis, using experimental methods, to act directly on tissue cells, causing the cells to part with their water; hydræmia results, and the excess of water in the blood is immediately excreted by the kidneys.

"Diabetes insipidus" is frequently due to disease of the pituitary gland or of the overlying hypothalamus, or to damage in this neighbourhood by syphilitic meningitis of the base of the brain. It is also probable that hysterical polyuria is due to a temporary inhibition of pituitary secretion through the sympathetic. This appears to affect the renal vessels directly, since pituitrin will check diuresis, even in the denervated kidney.

2.—ANURIA

Suppression, as opposed to retention of urine, may be due to—

1. Acute nephritis with intense congestion and nephrosis, whether the result of an infection or of drugs, such as turpentine, cantharides or carbolic acid.

2. Bilateral obstruction to the ureters.

3. Reflex causes, such as operations on the kidney or trigone of the bladder.

4. Vasomotor conditions, as collapse, shock or irritation of the vasomotor centre. Probably the anuria in diphtheria is due to the last of these (Garratt). In cholera there is not only collapse, but depletion of water by other channels.

5. Hysterical. This condition has been described by Charcot. It is, however, rare and the element of fraud must be eliminated. Thus, in one case, urea was found abundantly present in the contents of the washing-bowl, and this explained how the urine was disposed of.

3.—ALBUMINURIA

Albuminuria should be more correctly termed proteinuria—since blood serum contains two proteins—albumin and euglobulin—and either may appear in the urine, though search is seldom made for the latter. The ordinary tests of heat coagulation, nitric acid or salicyl-sulphonic acid give positive results with either. The presence of euglobulin may be shown by the addition of dilute acetic acid (33 per cent.) to urine in the cold. The acid is added drop by drop, and the precipitation of globulin is shown by an opalescence in the urine to which the acetic acid is added. Mucin is also deposited by the addition of acetic acid, but it is not redissolved by an excess of acid. A more distinctive test is the precipitation of globulin in distilled water. Single drops of urine are dropped into a glass vessel containing distilled water. As the drop of urine falls through the water it assumes a ring form, and the ring has a milky appearance due to precipitated globulin when the latter is present. The globulin can be precipitated for quantitative examination by making the urine alkaline with ammonia, and then half saturating it with ammonium sulphate.

Proteinuria may be classified thus—

I. Without Organic Diseases of the Kidneys, as in—

1. *Functional or orthostatic proteinuria.*—This is common in males between puberty and adolescence; it is much less common in females of the same age. Dukes found it in 16 per cent. of all boys entering Rugby School. Protein appears only in the urine secreted in the upright posture, and is absent from the urine passed on first rising. There is no evidence that the amount of protein in the food influences it, though some constituent of raw eggs may excite a transient albuminuria by a toxic action on the kidneys. Severe physical exercise will excite proteinuria in most healthy young adults. Collier found it present in every one of the Oxford crew of 1906 after rowing a course; to such a condition the term "physiological" proteinuria may fairly be applied. When the protein appears apart from exertion, the subject is often an anæmic weedy youth with a dull heavy aspect and a tendency to fainting. The heart is irritable, and the blood pressure unstable, and fluctuates with change of posture. There may also be a few hyaline casts, and frequently calcium oxalate crystals. In any case of proteinuria in a boy or young man the diagnosis of a kidney lesion should not be made unless casts other than hyaline are discovered, unless the tension of the pulse is definitely and permanently raised, and unless there are signs of cardiac hypertrophy. In the absence of such evidence, the urine passed on first rising should be examined. If this is free from protein, the condition is almost certainly functional. Then 15 grains of calcium lactate should be given three times a day for 3 days, after which the urine should be examined again. If this checks the proteinuria no further anxiety need be felt. Some milder forms of toxæmic kidney may simulate functional proteinuria, so that a search should be made for toxic foci, such as septic tonsils, tuberculous glands, or chronic appendix trouble, in all cases. A holiday is advisable if the patient has been doing hard mental work, as the condition is apt to appear under the strain of competitive examinations. A tepid bath, with cold sponging down the spine, and followed by vigorous towelling, is advantageous, and a general tonic such as strychnine, with iron if there is anæmia, should be prescribed. The condition soon rectifies itself when adolescence is past, and any case of proteinuria in a patient approaching thirty probably does not fall into this category.

2. *Febrile.*—Any acute specific fever may be accompanied by proteinuria due to cloudy swelling of the kidney. It should subside soon after the temperature falls to normal. This type of albuminuria is referred to again under the heading of Toxæmic Kidney, to which it more properly belongs.

3. *Congestive.*—In failing heart there is usually proteinuria from venous congestion of the kidneys. Hyaline casts may also be found. Unlike the urine of nephritis the urine is loaded with urates. After an epileptic fit there is often a transitory proteinuria, probably due to the congested condition of the veins during the fit. For a similar reason protein is apt to be present in the urine of any unconscious person.

4. *Toxic.*—This forms an intermediate group between those with and those without organic disease of the kidney, for if the action of the toxin be prolonged a definite nephritis may be established. Thus the proteinuria of pregnancy is generally regarded as toxic in origin, and may clear up

completely. The proteinuria sometimes seen in jaundice is also toxic in character.

II. With Organic Diseases of the Kidneys.—

1. *Nephritis, acute and chronic.*

2. *Residual albuminuria.*—This term is applied to cases in which albuminuria persists after complete recovery from an attack of nephritis. Observation of the case over a period of years may be necessary to exclude a low-grade progressive chronic nephritis. If and when residual albuminuria occurs it has the same significance as the scar of a perfectly healed wound in the skin. It would seem that residual albuminuria may persist throughout life unchanged, and there is no reason to think that the persistent passage of albumin of itself damages the kidney.

3. *Amyloid disease of the kidneys.*

4. *Tumours and infarcts in the kidney* may cause proteinuria, but more usually simple hæmaturia.

4.—ALBUMOSURIA

Albumose, or more correctly proteose, may be found in urine during autolysis of the tissues. It is not of great clinical importance except to distinguish it from Bence-Jones proteinuria. Proteose can be recognised by the fact that although it is precipitated by saturation with ammonium sulphate it is not coagulated by heat. Proteose precipitates disappear on heating and reappear on cooling. It can be separated from albumin by saturating the urine with crystals of ammonium sulphate, boiling and filtering. The precipitate on the filter paper is washed with water, when any proteose will be redissolved and carried through the filter paper. It can then be detected by the pink colour it gives on the addition of strong caustic soda and a drop of dilute solution of copper sulphate. With these reagents native proteins give a violet colour. The Bence-Jones protein, which is found in considerable amounts in the urine of sufferers from multiple myelomata, is not a true proteose though possessing similar solubilities. On treatment as above it yields a violet colour, showing that it has affinities with native proteins. It begins to be precipitated at 40°–55° C., but on approaching boiling-point most of the precipitate is redissolved. This is probably due to the influence of certain salts in the urine, and is not a property of the isolated protein. As Bradshaw showed, it also gives a ring of coagulum on contact with strong hydrochloric acid. Its recognition is of great diagnostic value, as it is pathognomonic of multiple tumours of the bone marrow, and enables them to be detected before there is any external sign, but only pain and tenderness in the bones. At a later stage the tumours may break through the investing bone and give rise to palpable swellings. Sometimes the Bence-Jones protein is spontaneously precipitated, causing the urine to appear milky. Considerable excess of phosphates may be found in this milky precipitate, probably derived from the autolysis of the surrounding bone.

True peptone is exceptionally found in the urine in pneumonia and phthisis, but is of no clinical importance.

5.—HÆMATURIA

When blood is intimately mixed with the urine it is held to be in favour of its renal origin. Bleeding from the bladder is more apt to occur into the last part of the urine voided, while urethral bleeding is said to occur chiefly into the first part. When the quantity of renal bleeding is not great, it imparts a smoky appearance to the urine, owing to the conversion of some of the hæmoglobin into methæmoglobin, which on spectroscopic examination gives an absorption band in the red in addition to the two bands in the green characteristic of oxyhæmoglobin. The chief causes of hæmaturia are best classified as follows:

1. *Prerenal.*—The altered condition of the blood which occurs, for instance, in scurvy, purpura hæmorrhagica and certain hæmorrhagic fevers, leads to the escape of some of the blood through the kidney without any evidence of a definite kidney lesion.

2. *Inflammations of the kidney*, due to (*a*) Bright's disease, both acute and chronic. Hæmaturia is a constant feature of acute nephritis and of exacerbations of chronic nephritis. It may also occur in the course of chronic interstitial nephritis and arterio-sclerotic kidney without any acute symptoms. "Renal epistaxis" is usually an early sign of an interstitial change, which is sometimes, as shown by Hurry Fenwick, confined to a single papilla where the vessels are dilated. There are a few cases in which no cause for the bleeding, either in the condition of the blood or the urinary tract, can be discovered in spite of the most careful examination of the kidney, the removal of which has been necessitated by the severity of the hæmorrhage. These are true cases of renal epistaxis or essential hæmaturia.

(*b*) Tuberculosis or a Bacillus coli infection. The latter more usually affects only the pelvis of the kidney.

(*c*) Certain drugs, such as turpentine, cantharides and carbolic acid, or occasionally hexamine.

3. *Vascular causes.*—Congestion due to heart failure, thrombosis and embolism (*e.g.* septic endocarditis) are common causes of hæmaturia.

4. *Irritation of the kidney by foreign bodies*, such as

(*a*) New-growth.

(*b*) Crystals, such as oxalates or uric acid, and calculi.

(*c*) Parasites, such as Bilharzia.

Traumatic, vesical and prostatic causes are not considered here.

6.—HÆMOGLOBINURIA

This is due to some hæmolytic agent. It may be—

1. *Paroxysmal*, as in Raynaud's disease and in syphilis. Most cases are syphilitic. The corpuscles are broken down by a hæmolysin which is present in the blood of 5 to 10 per cent. of cases of tertiary syphilis. Those who suffer from paroxysmal hæmoglobinuria are presumed to have some constitutional peculiarity which renders them susceptible to this hæmolysin. The hæmolysin acts as an amboceptor, unites with the red corpuscle in the cold and on return to warmth the normal complement in the plasma causes hæmolysis. In addition to this there are some rare forms of non-syphilitic paroxysmal hæmoglobinuria.

2. *Toxic.* In this group the toxic agent produces the hæmoglobinuria without an additional factor. Striking examples of this are blackwater fever (*q.v.*), poisoning by arseniuretted hydrogen, and transfusion of incompatible blood. Hæmoglobinuria may also occur in Lederer's anæmia. The chemical tests for hæmoglobinuria are the same as for hæmaturia, but the microscope will fail to reveal red corpuscles. Some of the pigment is excreted as methæmoglobin, especially after drugs of the aniline group, nitrites, or potassium chlorate.

7.—PORPHYRINURIA

Sometimes the hæmoglobin molecule is broken down in the blood stream and the pigmentary portion is excreted apart from the protein and iron. This is usually due to poisoning by sulphonal, trional or sulphanilamide, particularly when the drug has been taken regularly for a long time. It is then of grave prognosis ; large doses of alkalis should be given. It is commoner in females than in males. Occasionally porphyrinuria occurs apart from these drugs, when it is not of grave import. It has been met with in cirrhosis of the liver, gastric ulcer and as a congenital abnormality of metabolism, when it may be associated with sensitivity to light and with hydroa vacciniforme. Exceptionally toxic symptoms occur even when it is not associated with drugs, as in two cases recorded by Ranking and Pardington, and by one of us. In these, some intestinal toxin with a reducing action appeared to be at work. The intestinal flora has been found rich in yeasts in such cases. Hæmatoporphyrin sometimes imparts a port-wine colour to the urine, but sometimes it is excreted as a porphyrinate. In the latter case the urine is brown, from the admixture of some unknown pigment, and the spectroscope shows two bands closely resembling those of oxyhæmoglobin. On the addition of an acid, however, the characteristic bands of acid hæmatoporphyrin appear.

8.—CHOLURIA

Another derivative of hæmoglobin, bile pigment, appears in all forms of jaundice due to obstruction of the main or intrahepatic ducts. In a true hæmolytic jaundice, such as acholuric family jaundice, as the name implies, bile does not appear in the urine. Bile pigment can often be recognised by noting the tinging of the froth caused by shaking the urine, but is best detected by the addition of a drop of fuming nitric acid to filter paper dipped in the urine, when rings of colour appear, green being the essential one. The green colour given on addition of a solution of iodine to the urine is a less delicate test. Bile-salts are often absent from the urine when bile pigment is present. Matthew Hay's test is the only reliable one for their presence there. On putting flowers of sulphur on the surface of the urine, they sink to the bottom, owing to the lowering of surface tension by the bile-salts.

9.—MELANURIA

Melanin only appears in the urine in melanotic sarcoma. Garrod has shown that in all other diseases in which melanuria has been recorded the test employed has been unsatisfactory. The melanin is excreted as melano-

gen which darkens on standing, and gives a black precipitate on addition of ferric chloride, which is soluble in excess of the reagent, yielding a black solution. A more delicate test is made by the addition of sodium nitroprusside and sufficient caustic soda to render the urine alkaline. The ordinary ruby-red colour, due to creatinin, is developed. The urine is now made acid with acetic acid, and if melanogen is present a prussian-blue colour appears.

10.—ALKAPTONURIA

This is not the manifestation of a disease, but is rather of the nature of an alternative course of metabolism, harmless and usually congenital and lifelong (Garrod). The individual is incapable of completely breaking down the tyrosin in the protein molecule, so that the intermediate product, homogentisic acid, appears in the urine. The urine reduces Fehling solution on boiling, but it does not ferment, and it darkens on standing, or at once on the addition of alkalis. It may stain the linen brown. When a dilute solution of ferric chloride is allowed to fall drop by drop into the urine, each drop produces a transitory deep blue colour. The urine reduces ammoniacal silver nitrate in the cold, giving a silver mirror on the sides of the test tube. Ochronosis—a blackening of the cartilages and ligaments, and sometimes of the conjunctivæ—may occur, and usually there is also a chronic arthritis, which may lead to a curious "goose-gait."

[For other reducing substances in the urine, including sugar, see article on Diabetes.]

11.—KETONURIA

Ketonuria is a term used loosely to include the appearance in the urine of diacetic acid and its derivatives, acetone and β-oxybutyric acid. Acetone, however, being merely a decomposition product of diacetic acid, is relatively unimportant; β-oxybutyric acid, formerly regarded as the source of diacetic acid, is more saturated and less toxic and has been shown by Hurtley to be formed out of diacetic acid by the liver, as an attempt at detoxication. Diacetic acid is derived from the incomplete oxidation of fats or of the fatty acid groups in protein. It is probably always made in small quantities, but when there is an abundant consumption of carbohydrate, it is completely oxidised. In starvation the store of glycogen is quickly exhausted and the body chiefly lives on its fats; hence ketonuria. Persistent vomiting, advanced carcinoma of the digestive tract and rectal "feeding" also are equivalent to starvation, and will excite ketonuria, though without such a degree of acidæmia as to cause toxic symptoms. In conditions where the liver is thrown out of gear, such as post-anæsthetic poisoning, ketonuria may occur with toxic symptoms, because of the severe disturbance of all metabolic processes. But there are other agents at work besides diacetic acid which may be responsible for those symptoms. Only in advanced diabetes do we find toxic symptoms directly due to diacetic acid. Here there may be complete inability to utilise carbohydrates, so that the body perforce lives on protein and fats. If these are freely given in the food the amount of diacetic acid produced may be very large. But if a diabetic be fasted there is a great drop in ketonuria, showing that most of this is

exogenous in origin (see Diabetes). The test formerly used for diacetic acid was the mahogany red colour given on the addition of ferric chloride. This has the disadvantage of being masked if the patient is taking any salicyl body. The nitro-prusside test was formerly regarded as showing the presence of acetone, but Piper demonstrated that it is really a much more sensitive test than ferric chloride for diacetic acid. A crystal of nitro-prusside of soda is dissolved in the urine, and then a strong solution of ammonia is poured on the top. A ring, the colour of Condy's fluid, speedily develops at the junction of the liquids and spreads upwards. The intensity of colour is a rough measure of the degree of ketonuria. The reaction is made still more sensitive by previous addition of crystals of ammonium sulphate to saturation (Rothera).

12.—DRUGS WHICH ALTER THE COLOUR OF URINE

Methylene-blue is used as a colouring matter of sweets and also as an ingredient of certain proprietary pills. It is also given for coli infections of the urinary tract, gonorrhœa and bilharzia, or less commonly as an analgesic in rheumatism, sciatica and migraine. In small quantities it imparts a green colour to the urine, when it may be precipitated with the mucin. In larger doses it turns the urine blue. It can be recognised by its presence in suspension, so that it can be removed by simple filtration. It can be dissolved from the filter paper by chloroform, and is turned pink by the addition of alkalis. Eosin may be used in sweets and turns the urine a fluorescent pink. Prontosil rubrum and pyridium turn the urine a reddish-orange colour, though, if the urine is alkaline, this may not appear until it is acidified. Amidopyrine (pyramidon) may have a like effect. Rhubarb and senna may turn the urine reddish-brown from the chrysophanic acid they contain. The urine turns pink on the addition of an alkali. Santonin turns the urine a vivid yellow, which becomes rose-pink with alkalis. Carbolic acid may turn the urine greenish-black on standing, from the formation of hydroquinone. In carbolic acid poisoning the urine withdrawn by a catheter may even be found olive-green without exposure to the air. Other drugs, which may have this effect are salol, creosote, naphthalene and uva ursi. In chronic carboluria, ochronosis may occur as in alkaptonuria.

Certain drugs can readily be recognised in the urine by some colour reaction. Thus, salicylates are excreted as salicyluric acid, which gives a violet colour on the addition of ferric chloride. Copaiba, which is precipitated by nitric acid, can be distinguished from albumin by the solubility of the precipitate in alcohol. On the addition of hydrochloric acid a urine containing copaiba turns cloudy, the cloud soon becoming rose pink. Iodides in urine give a blue colour with guaiacum, and on the addition of hydrochloric acid impart a violet colour to chloroform shaken up with the urine.

13.—PYURIA

Pus may come from the urethra, prostate, bladder or kidney. The diagnosis of the source is discussed under septic diseases of the kidney. The best test for pus in the urine is the microscope. If the amount of pus be considerable it will yield a ropy mass on the addition of liquor potassæ.

If osanic ether be shaken with the urine, bubbles of oxygen are evolved. With tincture of guaiacum a blue colour may be given even without the addition of osonic ether.

14.—CHYLURIA

True chyluria is due to blocking of the thoracic duct, most commonly by the *Filaria sanguinis hominis*, but sometimes the result of inflammatory or neoplastic conditions, with consequent rupture of lymphatics of the bladder through back pressure. Fat may be found in the urine in the lipæmia of diabetes, in growths of the kidney, and after fracture of long bones, when fat may be liberated into the circulation. Accidental contamination by an oily lubricant for a catheter and fraudulent addition of milk to the urine must be excluded. Pseudo-chyluria is due to a lecithin compound of globulin, and is sometimes found when there is a great excess of globulin in the urine. Unlike true fat, this substance is not extracted by shaking up with ether.

15.—PNEUMATURIA

Osler gives the following causes for gas in the urine: (1) Mechanical introduction of air in vesical irrigation or cystoscopic examination in the knee-elbow position. (2) Infection of the urine as by the *Bacillus aerogenes capsulatus*. (3) Vesico-enteric fistula.

16.—CRYSTALLINE DEPOSITS IN URINE

These may be:

1. *Uric acid*, which is characterised by multiplicity of forms and the yellow colour due to the urinary pigment they absorb. The chief varieties found are derived from the barrel and the whetstone types. Thus with a small whetstone stuck at either end of a barrel we get the lemon-shaped crystal. If the whetstones at the end of the barrel are larger, we obtain the "bicycle-handle" crystal. A very characteristic form is that derived from two whetstones with their broader ends apposed. The rosette crystal is a group of whetstones joined by their bases. The factors in the excretion of uric acid are considered under renal calculi; the chief factors in the deposit of uric acid crystals as such are high acidity, high percentage of uric acid, and poverty in mineral salts. The first two are the most important, especially the first. Deposits of urates are usually amorphous, but ammonium biurate may crystallise out as spheres with projecting spines.

2. *Oxalate of lime* is found in the urine, usually as small regular tetrahedra, which under the microscope appear as "envelope" crystals. They may arise (*a*) from ingested oxalates. Rhubarb, spinach, asparagus and sorrel are the foods most likely to produce oxaluria sufficient to excite symptoms, for each contain more than 2 g. of oxalic acid per kilogram, though many other articles of diet contain some oxalates. Some individuals seem sensitive to strawberries which, however, only contain 0·06 g. per kilogram. (*b*) In either achlorhydria or hyperchlorhydria; the former permitting fermentation of carbohydrates, the latter promoting absorption of oxalic acid. (*c*) In crises in neurasthenics, with irritability, lassitude and neuralgic pains, without discoverable cause.

Oxaluria may cause smarting on micturition and may excite both albuminuria and hæmaturia. Its importance as a starting-point for renal calculi is considered later. Paralytic distension of the bowel has also been described in oxaluric crises.

3. *Phosphates.*—See Characters of Normal Urine (p. 1283).

4. *Cystin* is an amino-acid containing sulphur, and is contained in many proteins, being especially abundant in hair. Its presence in more than minute traces in the urine appears to be due to an inborn error of metabolism, affecting only the endogenous protein, since it is not increased by the administration of cystin by the mouth (Garrod). It is deposited as hexagonal plates, and is often accompanied by a variable amount of diamines, such as putrescin and cadaverin, pointing again to an incomplete breakdown of the tissue proteins. If the urine becomes infected, these cystin crystals may aggregate to form a calculus.

5. *Tyrosin* rarely appears in the urine as sheaves of fine glistening crystals. It is then generally accompanied by *Leucin*, which does not appear until the urine is concentrated by evaporation, when it forms spheres with concentric rings. The presence of these substances is sometimes regarded as pathognomonic of acute yellow atrophy of the liver, but they are occasionally seen in other severe disintegrations of the liver, such as cirrhosis.

17.—ORGANISED DEPOSITS

of red blood corpuscles, pus, epithelium, casts and spermatozoa do not call for detailed description here. The first two have already been referred to. For Epithelium and Casts see sections on Inflammatory Diseases of the Kidney.

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CIRCULATORY DISTURBANCES

1. *Active congestion.*—There is no distinction to be drawn between active congestion of the kidney and the early stage of acute nephritis.

2. *Passive congestion.*—Anything which raises the pressure in the renal vein must produce a passive congestion of the kidney. Failing compensation in valvular disease of the heart is the commonest cause of this; but it may also be brought about by respiratory diseases or by pressure on the renal vein by abdominal tumours or ascites. A transient congestion may result from an epileptic fit.

The cardiac kidney, as it is called, is the most typical example of passive congestion. The organ is firm and dark in colour, especially the pyramids. The capsule strips normally. The stellate veins are engorged. The kidney may drip with blood on section, and if placed in a dish after section soon exudes œdematous fluid.

The urine is scanty, high-coloured and of high specific gravity. Unlike the urine of chronic nephritis it is loaded with urates. It contains a variable amount of albumin and hyaline casts, with a few red blood corpuscles, if the congestion is at all considerable. Renal inadequacy does not reach

the high grade seen in true nephritis, nor is death from uræmia likely. The prognosis and treatment are those of the cardiac condition causing it. Stimulating diuretics are of much more service than in nephritis, since there is no primary disease of the secreting structures.

3. *Infarction.*—This, which is a common complication of infective endocarditis, may take two forms—(*a*) Multiple minute hæmorrhagic infarcts, producing the "flea-bitten" kidney, which may lead to foci of embolic nephritis with fibrinous exudate and leucocytic infiltration. (*b*) Larger anæmic infarcts, "map-like" areas of coagulation necrosis, roughly wedge-shaped, but with irregular edges and with the base reaching the surface of the organ. Their formation may cause a sudden pain in the loins, if they are large. Either of these conditions will cause both albuminuria and hæmaturia.

4. *Thrombosis of the renal vein.*—This is rare, and is usually significant of a terminal infection, as in a marasmic infant. In thrombosis of the inferior vena cava the process may reach as high as and spread into the renal vein. This would produce the same effects as the cardiac kidney, but in a much more intense form.

BRIGHT'S DISEASE

Bright described an acute inflammation of the kidney accompanied by dropsy and albuminuria, and a chronic form in which dropsy is absent. There has been much controversy as to what should be included in the category of "Bright's disease," but there is no doubt as to its essential features. It is a bilateral, non-suppurative affection of the kidneys, accompanied by albuminuria and cylindruria. Except in nephrosis, there is generally hæmaturia in the acute or active stages; œdema and effusion in the serous sacs are commonly present. The renal lesion is diffuse in acute and chronic nephritis, but in "chronic interstitial nephritis" it is chiefly localised in wedge-shaped areas, separated by renal tissue which remains relatively normal. The actual lesion in all forms of nephritis is obviously inflammatory, as shown by proliferation of cells, particularly the cells of Bowman's capsule, the layers of which become adherent while the multiplication of their cells leads to crescent formation. There is also small-cell infiltration and œdema of the interstitial tissue of varying degree. Accompanying these inflammatory changes are degenerative changes, chiefly evident in the renal tubules, namely, cloudy swelling, fatty, hyaline and other forms of cellular degeneration, and necrosis. In some forms of Bright's disease the inflammatory changes predominate; in others the degenerative. In one uncommon form the degenerative changes are so marked a feature of the histological picture, while the changes which are without doubt inflammatory are so slight or even absent, that this form is called Nephrosis in contradistinction to Nephritis.

There are other affections of the kidney, such as toxæmic kidney, hyperpietic kidney (benign nephrosclerosis) and senile or atheromatous kidney, which would be better separated from the category of Bright's disease, because in them the disease of the renal parenchyma is neither the first established nor the primary condition of disease. It is, indeed, but part of a widely distributed pathological change in other organs of the body.

They are, however, included in the present classification and description of Bright's disease, because there are intermediate forms which link them to Bright's disease, and because in some cases they develop into Bright's disease.

There is so much overlapping of the various types of Bright's disease that more is lost than gained by pressing distinctions in detail. Volhard, Van Slyke and others recognise three types of Bright's disease which are essentially different in their genesis and pathological nature, namely (1) the hæmorrhagic or glomerular, marked primarily by glomerular inflammation, with hæmaturia and usually diminished renal function (even in the acute stage); (2) the sclerotic disease, marked primarily by pathological changes in the small arteries of the kidneys (and usually other organs), with hypertension as the first sign, and diminished renal function only as a terminal phenomenon; and (3) the degenerative disease or diseases, called nephrosis, marked primarily by degenerative changes in the kidneys, without hypertension or hæmaturia. This classification has long been the accepted basis for the description of Bright's disease, and in our opinion it best harmonises the anatomical, pathological and clinical phenomena.

I. Degenerative Forms:
   (A) *Toxæmic kidney.*
   (B) *Nephrosis.*

II. Inflammatory Forms.
   (A) *Glomerulo-tubular nephritis.* (*Diffuse nephritis*). 1. Acute nephritis. 2. Chronic nephritis: (*a*) secondary type; (*b*) primary type.
   (B) *Embolic focal nephritis* set up in infective endocarditis.

III. Vascular Group.
   (A) *Chronic interstitial nephritis, including malignant nephro-*
   (B) *Hyperpietic kidney* (benign nephrosclerosis).
   (C) *Senile or atheromatous kidney.*

TOXÆMIC KIDNEY

Definition.—Certain toxic substances may excite degenerative rather than inflammatory lesions in the kidneys, which are nevertheless capable of complete recovery. Characteristically, as in febrile albuminuria, the affection of the kidneys is dependent, both for its inception and persistence, on some other disease, and, generally speaking, its intensity varies with the severity of the primary disease. In its onset, intensity, course and termination, it simply reflects the toxæmia which causes it.

Ætiology.—The commonest cause is bacterial toxæmia. As fever in itself does not necessarily cause albuminuria, all the so-called "febrile albuminurias" should be referred to this group. Thus the acute specific fevers—pneumonia, typhoid fever, diphtheria, small-pox, tonsillitis and scarlet fever (notwithstanding the fact that the two last often cause a true nephritis)—are common causes of the slighter degrees of toxæmic kidney. More potent are exogenous and endogenous poisons. Mercurial salts, arsenic,

phosphorus and cantharides are important causes clinically, while uranium and bichromate salts are frequently used in the experimental production of the condition. Jaundice and the ketosis of diabetes mellitus are not uncommon causes. The toxæmias of pregnancy belong to this group, but in their tendency in some cases to develop into chronic nephritis and their frequent association with a raised blood pressure and visual disturbance, these cases differ from other members of the group.

Pathology.—The post-mortem appearances are not distinctive. The cardio-vascular system is normal. The kidneys are pale and likely to be increased in size and weight. On section the cut surface of the cortex is pale in contrast to the congested pyramids: it is increased in thickness and its structure is blurred. On microscopical examination the parenchyma shows degenerative changes, particularly affecting the convoluted tubules. Apart from the presence of some swelling of the glomerular tufts, and the presence of an albuminous exudate in the intercapsular space, the glomeruli show little damage. The absence of tissue reaction that is undoubtedly inflammatory and the presence of tissue changes that are certainly degenerative are the distinctive features of the histological picture. Similar changes are to be found in other organs of the body, and especially in the liver, which may show various degrees of damage, namely, cloudy swelling, fatty degeneration and focal or diffuse necrosis.

Symptoms.—When due to bacterial toxæmia the condition does not give rise to symptoms. It is recognised by the presence of a trace or cloud of albumin in the urine on boiling, and by the presence, in the centrifugalised deposit, of granular, hyaline and epithelial casts. In addition, there may be a few white blood corpuscles; when red blood corpsucles are present, or when there is frank hæmaturia, the differential diagnosis from an acute nephritis cannot be made with certainty. In the severer types with insidious onset, as in mercurial poisoning or in the toxæmia of pregnancy, the first symptom is often malaise, disturbance of digestion and constipation, accompanied by albuminuria and oliguria. Headache is a prominent symptom, and is often persistent. In the toxæmia of pregnancy a rising blood pressure or œdema may be the initial sign; the œdema is either general or it appears first in the lower extremities, as in cardiac œdema. Eye symptoms are important; there may be dimness of vision and flashes of light before the eyes, or rarely sudden blindness. On examination of the fundus oculi the disc may appear normal, or there may be œdema of the disc or partial detachment of the retina. The vessels are normal and hæmorrhages are rare. These symptoms may be followed by fits (hypertensive crises), but sometimes the fits occur without previous warning. In general, the symptoms of a fully developed case are clinically indistinguishable from those occurring in the uræmia of true nephritis. The urine contains up to 3 or even 4 per cent. protein. Hyaline, granular and epithelial casts may be present, and may be very numerous; white blood corpuscles may be present, though few in number. In severe cases, the urine contains blood-cell casts, the result of capillary thrombosis and extravasation of blood.

Diagnosis.—The diagnosis depends on the recognition of the signs and symptoms of kidney disease in a patient affected by one of the known causes of toxæmic kidney, and on certain biochemical tests by which a true nephritis can be reasonably excluded. In milder cases, the possibility of the symptoms

being due to heart failure must be excluded. Complete recovery is in favour of the diagnosis of toxæmic kidney. Exacerbation of a chronic nephritis can be recognised by a history of previous nephritis and the presence of definite cardiac hypertrophy and arterial changes. The difficulties are sometimes considerable, however, since a marked rise of blood pressure may occur in a toxæmic kidney, while advanced degrees of chronic nephritis may occur without cardiac hypertrophy, increased blood pressure or clinical evidence of arterial disease. The blood urea is normal in the toxæmic kidney; whereas in chronic nephritis the blood urea tends to rise, and may reach 300 mgm. or even more. In the toxæmia of pregnancy, the appearance of albuminuria in the early months of pregnancy is in favour of the condition being one of chronic nephritis, whereas the albuminuria due to toxæmia generally makes its first appearance in the later months.

Prognosis.—The importance of recognising the toxæmic kidney is that both the immediate and ultimate outlook are better than in nephritis of apparently equal severity. The prognosis in the single case depends on the nature of the cause, the degree of its severity, and the possibility of its early and complete removal. Recovery, when it occurs, is complete, but in the severe cases chronic nephritis may supervene.

Treatment.—If not already in bed on account of the condition responsible for the toxæmic kidney, the patient should be immediately confined to bed. Treatment is directed towards eliminating the toxins and resting the kidneys. Barley water and milk and soda should be given. An easy but not loose evacuation of the bowels must be secured daily by the use of magnesium sulphate, jalap, senna, or compound liquorice powder. A simple diuretic and diaphoretic mixture, such as potassium citrate grs. 15, liq. ammon. acetatis min. 60, sp. ætheris nitrosi min. 15, aq. chloroformi ad ½ oz., is given in water every four or six hours. The intake of solids is limited. At the same time, since there is no retention of urea in the blood, it is unnecessary strictly to limit the intake of protein. Soups, meat extractives and condiments are to be withheld. The action of the skin may be stimulated with hot packs or hot baths. The fits are best treated by venesection. The above outline of treatment is for the severer cases; for the febrile albuminurias, special treatment for the renal condition is not required.

NEPHROSIS

This form of Bright's disease is characterised by œdema, marked albuminuria, and two characteristic changes in the blood, namely, a fall in the plasma albumin and increase of cholesterol. It is distinguished from the glomerulo-tubular type of acute nephritis by the absence of hæmaturia, cylindruria, hypertension and urea retention, and also by the fact that anæmia is less often present in nephrosis or, if present, tends to develop only at a late stage.

Ætiology.—In most cases no ætiological factor is established, and the first evidence is the onset of œdema without previous illness. In the remainder the best established cause is syphilis. Tuberculosis and osteo-myelitis may be ætiological factors. There may be a recent history of chill, of upper respiratory tract catarrh, or of gastro-enteritis. It may be that streptococcal

infection, more especially of the upper respiratory tract, is a cause of the complaint.

Pathology.—The condition of the kidney is that of toxæmic kidney in a more severe form, the fatty changes in the tubules being very marked.

Symptoms.—The disease is generally first recognised by the gradual or rapid onset of œdema, which gradually increases and tends to become massive. The œdema may be generalised, affecting the scalp, hands, trunk and legs. It is often first noticed as puffiness of the eyelids, or it may first appear as a swelling of the feet and ankles extending up the legs. The patient may feel quite well apart from the disability caused by œdema. On the other hand there is more usually complaint of malaise and fatigue, loss of appetite and nausea, and sometimes of epigastric pain. There may be cough and slight shortness of breath due to slight bronchial catarrh, œdema of the lungs or hydrothorax. Swelling of the abdomen may be the result of œdema of the abdominal wall or ascites. The face is pale and the eyelids and cheeks are puffy, but the mucous membranes are of a good colour, and the blood count is normal. The urine is reduced in quantity, its specific gravity is normal or raised, it contains a large amount of albumin, often amounting to 0·5 or even 1 per cent., and readings of 4 per cent. or even more have been recorded. The urinary deposit contains but a slight excess of cells and few or no casts. Red blood corpuscles are generally absent. The heart and blood pressure are normal, but a pericardial effusion may develop. There is no retinitis and no urea retention. Characteristic changes are found in the blood. The plasma albumin falls more considerably in nephrosis than in other forms of Bright's disease. The normal figures are plasma albumin 4·1 g. per cent., globulin 2·6 g. per cent., total protein 6·7 g. per cent., which gives an albumin-globulin ratio of 1·6 to 1. In nephrosis, plasma albumin may be 2 to 1 g. per cent., globulin 2·6 to 3 g. per cent., so that albumin-globulin ratio varies between 1:1 and 1:3. The blood cholesterol is raised to 300–800 mgm. per cent. (normal 130–200 mgm. per cent.).

Course.—The disease pursues a chronic course. In the first stage there is a gradual increase of symptoms. When the disease is fully developed it may remain more or less stationary for a number of months, at any time during which there may be some exacerbation or remission of symptoms. During an exacerbation the symptoms increase and convulsions may occur. After remaining stationary for some time, even up to 6 or 12 months, there may be a gradual remission of symptoms, and then complete recovery. In other cases an intercurrent infection, such as pneumococcal peritonitis, broncho-pneumonia, or erysipelas, is responsible for a fatal termination. Or the clinical picture of the disease may gradually take the form of chronic nephritis, in which case the œdema tends to become less, lethargy and fatigue increase, anæmia develops, the blood pressure gradually rises, cardiac hypertrophy follows, and death results from uræmia.

Diagnosis.—The differential diagnosis from nephritis is made on the absence of hypertension and hæmaturia, and the presence of a normal or low blood urea. The fall in plasma albumin and the rise in blood cholesterol are both greater in nephrosis than in nephritis. In nephrosis, cylindruria is relatively slight or absent, and anæmia is uncommon. The differential diagnosis from amyloid kidney may not be possible during life. The presence of splenomegaly, anæmia, and especially a chronic infection, such as chronic

osteo-myelitis (a potent cause of amyloid disease), would be in favour of the diagnosis of amyloid change.

Prognosis.—The importance of the recognition of nephrosis depends largely on the fact that complete recovery may occur even after the disease has been present for many months.

Treatment.—The possibility of a toxic cause, particularly syphilis, and to a slight extent bacterial or other toxæmia, should be borne in mind. Syphilitic cases may respond to specific treatment, which, however, must be prescribed with caution. Obvious sources of sepsis should be removed wherever possible. During the first stage of the disease, and indeed as long as there is good hope of recovery, the patient should be kept in bed and nursed between blankets. Fluid intake is limited to that short of causing thirst. During the early stage, when there may be some doubt as to the differential diagnosis from subacute nephritis, the patient should be put on a diet of low protein and salt content. When the diagnosis is established, and the low plasma protein confirmed, adequate protein is given to maintain nitrogen equilibrium. This means something more than 1 gr. per kilo of body weight per diem : in some cases a high protein intake seems to be beneficial, though this treatment has not fulfilled the expectations originally formed. It is not usual now to order a completely salt-free diet, though it is advisable not to permit the addition of salt at the table. If the blood cholesterol is high, the intake of fat should be restricted. The bowels are regulated with magnesium sulphate or some other bland laxative, such as senna pods or compound liquorice powder. Constipation and loose stools are both to be avoided. In some cases the administration of potassium salts is effective in producing diuresis and reducing the œdema, but must be given very cautiously to avoid depressing the heart. The maximum dose given is 120 grs. daily of a mixture containing equal parts of potassium bicarbonate and potassium citrate. Perhaps the best diuretic in such cases is urea by the mouth in doses of 30 to 60 grs. three times a day ; considerably larger doses are sometimes given, but in that case the blood urea should be watched. Thyroid has been advocated by some observers. It acts presumably by raising the basal metabolic rate, which is often low in nephrosis. When other means have failed and considerable œdema persists, decapsulation should be seriously considered. It is quite often temporarily or even permanently effective in curing, or at least greatly reducing, the œdema. It has not, in our experience, affected the albuminuria so dramatically as it may the œdema, but on occasion it has seemed to determine a favourable turn in the course of the disease. Opportunities for symptomatic treatment should be looked for, such as the treatment of anæmia with iron, or some slight degree of heart failure with digitalis, or the control of sleeplessness, loss of appetite and dyspepsia, depression and nervous agitation.

ACUTE NEPHRITIS

The classical form of acute nephritis is hæmatogenous in origin and essentially glomerulo-tubular in distribution. Such a definition would exclude an ascending infection of the tubules from the pelvis of the kidney, such as occurs in pyelonephritis. It would also exclude the embolic nephritis of

infective endocarditis, where inflamatmory foci are set up in the kidney as the result of septic emboli reaching it from the heart. These produce marked fibrinous exudation and infiltration with leucocytes; but only some capillaries in some of the glomeruli are affected.

Ætiology.—Acute nephritis was formerly not a common disease. Herringham found, at St. Bartholomew's Hospital, where the average number of medical cases is 7000 a year, that there were, in a period of 9 years, only 166 cases, 120 being in males. On the other hand, a large number of cases occurred in the epidemic of acute nephritis in the War of 1914–1918, 1500 being recorded in Flanders alone during 1915. Since the War of 1914–1918 it would appear to have become more frequent.

The causes usually given for acute nephritis are as follows:

1. Acute Specific Fevers.—Scarlatina is undoubtedly the commonest specific fever to produce it. Goodall found nephritis in 8·4 per cent. of all cases of scarlatina. Nephritis is an occasional complication of typhus, small-pox, chicken-pox and mumps. Syphilis, malaria and yellow fever may also cause it. Many cases of nephritis are preceded by tonsillitis, or otitis media, and it is probable that the throat is often the door of entry for the infection.

2. Diseases of the Respiratory Tract.—It may also occur as a complication of other acute infections of the respiratory tract. The commonest bacterial agent is the streptococcus.

3. Diseases of the Skin.—The frequency with which acute nephritis may follow burns or extensive skin diseases is interesting, in view of the physiological connection between the kidney and the skin. It is a not infrequent complication of erysipelas, impetigo, boils, pemphigus and dermatitis. It must be remembered, also, that children who have been burnt are very liable to develop true scarlatina as well as a mere septic rash, and that streptococcal infection may be the responsible agent.

4. Diseases of Other Systems.—Acute nephritis may also be a complication of acute infections of other systems. Purpura, which is probably toxic in origin, may be accompanied by a true nephritis.

5. Epidemic Type.—In the American Civil War and in the War of 1914–1918 acute nephritis occurred as a primary disease in an epidemic form, characterised by dyspnœa at the onset, and in general by a benign course. In the fatal cases, inflammatory and thrombotic lesions were found in the lungs and spleen.

It is a very common idea that cold or chill is a cause of acute nephritis. The statistics of the army epidemic go far to disprove this. For, during the first winter, when there was much wet weather, and the men were much exposed, cases were few and far between, and not until the weather was better did the disease assume epidemic proportions. On the other hand, a patient who has nephritis is more susceptible to cold, which may provoke an exacerbation. Where exposure seems to be responsible for acute nephritis, examination will generally reveal some definite evidence of an old-standing lesion of the kidneys. Conformably with that, after the first winter of the war, there was an agreement between the incidence of nephritis in the army and low temperature.

Pathology.—The kidney is swollen, with occasional punctiform hæmorrhages over a pale, greyish surface. The cortex is increased and, on section, its pallor contrasts with the deep red medullary cones. Microscopically, the

Quaeckie Dysentery also gives rise to
acute diffuse [illegible]

glomeruli are swollen, becoming pear-shaped and protruding into the first part of the convoluted tubules, with Bowman's capsule tightly stretched over them. In these glomeruli the nuclei are less distinct, and the capillaries show fatty changes in their walls. The capillary loops become filled with exudate and empty of red blood corpuscles; their lumina contain a fine network of coagulated substance and leucocytes. There is proliferation of the endothelial cells, and mitotic figures are not infrequent. A serous exudate and a varying number of red and white blood corpuscles may be extravasated between the layers of Bowman's capsule. The convoluted tubules have their lumen blocked either by the swelling of their epithelium or by débris, casts and blood. The interstitial tissue is swollen and œdematous, with hæmorrhages here and there, and sometimes lymphocytic infiltration. The arteries of the kidney show little alteration except that some of the afferent arterioles share in the glomerular changes.

Symptoms.—The onset is usually acute, though occasionally it may be rather insidious. In the latter instance the patient may complain of biliousness, nausea, vomiting and abdominal pain, with headache and sometimes diarrhœa before the onset of renal symptoms. In the cases with acute onset, he may have more or less severe pain in the back, and œdema soon develops. It usually starts in the face; the legs and scrotum are generally involved next, and the swelling soon spreads all over the body. Occasionally the dropsy is curiously localised and fugitive. Though dyspnœa is not regarded as a common feature of acute nephritis apart from uræmia or cardiac failure, in the army epidemic it was almost invariable at the onset. As a rule, shortness of breath started at the same time as the dropsy, but did not last so long, having ceased at the end of 2 or 3 days. There is usually only slight fever, though occasionally a temperature of 102° or 103° may be reached. Some irregularity of temperature, however, is common in the first week or 10 days. The pulse may be raised in tension and the blood pressure is generally raised. Occasionally the serum is milky, as was pointed out by Bright. The skin may be dry and itching, with occasionally a papular or erythematous eruption. Retinal hæmorrhages rarely occur.

The urine is greatly reduced in volume, and may be entirely suppressed. Eight to 12 ounces would be an ordinary figure. It is dark in colour and usually contains obvious blood. This may render the urine as dark as porter, but it may be bright red or merely smoky. Sometimes the blood forms a flocculent, reddish-brown precipitate. The urine is usually loaded with albumin, and casts will be found on microscopical examination. At first blood casts and epithelial casts will alone be found; but, at a later stage, granular and hyaline casts will appear. Fatty casts are not found in the first attack of acute nephritis. Their presence suggests a recrudescence of a chronic disease. Isolated renal cells, transitional epithelium and squamous cells from the lower urinary tract are also commonly found. Micro-organisms are not usually observed, and their presence in any number would suggest that the case is more probably one of pyelonephritis. A sudden rise in the secretion of water after a few days is usually a sign of definite improvement.

The sedimentation rate is raised in acute nephritis, and, in favourable cases, its fall is closely related to the reduction in hæmaturia, but when there is continued activity of the disease-process a raised sedimentation rate is the

rule (Oakley). In the presence of nephritic œdema the sedimentation rate is very high in contrast to the low rate of cardiac œdema. This is due to the alteration in plasma proteins in the former condition, and especially to the increase in plasma fibrinogen.

Complications may be due to three main causes.

1. *Renal failure, i.e.* uræmia may develop. Some slight uræmic symptoms are common in acute nephritis, such as headache, dizziness, nausea and vomiting. But any of the forms of uræmia described later may assert themselves. Convulsions are the most common of the severe symptoms, but are not as grave in significance as in chronic nephritis. If treated promptly, recovery may follow.

2. *Extension of the œdema.*—Water-logging of the lungs may occur, producing serious dyspnœa; but this is sometimes chiefly due to cardiac failure. In any case it is serious. A milder degree of bronchial catarrh is quite common. A rare but very dangerous complication is œdema of the glottis, which calls for prompt treatment.

3. *Secondary infections.*—The subjects of nephritis are always liable to secondary infection, and these are particularly apt to affect the serous membranes; therefore pleurisy, pericarditis, and peritonitis are not uncommon complications. The last two are very dangerous.

Sequelæ: If complete resolution does not occur, the patient will develop chronic nephritis of the secondary type (see p. 1309).

Diagnosis.—The combination of dropsy, albuminuria, hæmaturia, casts and scanty urine usually makes the diagnosis quite easy. The differential diagnosis of acute nephritis from an exacerbation of chronic nephritis may be difficult. Definite evidence of cardiac hypertrophy and arterial changes would be in favour of the latter. The presence of granular casts at the outset, or of fatty casts at any time, is suggestive of chronic disease. An infarct in the kidney which causes a pain in the back and hæmaturia may simulate nephritis, but general dropsy is not likely to occur, nor are casts present in the early stages. Great reduction in the volume of urine is not usual. It must be remembered, however, that infarcts may start foci of nephritis. Signs of septic endocarditis would suggest infarction. In chronic interstitial nephritis there may be a smart hæmorrhage, but the abundant urine of low specific gravity and the cardio-vascular signs would lead to a correct diagnosis. The renal hæmorrhage in the early stage of new-growth of the kidney is so profuse that confusion with acute nephritis is not likely to occur. Moreover, epithelial casts would not be found, though a large blood cast from the pelvis of the kidney is a very characteristic feature. Pyelitis may give rise to some confusion, as there may be small hæmorrhages, especially at the beginning. The presence of micro-organisms in a catheter specimen and abundant blood corpuscles, with only a haze of albumin, in the absence of casts, will generally make the diagnosis clear. Moreover, general dropsy does not occur in pyelitis unless it sets up severe nephritis as a sequel. In any case of hæmaturia, especially when it is associated with profound constitutional disturbance, loss of weight, tachycardia, continued fever and peripheral neuritis, the diagnosis of peri-arteritis nodosa must be considered (*q.v.*). Lastly, in septicæmia, particularly streptococcal and complicating an ascending infection of the urinary tract, the possibility of acute interstitial nephritis should be borne in mind. The diagnosis will be suggested by the presence of albumin-

uria and oliguria, or by symptoms of uræmia complicating septicæmia. The diagnosis is usually made post mortem.

Prognosis.—The prognosis naturally depends on the severity of the disease. It is better in those cases where there is a discoverable cause, an acute onset, and where the patient comes under treatment promptly. Recovery is usually slow, and the criterion of the cessation of the acute stage is the disappearance of red blood corpuscles from the urine.

Volhard distinguished a separate form of acute nephritis under the name of acute focal nephritis. Its onset is sudden, and recovery is the rule. It is recognised clinically by the presence of hæmaturia and albuminuria without œdema, hypertension or urea retention. There is little constitutional disturbance. It is more frequent in children than in adults, and it is said to occur in epidemics. Its ætiology is the same as that of acute diffuse nephritis. It is doubtful if it can be regarded as a distinct clinical entity, but we recognise it to this extent that acute nephritis having these clinical features carries with it a good prognosis, and recovery is to be anticipated in 2 to 4 months. Mild cases recover sooner. When in addition to the above clinical picture there is added hypertension, urea retention, moderate albuminuria and some degree of anæmia, the course of the disease is likely to be longer, and 12 months' duration with complete recovery is not uncommon. We have experience, too, of complete recovery after an illness of 2 years' duration in severe cases of the above type. When in addition to the above there is considerable œdema and massive albuminuria with hæmaturia, and with or without hypertension, the ultimate outcome of the disease cannot be foretold, but in general terms a somewhat better prognosis should be given in acute and subacute nephritis than the present condition of the patient seems to justify, especially for the reason that it encourages persistence with treatment. The disease is rarely fatal in the acute stage. In the subacute stage, namely, after the first 3 weeks of illness, it may enter a stationary phase, or become slightly progressive. The patient may die from uræmia, secondary infections or extension of the œdema to vital structures. The longer the duration of the hæmaturia, even if it be a microscopic hæmaturia, the more likely is there to be some permanent damage to the kidney, and the development of chronic nephritis.

Treatment.—(*a*) PROPHYLACTIC.—The best prophylactic measure is prompt and efficient treatment of any infective process liable to set up nephritis. There is evidence to show that the routine administration of alkalis in scarlet fever diminishes the incidence of acute nephritis. The enucleation of obviously infected tonsils, especially when an attack of tonsillitis has been accompanied by albuminuria and cylindruria, is advisable. The early administration of scarlatina antitoxin serum in a severe case of scarlet fever is prophylactic treatment of nephritis complicating this disease.

(*b*) CURATIVE.—The indications are to remove, if possible, the microbic or toxic cause at work and to ensure such physiological rest for the kidney as is practicable; to promote elimination of nitrogenous and saline waste by other channels; to treat complications as they may arise and to correct the resulting anæmia. In this way much may be done to steer the patient towards recovery, although we can do little to control the course of the inflammatory process. The patient is naturally kept recumbent in bed. To counteract the congestive effects of gravity, it is well to move him from

side to side, and occasionally to put him on to his chest. He should be clad in a flannel nightgown, and be placed between blankets to guard against chills and to encourage free action of the skin. The room should be warm and well ventilated. If suppression of urine threatens, dry cups or poultices should be applied over the loins. This measure is sometimes successfully adopted to diminish hæmaturia.

Diet.—In acute nephritis, the danger of overloading the inflamed kidney with nitrogenous substances is hardly sufficiently recognised; whilst in chronic nephritis the dietetic restrictions are apt to be too severe. The dictum that "in acute affections we concentrate our attention on the diseased organ, whilst in chronic cases we keep the general condition of the patient more in view," applies particularly to the treatment of nephritis. Nitrogen retention is common and a source of danger, so that the free administration of milk usually recommended is open to objection, since cow's milk contains 4 per cent. of protein, which equals 0·56 per cent. of nitrogen. It will do little harm to deprive the patient of nitrogen for a time, and von Noorden advises restriction of the diet at the outset to fruit juice, water and sugar. Where there is no nausea, toffee is allowed, which, being composed of butter and sugar, throws no work upon the kidney. It is generally appreciated by children and allays hunger. Barley water, with a little milk added, may also be given, and as the patient improves the proportion of milk may be increased. It is quite unnecessary to give anything else for a few days, and the relatives' fear of starvation may be allayed by explaining the rationale of the treatment. The excretion of nitrogen is reduced to its lowest level by giving a diet of fats and carbohydrates, when it may fall below that of a fasting person, as was shown by Folin; but excess of fat is inadvisable for reasons given under chronic nephritis. It is well to restrict or withhold table salt and substitute a mixture of formates, citrates and phosphates, such as ruthmol. The fluid intake and urine output should be measured, and a written record kept of total quantity of fluid taken in and excreted every 24 hours. The patient should not be allowed to be thirsty, but generally speaking the amount of fluid allowed in the day should not exceed 3 pints for an adult or 30 oz. for a child of 12. There may be a sudden diuresis after some days, and it is a sign of recovery. It is sometimes termed a "critical diuresis," and after its occurrence the quantity of water and milk taken may be increased. A drink prepared by adding 1 pint of boiling water to 60 grains of potassium acid tartrate, half a lemon, and some sugar, stirred occasionally until cold and then strained, may be allowed throughout in moderate quantities. The citric acid and the tartrate become bicarbonates in the blood and may render the urine less irritating by making it less acid; apparently it is not as easy to render urine alkaline in a severe case of acute nephritis as it is in the normal individual. Beef-tea, broth and meat juices are all to be condemned as imposing work on the kidney with very little corresponding nutritive advantage.

General Treatment.—The bowels are kept open by a daily laxative such as pulv. jalapæ co., magnesium sulphate or sodium sulphate, or a preparation of cascara. It is important to secure an adequate and easy evacuation of the bowels, but loose stools should be avoided. Occasional constipation is better treated with an enema than by a large dose of laxative. The function of the skin is promoted, and protection from chill is secured by

keeping the room warm and well aired. The patient is nursed between blankets, and wears a flannel nightgown or a vest, preferably with long sleeves, under the night attire to which he is accustomed. By this means the skin is kept warm and at an even temperature. In addition, the patient should be sponged with hot water followed by friction with warm dry towels. More drastic measures are seldom called for in acute nephritis unless uræmia is impending, when the hot-air bath may be of service.

In the acute stage stimulating diuretics are contra-indicated. Saline diuretics, such as potassium citrate, may be given. In so far as saline diuretics, such as potassium citrate, produces diuresis, they do it by raising the osmotic pressure of the blood, and thus drawing water from the œdematous tissues. The following prescription is mildly diaphoretic and diuretic:

Pot. cit., grs. 15.
Liq. ammon. acetatis, min. 60.
Sp. æth. nitr., min. 15.
Aq. camph. ad fl. oz. 1. To be taken every 6 hours.

The addition of 5 minims of tincture of digitalis is advisable if the heart's action becomes weak.

Treatment of Complications.—For the treatment of renal failure, see Uræmia. Pleurisy, pericarditis, or peritonitis should be treated on ordinary lines. Œdema of the glottis may call for scarification of the larynx or even tracheotomy.

After-treatment.—Bed is imperative until red blood corpuscles have disappeared from the urine and is advisable until albuminuria has ceased altogether. This may be impossible, since acute nephritis may go on to chronic nephritis, but there is a considerable advantage in prolonging the rest as much as possible. Bread, butter, vegetables, puddings, eggs and then fish may be gradually added to the diet, according to the scale given under chronic nephritis, as the hæmaturia and albuminuria diminish, but abstention from meat is advisable for some time, and meat extracts had better be altogether avoided. If anæmia develops, iron is given in the form of ferrous carbonate 45 grains, or ferrous sulphate 9 grains, daily in divided doses after food. Chills should be guarded against in every possible way, and the loins may be protected by wearing a well-fitting cholera belt.

CHRONIC NEPHRITIS

(*a*) Secondary Type.

It is generally agreed that chronic nephritis involving the parenchyma of the kidney is diffuse from the first, though naturally the interstitial changes take longer to manifest themselves. It is certain that when parenchymatous nephritis has existed for any length of time, there will be interstitial change as well. On the view here adopted, "chronic parenchymatous nephritis" or large white kidney is the subacute stage of a glomerulo-tubular inflammation. If the patient lives long enough, the kidney will pass into the contracted stage, formerly known as small white kidney.

Ætiology.—It is most frequently the sequel of acute nephritis, though

the initial attack may have been so mild as to have escaped notice. Severe forms of toxæmic kidney, such as mercury poisoning, and the kidney of pregnancy, as also nephrosis, develop into chronic nephritis if they fail to clear up.

Pathology.—The kidneys are swollen. The capsule strips easily, leaving a smooth whitish-grey or mottled surface on which the engorged stellate veins are very obvious. On section the cortex is increased in thickness and pale in colour; the normally distinct fine radial markings are blurred; the pyramids are relatively engorged and contrast with the pale cortex. Microscopically, the glomeruli are large and irregular, with an increase in the number of nuclei, and individual endothelial cells have undergone hyaline or fatty degeneration. Proliferation of the cells of Bowman's capsule is found with crescent formation, and adhesion of the visceral to the parietal layer of Bowman's capsule. There is peri-glomerular infiltration of leucocytes, and the capillaries outside the glomeruli are engorged with blood, the glomeruli themselves being relatively bloodless. The cells of the convoluted tubules undergo cloudy swelling and fatty degeneration to a greater or less extent. Desquamation of the cells occurs, and the tubules contain hyaline and epithelial casts, or red and white blood corpuscles. In some cases of chronic nephritis the tubule changes are most marked, and the glomeruli are relatively little affected in the earlier stages of the disease. As time goes on fibrosis increases, the kidneys shrink in size, their surface becomes granular, and the capsule thickened and adherent. The kidneys are tough on section; the whole surface is a more uniform brownish colour, or in extreme cases of fibrosis, whitish-grey. The cortex is narrowed; the cut vessels may be a little prominent. Microscopically, many of the glomeruli may have undergone hyaline degeneration and fibrosis. In others, crescent formation is marked; there is increase of fibrous connective tissue around the capsules, and small cell infiltration. The tubules tend to dilate and become tortuous, and their lining cells flattened. In others there is hypertrophy of the tubules to compensate for units which atrophy and disappear completely. In some cases the vasa afferentia undergo intimal hyperplasia and fatty degeneration, and there may be hypertrophy of the media. When the blood pressure was persistently raised during life, the heart, especially the left ventricle, will be found hypertrophied. The aorta is thickened, and ordinary atheromatous changes may occur at an unusually early age.

Pathology of œdema in chronic parenchymatous nephritis.—Dropsy is one of the most characteristic features of the disease. Various explanations have been given of its causation. One of the earliest was that it was due to hydræmia from retention of water which the kidney could not excrete. But even total anuria need not cause dropsy, and Rowntree has shown that in glomerulo-nephritis the blood volume may be within normal limits. The next hypothesis was that the capillary endothelium was damaged by toxins, and therefore became unduly permeable (Cohnheim). It has been shown experimentally, however, that such damage may actually hinder the passage of fluid from the blood to the tissues. Widal attributed œdema to the defective elimination of salt by the kidney, which led to accumulation of water by raising the osmotic pressure of the tissues. But if water is retained, salt must also be retained, and when diuresis is produced, salt is excreted also. An important observation was made when Epstein showed that a feature peculiar to nephrosis and to chronic nephritis with marked

œdema was a great reduction in the protein content of the blood and exudates, almost entirely affecting the albumin, so that the amount of globulin is always increased relatively and sometimes absolutely. The daily drain on the protein may even amount to 10 per cent. of the total protein in the blood. This causes a fall in the osmotic pressure of the blood, giving the tissues the controlling power to absorb and retain fluid. In support of this view it may be mentioned that the œdema produced in perfusion experiments with normal saline or Ringer's solution is prevented by the addition to the perfusing fluid of colloids which are in osmotic equilibrium with the colloids of the lymph and tissues. A weak point in this hypothesis is its failure to explain the dropsy of acute nephritis, which comes on long before any depletion of the proteins of the blood can occur.

But the most usually accepted explanation of renal dropsy to-day is an alteration of the affinity of the tissue cells for water as the result of an altered salt metabolism, especially in respect of the sodium ions. In other words, the œdema is regarded mainly as a result of damage to the extra-renal tissues by the same agent that damaged the kidneys, rather than as a consequence of the failure of renal function.

That the blood serum in nephritis may be milky was noted by Bright, and subsequent observers have called attention to pseudochylous ascites in this disease. This is due to the increased cholesterol content, which is more marked in this type of Bright's disease than in any other, except nephrosis.

Symptoms.—These may be continued from those of acute nephritis. More usually there is an interval of apparently normal health. Then the patient begins to suffer from languor and digestive disturbances, followed by the combination of anæmia and dropsy, which gives rise to a very characteristic aspect. Hence the saying "large white kidney, large white man." The dropsy may extend to the serous sacs. The urine is scanty, probably 20 ounces or less in the day; its specific gravity is high, but urates are not so abundant as in the urine of the cardiac kidney. It contains a large amount of protein, usually about 0·5 per cent., as measured by Esbach's method. Numerous tube casts will be found on sedimenting the urine, epithelial, fatty, granular and hyaline forms all being present. Red blood corpuscles may be found from time to time. Examination of the blood may show no increase in the blood urea.

Vomiting and diarrhœa are common and troublesome. Ulceration of the colon, probably due to the vicarious elimination of toxins by the bowel, is an occasional and dangerous complication. Areas of exudate, known as "cotton-wool" patches, and œdema of the optic disks—constituting albuminuric retinitis—may be found in severe cases. There may be dyspnœa, due to acidæmia, the result of diminished excretion of acid sodium phosphate. Secondary infections of the lung, pleura, pericardium or peritoneum may occur.

If hypertrophy of the heart and a rise of blood pressure fail to take place, the outlook is very grave, and death from uræmia or secondary infection is likely to close the scene. If, on the other hand, the blood pressure rises, the heart hypertrophies, the dropsy subsides, and a more chronic stage supervenes. The output of the urine then increases, probably up to 80 oz. or more; the specific gravity being persistently low. This is due to failure of the kidney's

capacity to concentrate the urine. The quantity of albumin is very variable, but is always more than that of "chronic interstitial nephritis." Epithelial, fatty, granular and hyaline casts continue to appear unless they are disintegrated by the extreme dilution of the urine. Towards the end the secretion is sure to fail, and uræmia is likely to follow. Signs of cardiac hypertrophy can be detected, and the blood pressure is generally raised to something between 160 and 220. Albuminuric retinitis is more likely to occur now. Later, silver wire arteries, retinal hæmorrhages, which are often flame-shaped, and even glistening white patches are sometimes to be noted. Infarction of the lung may occur, causing pain, dyspnœa, hæmoptysis with signs of consolidation, and perhaps pleural friction. It results from detachment of a clot in the right auricular appendix, and, being generally due to a secondary infection, marks a definite step downwards. There may be other signs of infection, such as pericarditis or peritonitis. But in the absence of complications life may be prolonged for several years.

Diagnosis.—The combination of dropsy, anæmia, albuminuria and cylindruria generally makes the diagnosis of chronic nephritis easy. In the dropsy with albuminuria of failing heart the œdema first occurs in the most dependent parts, while in nephritis the eyelids are first affected. In cardiac dropsy the liver will probably be enlarged and tender, and the urine will be high in colour and loaded with urates; the only casts it will contain are hyaline; renal function is not seriously impaired. Amyloid kidney may be accompanied by cachectic dropsy; but the heart will not be hypertrophied and the blood pressure is not raised. Moreover, a cause for amyloid disease, and the presence of amyloid disease elsewhere, are usually obvious.

If there is no œdema the diagnosis has to be made from functional albuminuria, residual albuminuria and chronic interstitial nephritis. Functional albuminuria only occurs before thirty and generally about puberty, albumin is absent from the urine secreted in the recumbent posture, casts are absent, with the possible exception of the hyaline variety, and calcium lactate may clear up the albuminuria for a time. Residual albuminuria, an uncommon condition, is not an indication of a progressive disease. The albuminuria is detected accidentally, there being no symptoms. The blood pressure may, however, be slightly raised. There are no cells in the centrifuged deposit of urine. In "chronic interstitial nephritis" the specific gravity of the urine is very low, and there is little albumin. Unless the heart is failing there will be no œdema. The estimation of blood urea should be carried out whenever there is a question as to renal efficiency. As in acute nephritis the erythrocyte sedimentation rate is always raised.

Prognosis.—The outlook in chronic nephritis is always serious. It is essentially a progressive disease, but with care life may be prolonged for several years. Death may occur from uræmia, heart failure or secondary infections. Retinal changes make the prognosis more serious, and "woolly" exudate with swelling of the optic disc generally foretells death within two years. Retinal hæmorrhages and discrete white patches of degeneration in the retina are, however, of less serious significance.

Treatment.—It is essential, as a prophylactic measure, that the treatment of all cases of acute nephritis should be thorough and prolonged. Septic foci, especially in the tonsils, should be looked for and thoroughly treated, as also should any syphilitic or malarial infection Confinement to

bed is only advisable during exacerbations, when dropsy is extreme, or when uræmia is threatening. The skin should always receive attention, and patients should sleep between blankets and be careful to avoid exposure to cold and wind.

Diet.—There has been a tendency to restrict the protein intake too much, since there is no evidence that the albuminuria is influenced by the amount of protein in the food. Epstein has urged, indeed, that a high protein diet is indicated in order to raise the low protein content of the blood, while fats should be avoided to diminish lipæmia. That such a diet may markedly reduce œdema is true, but not necessarily by raising the protein content of the blood. Probably the diuretic action of the urea formed from the high protein diet is partly responsible. It is, therefore, wise to estimate the blood urea and, if it is not raised, to carry out the urea concentration test (p. 1286), and only to make use of the high protein diet if this test shows at least 2 per cent. of urea. If it is below that figure the protein intake may be calculated on the basis of 1 G. of protein a day for every kilo of body-weight. Naturally, meat extracts and cellular organs, such as liver, kidney and sweetbread, should be avoided, because they contain a large amount of purin; that has to be excreted by the damaged kidney, which eliminates uric acid with difficulty. This is contrary to the principles of physiological rest but, equally, such restrictions of diet must be avoided as would lead to failure of appetite and consequent wasting, while incapable of diminishing the albuminuria. A much greater variety of diet than is usually allowed might be permitted; cooked eggs and dishes made from eggs may certainly be taken. Raw eggs, however, contain certain indeterminate substances which may irritate the kidney. The distinction drawn between red and white meat is fallacious. Red meat is assumed to be more injurious, presumably because it is supposed to contain more purin, whereas the reddest meat contains far less than sweetbread. Chronic nephritics should not be restricted to milk, which is too dilute a form of food for them, and may increase the dropsy. An entirely salt-free diet is not to be recommended, though moderate restriction in this respect is probably wise. Salt can be replaced by lemon juice or ruthmol. In this way we can avoid increasing the miseries of an incurable disease by unnecessary restrictions. If nitrogen retention exists as shown by estimations of blood urea, a diet poor in protein should be taken on one day in each week. Indeed, a day when the diet is restricted to fruit and sugar is often as useful in chronic nephritis as is the day of vegetable and egg diet in diabetes. But prolonged nitrogen starvation is as bad for the nephritic as for any one else, and in some cases increases the water-logging of the tissues.

Generally speaking, alcohol is inadvisable in any form, and should never be ordered to those unaccustomed to it. In those who have been taking it regularly, deprivation may interfere with appetite, in which case a little well-diluted whisky is probably as innocuous as any form of alcohol can be. But the strictest moderation must be enjoined. Tea and coffee used to be forbidden, because of the methyl-purins they contain, but in our opinion this restriction is unnecessary.

Diuretics.—Diuretics should be used with caution in chronic nephritis. When there is marked œdema the fluid intake should be limited to a litre or perhaps 2 pints in the 24 hours, but the patient should not be allowed to be thirsty. In some cases the administration of potassium salts by mouth acts

as an efficient diuretic (*vide* treatment of nephrosis). Saline diuretics in the form of citrates and acetates may be safely given, provided that the dose is moderate, and that the possibility of alkalosis developing in severely damaged kidneys is remembered. Urea may be given in those cases in which the blood urea is low, and in which the danger of a rising blood urea is not anticipated. The caffeine group of drugs should be employed with caution, and when used they are best given in small doses, and then withheld if diuresis does not result. Theophylline and sodium acetate grs. 4, or theobromine and sodium salicylate (diuretin) grs. 10, administered twice or three times daily may be prescribed if there is no hæmaturia. In general terms organic mercury preparations are contra-indicated in chronic nephritis on account of the danger of mercury-poisoning. Nevertheless, in cases in which œdema is persistent, renal function is adequate and there is an absence of anæmia, injection of mersalyl (salyrgan) may sometimes be used with advantage. Sixty or 120 grains of ammonium chloride are given on each of 2 days before ½ to 1 c.c. of the drug, and, if tolerated, this treatment is repeated at intervals of 5 to 9 days. Œdema in chronic nephritis may be in part due to heart failure. In this case digitalis may prove a valuable and efficient diuretic. A raised blood pressure is not a contra-indication to its use.

A marked feature of chronic nephritis is the defective adjustment of the kidneys to varying water supply. As in acute nephritis, the drinking of large amounts of fluid may, therefore, merely increase the œdema.

As explained under Acute Nephritis, the saline diuretics are the least open to objection; since they draw the extra water from the tissues they cannot increase and may diminish the œdema. Urea as the natural diuretic of the body is often given in doses of 45–60 grains three times a day, when there is no nitrogen retention.

Diaphoretics.—The arguments for and against diaphoretic measures will be found under uræmia. Diaphoretic drugs are not suitable for the routine treatment of chronic nephritis, as a moist perspiring skin renders the patient more liable to chills—always a danger in this disease. A course of hot-air baths may sometimes be helpful when there is evidence of salt retention. If they are followed by diuresis they are doing good.

Purgation.—Although efficient action of the bowels must be maintained, habitual loose stools are to be avoided, because they weaken the patient and promote the absorption of intestinal toxins. The special liability to mercurialism renders calomel unsuitable for routine treatment.

Acupuncture.—The patient is placed in a cardiac bed with the head raised and feet lowered for a day or two before acupuncture is performed so that the fluid gravitates into the lower limbs. The preparation for acupuncture consists of a mackintosh sheet placed under the lower limbs, and arranged to form a chute leading into a pail on the floor: the lower limbs from the knees to and including the toes are cleaned with ether soap, and then with spirit, and placed on sterile towels: the skin is covered with a coating of Lassar's paste. Acupuncture is performed with a medium-sized trocar from a Southey's tube set, the trocar being stabbed through the paste and skin to the subcutaneous tissues. Beginning at the side of the tendo Achillis, 15 punctures are made in line posteriorly in the lower two-thirds of the leg. Two lines of punctures about one inch apart are made in each

leg. Each leg is then wrapped in a piece of sterile jaconet, wrapped firmly round the thigh immediately above the knee, and secured with adhesive tape. Below the jaconet is wrapped loosely round the limb forming a tube which conducts the fluid into the mackintosh gutter at the foot of the bed. Drainage may continue for a week. By this method fluid may even be drained from serous cavities when there is marked dropsy.

Decapsulation.—This procedure is now reserved for the treatment of œdema in the nephrotic type of Bright's disease if adequate treatment on conservative lines has failed to relieve it.

Climate is a valuable help. In this country, Ventnor or anywhere on the south coast from Bournemouth westward is the most suitable climate that can be obtained. Egypt generally suits such patients particularly well. Madeira or California are also quite suitable. The wind and the more violent fluctuations of temperature on the Riviera render it much less advisable.

Treatment of complications. — These are uræmia, heart failure and secondary infections, such as pericarditis, pleurisy, colitis and peritonitis. Their treatment is discussed under those headings.

In conclusion, it must be recognised that the kidney, once chronic nephritis is established, cannot completely recover, and the main thing is to attune the mode of life to a low key, subjecting the patient to as little strain as possible. He may have a considerable variety of food, provided that the intake of protein is regulated in the way described above, and that he takes very little purin and salt. He can be helped by saline diuretics and unirritating preparations of iron, such as liquor ferri acetatis. He will do all the better if his medical man realises that many of the methods recommended in the treatment of this disease are impotent, where not actually harmful.

(*b*) Primary Type—Renal Dysbiotrophy

Chronic nephritis may develop without any known cause. In such a case there is no past history of acute nephritis; of symptoms of Bright's disease, such as œdema, hæmaturia or pain in the back; nor indeed any history of infection, such as scarlet fever or tonsillitis to which the onset of the disease can be attributed. The complaint may be found accidentally by the discovery of albuminuria in the course of routine examination. More often the diagnosis is first made at a later stage of the disease when there is complaint of asthenia, anæmia, or liability to fatigue. Sometimes, indeed, there are no symptoms of the disease until it has reached the terminal stage of uræmia.

Ætiology.—This form of chronic nephritis probably belongs to the group of congenital-developmental diseases of inborn and familial type, as defined by Parkes Weber. According to this view certain forms of chronic nephritis are inborn constitutional diseases which, though they may manifest themselves soon after birth, may sometimes be delayed in their appearance until years later. When the disease runs its course and ends fatally within a few weeks or months of birth, there can be no doubt of its having been present in utero. When it does not manifest itself until after many years of antecedent good health, we may assume that the disease was only potentially present at birth, the inborn tendency to its development being due to a congenital tissue inferiority or dysbiotrophy. The reasons for this view are: (1) the absence of a discoverable ætiology already referred to; (2) the not

uncommon familial occurrence of the complaint; (3) the finding post mortem of congenital abnormalities in the kidneys or urinary tract; and (4) that in its course, which is latent, progressive and invariably fatal, the malady resembles many other diseases which belong to this congenital-developmental class.

Familial hæmorrhagic nephritis, which is also hereditary and apparently congenital, is a rare condition. In one family 16 cases occurred among 28 individuals in 3 generations, 8 being in males, 7 of which ended fatally in early life, and 8 in females with only 1 death. The disease evidently runs a more benign course in the female. In one patient the first symptom occurred when only 3 weeks old, in another when 2 years old, while in the remaining cases the onset was quite early in life. Most of the cases have been characterised by recurrent attacks of hæmaturia, sometimes considerable in amount. As such attacks may be preceded by an increased nitrogen output, some inherited form of protein sensitivity seems a probable factor. As deafness may also be familial, it is interesting to note that it was marked in 5 of the 16 patients, and one otherwise healthy member of the family was also deaf. The condition usually terminates in uræmia.

Pathology.—The kidneys are small, pale and fibrosed. One kidney may be smaller than the other. Congenital deformity is not uncommon: occasionally one kidney is absent or represented by only a nodule of fibrosed tissue, from which an atrophied ureter has its origin. On microscopic examination there is diffuse fibrosis of the kidneys; many glomeruli are atrophied, others show varying degrees of inflammatory reaction.

Symptoms.—In the rare cases that appear in infants of a few weeks or a few months old, the symptoms are those of uræmia, namely, dyspepsia and loss of weight leading to diarrhœa, vomiting and cachexia. In those that develop about the age of puberty the disease may cause infantilism (renal dwarfism); and bone deformities resembling rickets often develop, and may be associated with a low calcium content of the blood, leading in some instances to a compensatory enlargement of the parathyroids. In one group of cases there is cardiac hypertrophy, a considerably raised blood pressure, and retinitis. In these arteriolar changes (diffuse hyperplastic sclerosis) are found post mortem. In others the blood pressure is normal or subnormal. In another group (first described by Rose Bradford in 1904) the disease makes its first appearance between the ages of 20 and 30 years. It may appear suddenly in the form of uræmia without warning, and become rapidly fatal. Even in those cases in which the kidneys are found post mortem to be white, fibrotic and greatly reduced in size, with diffuse inflammatory changes of long standing, early adult life may have been apparently perfectly healthy, and symptoms of the disease may have been present for only a few months.

Differential Diagnosis.—Loss of weight, a sense of fatigue, anæmia and dyspepsia, may have been so marked as to raise the question of tuberculous disease or neoplasm. When there is marked asthenia and pigmentation, Addison's disease may be suggested, or the differential diagnosis may lead to the suspicion of pernicious anæmia. In cases with high blood pressure a juvenile form of hyperpiesia must be excluded. When there is marked polyuria with urine of low specific gravity, the possibility of diabetes insipidus arises.

Treatment.—The disease is essentially progressive, and treatment can only be symptomatic.

CHRONIC INTERSTITIAL NEPHRITIS, INCLUDING MALIGNANT NEPHROSCLEROSIS

Synonym.—Granular Kidney.

When this term was first used it included a number of clinical entities, which together formed a somewhat motley group. Among these certain forms of chronic nephritis have now been identified as such, particularly the type recognised by Rose Bradford as the small white kidney, and classified by us under chronic nephritis, primary form. Clifford Allbutt identified hyperpiesia, Samuel West and others recognised the senile kidney. Some authors are inclined to think that after excluding these clinical forms only a single entity, malignant nephrosclerosis, remains. "Chronic interstitial nephritis," however, probably still includes more than one clinical entity, and it is for this reason that we have retained the term.

Ætiology.—The causation of malignant nephrosclerosis is unknown, but probably those factors which apply to hyperpiesia already described are concerned. Malignant hypertension, however, tends to make its appearance at an earlier age, and is not uncommon at any age after 35 years, and is frequent between the ages of 40 and 55. According to Ellis it is more common in men than in women. As to the other cases included under the term "Chronic Interstitial Nephritis," the ætiology is unknown, but gout, lead poisoning and alcohol are thought by some to be factors. Syphilis is not a cause.

Pathology.—The kidney tends to be reduced in size, is tough, and red in colour. The capsule is adherent, leaving a finely granular surface on stripping. Sometimes the capsule is thickened and splits on attempting to strip it, thus giving an erroneous impression of a smooth surface. Retention cysts may be seen, both on the outside and the inside of the organ. On section the cortex is reduced; not only is it shrunk from without inwards, making the organ smaller, but the increase of intrapelvic fat shows that it has also shrunk from within outwards. The vessels are unduly prominent. The glomeruli show signs of inflammatory reaction, and the interstitial tissue in their neighbourhood is increased and infiltrated with small cells, generally of the mononuclear type. These areas of disease are patchy, and form wedge-shaped areas, with their apex towards the cortico-medullary zone. The intervening areas of renal tissue show little or no change. The histological lesions in the arteriæ interlobulares and vasa afferentia, as also the patchy small-cell infiltration in the kidneys and evidence in some glomeruli of proliferation of the cells of Bowman's capsules, provide evidence of inflammatory reaction. The cardiovascular changes are those described under hyperpietic kidney (benign nephrosclerosis). In addition a characteristic lesion is acute arteriolar necrosis, while focal necrosis of the capillary tuft is common. Hæmorrhagic infarction of some glomerular tufts may be found. The distribution of the renal lesion in chronic interstitial nephritis is distinct from that in chronic nephritis, for in the latter the lesion is diffuse and every glomerulus is more or less altered in structure. In advanced cases of chronic interstitial nephritis, however, the extent of structural alteration extends and becomes more diffuse.

Symptoms.—The subject of chronic interstitial nephritis often fails to seek medical advice until the condition has become well advanced, and this

is partly because the body adjusts itself to the changes which are taking place in it as a result of the disease, and partly because the disease may develop very rapidly in its early stages. Common early symptoms are loss of energy, proneness to fatigue, lack of power of concentration, headache and dyspepsia. In other cases the patient feels well, and consults his doctor on account of hæmorrhage. The source of the bleeding is most commonly from the nose (epistaxis), or frank hæmaturia. In other cases it may be a cerebral vascular accident, thrombotic or hæmorrhagic: less often it takes the form of hæmatemesis or melæna. Disturbance of vision due to retinal hæmorrhages, or sudden blindness due to hæmorrhage into the vitreous are not uncommon early symptoms. A woman may complain of bleeding from the uterus, and rarely a blood-stained seminal discharge is the initial symptom in a man. In other cases the initial symptoms are cardiac, and the patient complains of cardiac pain, shortness of breath, or consciousness of the heart's action. Nocturnal frequency of micturition may be an early symptom. On examination the patient will be found to have an increased blood pressure, the systolic ranging between, say 200-240 mm. or even higher, and the diastolic over 120 mm. There is also cardiac hypertrophy, but the case differs from a hyperpietic kidney (benign nephrosclerosis) in one or more of the following ways. Thus, the complexion tends to be sallow, and often there is loss of weight and some degree of secondary anæmia. The urine may contain only a trace of albumin, but more frequently it contains an appreciable quantity, namely 0·1 per cent. or more. The urinary deposit characteristically contains red blood corpuscles and granular and hyaline casts. When the disease is fully established, the urine has a low fixed specific gravity, varying between 1008 and 1012. Further examination may show impairment of renal function, and the blood urea may be raised to 70 mgm. per cent. at least. On examination of the eyes, in addition to arterio-sclerosis of the retinal vessels, retinal hæmorrhages and exudates, œdema of the disc and retina, and some detachment of the retina may be found. Ellis has emphasised the diagnostic importance of papillœdema in malignant nephrosclerosis.

There are cases of chronic interstitial nephritis which run a most rapid course in the initial stage. The clinical features are hypertension, cardiac hypertrophy and hæmorrhage. Toxic symptoms make their appearance within 3 to 6 months of the onset, and by this time some degree of failure of renal function may be demonstrated by clinical tests, or the patient's symptoms may already be those of uræmia. The whole evolution of the disease and its fatal termination in uræmia, cerebral hæmorrhage or cardiac failure, may take place within a period of 12 to 18 months.

There are other cases in which there may be a preceding period of five or more years during which time the patient is known to have hyperpiesia, and complains only of cardiac symptoms which are readily explained in terms of it. Meanwhile the disease-process seems to be more or less stationary, and then for no obvious reason the disease takes a progressive form, and a terminal acute phase lasting only 3 to 6 months is ushered in by an attack of hæmaturia or epistaxis, by retinitis, or by symptoms of renal failure, and the toxic picture of chronic interstitial nephritis rapidly develops.

On the other hand, there are chronic forms of the complaint which pursue a varied course different from the grave progressive course of malignant hypertension. The variety of the clinical picture which these cases present

makes their description difficult, and it is to allow of their recognition, and in order to leave the subject open for further clinical and histological observation, that the term "chronic interstitial nephritis" has been retained. Thus, a man complains of malaise, loss of health and strength, undue fatigue or loss of weight. On examination, the chief finding is an appreciable albuminuria. At this stage there may be no abnormal cellular deposit, or there may be a few red blood corpuscles and hyaline casts in the urinary deposit. Renal function may be normal. With limitation of his activities and general measures of medical treatment, the patient may recover his health to a considerable extent, though the albuminuria persists. From now on, over a period of 2 to 5 years, or perhaps longer, reasonably good health is maintained. Sometimes the blood pressure is but little raised. There may be an attack of hæmaturia or epistaxis from time to time. The blood urea may be a little raised, and may even remain more or less stationary at a level of 60 to 80 mgm. urea per cent. for several years, until finally physiological adjustments fail, and uræmia, a vascular accident, cardiac defeat or an intercurrent infection determines the fatal termination.

Complications.—The principal complications are due to failure of the pump, the tubing, or the filter. In other words, the heart may fail, causing venous congestion; the artery may give way, as in cerebral hæmorrhage; or the renal excretion become so inadequate as to lead to uræmia. Glycosuria is sometimes found. This may be due to alcoholic excess, a factor in the causation of the interstitial nephritis.

Diagnosis.—This rests on the combination of urinary and cardiovascular signs. The differential diagnosis from hyperpiesia is discussed on p. 1068, and that from secondary contracted kidney on p. 1312.

Prognosis.—The disease is usually progressive. Its course may be very slow, but after the development of retinitis a fatal ending occurs in the great majority of cases within 2 years. In some cases, however, even including those in which all the characteristic signs of the disease are present, including microscopic hæmaturia, persistent hypertension and retinitis, the disease may reach a stationary phase, and considerable recovery may occur, the fatal termination being delayed on occasion for as long as 6 years. For this reason a definite prognosis should not be given until a late stage in the disease. Tests of renal function afford useful prognostic evidence. Any evidence of cardiac dilatation, or of uræmia, even of the chronic variety, makes the outlook much less satisfactory. Retinal changes are of ill-omen.

Treatment.—In general terms, this should be carried out on similar lines to that for hyperpietic kidney (*q.v.*), though the response is not likely to be satisfactory. In addition, the anæmia often calls for treatment.

HYPERPIETIC KIDNEY

Synonym.—Benign Nephrosclerosis.

In this form of renal disease the vascular changes are of greater importance than the renal, and it will only be necessary to make a brief reference to it here.

Ætiology.—This is the same as that described under Hyperpiesia (see page 1065).

Pathology.—The chief kidney changes are in the small vessels. They consist of thickening of the intima and medial hypertrophy. The former may go on to fatty degeneration and obliteration of the lumen of the vasa afferentia, and so cause ischæmic fibrosis of the glomeruli with atrophy of the associated tubules. Thus, the changes in the renal parenchyma are largely degenerative in character, rather than the inflammatory changes seen in chronic interstitial nephritis. The kidney is slightly reduced in size and is somewhat firmer than normal. On section, the fine radial striation in the cortex is preserved, and throughout the organ the small arteries are prominent. Histologically the essential lesion is a thickening of the intima of the vasa afferentia and the interlobular arteries, with hypertrophy of the media. In the early stages there is cellular proliferation in the intima and increase of hyaline material. At a later stage there is fatty degeneration in the terminal arterioles in contrast to their parent vessels, in which little or no fatty degeneration is found. The thickening of the intima may lead to obliteration of the lumen, with fibrosis and atrophy of the glomerulus and its tubules. At a later stage, too, owing to fatty degeneration and atrophy of the muscle fibres of the media, the media may be actually thinner than normal. These changes, like those described in chronic interstitial nephritis, have a patchy distribution in the organ. The fibrous connective tissue in the immediate neighbourhood is thickened, but there is no glomerulitis and little or no small-celled infiltration, in contrast to the inflammatory reaction found in chronic interstitial nephritis. The vascular changes described above were originally termed arterio-capillary fibrosis by Gull and Sutton. They were first accurately described by Jores under the term diffuse hyperplastic sclerosis.

Symptoms.—These are those of hyperpiesia (see pp. 1066, 1067).

Treatment.—See that of hyperpiesia (pp. 1068–1070), the heart in hypertension (p. 996), and renal uræmia (pp. 1327, 1328).

SENILE OR ATHEROMATOUS KIDNEY

In this form of kidney disease also the vascular changes are of greater importance than the renal, and it is only necessary to deal briefly with the affection.

Pathology.—The kidneys show depressed red areas, which are due to contraction of fibrous tissue along the distribution of particular interlobular arteries, and, therefore, tend to be conical in form, with their base to the surface of the organ. There is an absence of cardiac hypertrophy; the pressure in the diseased arteries falls below that necessary for glomerular excretion. The affected glomeruli accordingly shrink, and the connective tissue around them becomes condensed and thickened. The degenerate glomerulus and its capsule fuse together, and undergo fatty and fibrotic changes. The atheromatous kidney is, therefore, generally due to atrophy following insufficient circulation, with consequent fibrosis.

Symptoms and Diagnosis.—There may be gradual failure of the physical and mental powers—described by Allbutt as "contraction of the spheres of bodily and mental activity"—rather than the more dramatic events of chronic interstitial nephritis. There is a trace of albumin in the urine. The radial artery is thickened and tortuous. The blood pressure is not high, and

there is an absence of cardiac hypertrophy. Death by cardiac failure or intercurrent affections is the commonest ending, while cerebral hæmorrhage and uræmia are unlikely.

URÆMIA

Uræmia is the name which has been given in the past to the toxic state which complicates or terminates severe kidney disease, and in which urea retention occurs. More recently it has been recognised that a high grade of urea retention may develop as a result of extra-renal factors. It is proposed to group these conditions under the name of Extra-renal Uræmia in order to emphasise the fact that although the kidney fails in its function, organic disease of the kidneys is not the primary fault.

Extra-renal Uræmia

Alkalosis (see also Alkalosis, pp. 405–408).—This is a toxic state characterised by malaise, gastro-intestinal disturbance, and a variety of nervous symptoms due to an increase of the CO_2 combining power of the blood plasma.

Ætiology.—Alkalosis is caused by giving too large doses of sodium bicarbonate or other alkali. The minimum normal tolerance of alkali by mouth seems to be the equivalent of 15 g. of sodium bicarbonate in 24 hours. If a patient develops alkalosis when taking this quantity of alkali or less, some predisposing factor will be found. Such factors are anæmia, kidney disease, or vomiting. Of these factors anæmia is important, because of the action of hæmoglobin as a buffer helping to maintain a constant *p*H in the blood. With a low hæmoglobin content in the blood an extra tax is thrown on the kidneys, so that in anæmia a smaller quantity of alkali given by the mouth may be the cause of alkalosis. Impaired renal function, such as results from kidney disease, is another factor predisposing to alkalosis, because the kidneys are unable to excrete the excess of alkali. As alkalosis may itself be responsible for kidney damage a vicious circle is set up. It has been suggested that chloride loss and the consequent hypochlorræmia is the cause of the rise in blood urea. This explanation cannot, however, account for the whole condition, because there are other conditions in which there is a considerable loss of blood chlorides without uræmia. The uræmia which develops in repeated vomiting, however, is probably due to loss of hydrochloric acid in the vomit.

Symptoms.—The toxic symptoms caused by giving too large doses of sodium bicarbonate or other alkali appear from 4 days up to 4 weeks from the beginning of treatment (Cooke). The patient complains of malaise, dizziness, constipation and headache, which commonly takes the form of a sensation of pressure on the vertex. He becomes nervous and irritable, often resentful. There is loss of appetite, distaste for food, nausea and vomiting. The patient becomes drowsy in the day and sleepless at night. Respiration is slowed, the pulse rapid, the face flushed, and the body perspiring. There is aching or actual pain in the trunk and limbs, with tenderness of the muscles on pressure, and increased muscular irritability. In the severest cases there may be tetany or epileptiform convulsions, and if the condition is unrecognised

the patient may become comatose, with incontinence of urine and fæces, and die. In addition to the above symptoms, a dry furred tongue, thirst, and at a later stage diarrhœa are common. The urine is alkaline, except sometimes in the early stages. It contains a trace or cloud of albumin. The deposit may contain hyaline or granular casts, and a few red and white blood corpuscles. Renal function is impaired, as is shown in nearly all cases by urea retention, and in some by failure of the power of urine concentration, which results in the excretion of urine of a constantly low specific gravity. There may also be a considerable polyuria, amounting to 2 or 3 litres in 24 hours. In most cases reported the dose of alkali which has caused alkalosis has been the equivalent of 20 g. of sodium bicarbonate given daily for 4 days or more. More usually the toxic dose has been the equivalent of 30 to 60 g. of sodium bicarbonate daily, and larger doses than this are naturally all the more likely to produce the condition.

Diagnosis.—Alkalosis must be suspected whenever a patient taking alkali develops symptoms of malaise, headache, constipation, digestive disturbance, or change in the personality. The diagnosis is established by an examination of the blood. The blood urea is commonly raised to 60 or 80 mgm. per cent., and may reach the high figures found in renal uræmia. The alkali reserve, which normally varies between 50 and 75 c.c. CO_2 per 100 c.c. of plasma, increases to 90 c.c. or more. The chloride content of both blood and urine may be low. The CO_2 combining power of the plasma is the most important observation to make, because it precedes the rise of blood urea.

Treatment.—The administration of alkalis is immediately discontinued. Acid sodium phosphate, gr. 10, three times daily after food is administered. If the case is under close observation, and if repeated estimations can be made of the alkali reserve, larger doses may be prescribed, but on account of the danger which exists, owing to renal damage, of a rapid change from alkalosis to acidæmia, some authorities are opposed to giving acid in any form. In any case, it is unwise to prescribe ammonium chloride.

Gastro-renal Uræmia

Repeated vomiting from any cause may induce alkalosis and thus be responsible for uræmia. In acute cases with albuminuria the differential diagnosis from renal uræmia is made clinically on the high specific gravity and high urea content of the urine. In chronic cases a complete blood examination and the observation of the degree of alkalosis may be required to exclude renal uræmia.

Diarrhœa may be responsible for uræmia, both on account of the loss of fluid and the resultant loss of chloride. But in this case the uræmia is associated with the opposite condition of acidosis, as may be established by the estimation of the alkali reserve. In acute cases, treatment is by intravenous injection of 200 to 400 c.c. of a 2 per cent. sodium bicarbonate solution.

Renal Uræmia

This type of uræmia belongs to a different category from that of Extra-renal Uræmia, because it is primarily due to severe kidney disease of which it is a complication or a terminal phase. A raised blood urea is the distinguish-

ing feature of uræmia. Nevertheless, the term renal uræmia is used in a clinical sense, both because the diagnosis can be made without an estimation of the urea in the blood, and because, on occasion, the patient may suffer from uræmia before the blood urea is appreciably raised. Renal uræmia varies greatly in its symptomatology, but, as Clifford Allbutt pointed out, it is generally characterised by anæmia, headache, nausea, lethargy, retinitis, convulsions or coma.

Although there are many factors in support of the so-called retention theory of uræmia, its complete explanation in biochemical terms is not yet clear.

In view of the high blood urea in severe uræmia, urea retention might be regarded as the simplest explanation of the condition. It has been shown experimentally that the administration of massive doses of urea causes headaches, giddiness, apathy, drowsiness, bodily weakness, nausea and diarrhœa—a group of symptoms characteristic of chronic uræmia. But that this is not the whole explanation of uræmia is shown by the fact that symptoms of uræmia may be present before the blood urea has risen to a level proportionate to the symptoms. It has been suggested, therefore, that other renal excretory products, such as indican, uric acid and the salts of urine, may contribute to the uræmic state. When the hypobromite method is used for the estimation of urea in the blood or cerebro-spinal fluid other nitrogenous products than urea are estimated. The urease method gives the amount of urea only, so that the difference between the results obtained by these two methods is an indication of the quantity of amine bodies other than urea, and to these bodies some at least of the clinical syndrome is probably due. But even this expansion of the retention theory to include nitrogenous bodies other than urea does not explain uræmia, because in complete suppression of renal function, such as occurs when the ureter of a single kidney is completely destroyed by any cause (Ascoli's urinæmia), the clinical picture is entirely different from that of uræmia complicating acute and chronic Bright's disease. Ascoli says: "Severe urinæmia in man is chiefly manifested by bodily weakness and languor, which often appear before any other symptoms, but generally lead to progressive mental weakness and exhaustion, often terminating with great suddenness. The greater part of the most prominent symptoms of uræmia are, however, lacking, especially the severe and acute mental disturbances, the sudden amaurosis, and the epileptic phenomena in general. Only in occasional cases do the symptoms resemble uræmia." The name of *latent uræmia* is sometimes given to this condition, but it is hardly suitable. It has also been held in the past that uræmia may be due to some precursor or derivative of urea or other nitrogenous body normally secreted by the kidneys, but there is no convincing evidence of the accumulation of such bodies in the blood at least in such quantity as to cause uræmia.

It is evident that the retention theory and a failure of the excretory function of the kidneys do not provide a complete explanation of renal uræmia. But the kidneys have two other important functions, namely, the regulation of the osmotic pressure of the blood and the regulation of its hydrogen-ion concentration. Now, in uræmia the acid-base equilibrium is disturbed, and there is a fall in the CO_2 combining power of the blood plasma; that is to say, acidæmia. If this state of acidæmia is corrected by the administration of alkali in such dosage as to restore the CO_2 combining power of the

plasma to normal, the patient may be relieved of the more acute symptoms of uræmia, and may be maintained symptom-free for several weeks or months. Or, if the uræmic state is the complication of a recoverable disease, as in the uræmia of acute nephritis, or the uræmia complicating or following operations on the urinary tract, the restoration of the acid-base equilibrium in the blood may save the patient's life. The fact is that when diseased kidneys fail in their function of maintaining acid-base equilibrium, and even when the disease is not so severe as itself to have determined the onset of uræmia, the administration of alkali or acid in excess readily causes uræmia. Further, both acidæmia and alkalosis in themselves cause renal damage, and thus aggravate pre-existing renal disease. In this way a vicious circle is set up.

In order to realise fully the way in which a grave disturbance of the acid-base equilibrium of the blood caused by giving too much alkali to a patient with presumably previously healthy kidneys, the reader is referred to alkalosis. In a severe case of alkalosis the clinical syndrome may be indistinguishable from renal uræmia, including albuminuria, low specific gravity urine, cylindruria, high blood urea, polyuria, thirst, lethargy, loss of appetite, nausea, vomiting, constipation, diarrhœa, coma, convulsions and death.

There is another approach to the interpretation of some of the symptoms of uræmia. Symptoms similar to those occurring in the cerebral type of uræmia may be produced by a disturbance of the cerebral circulation due to œdema of the brain, or to spasm of one or more of the cerebral arteries without a rise in the blood urea. In either case a raised blood pressure is the determining factor. In the acute cases, headache, vomiting and bradycardia are the important clinical features, and because of the rise of blood pressure which characterises the attack, it is described as a hypertensive cerebral attack. Even in cases with a high blood urea the cerebral symptoms may be due to disturbance of the cerebral circulation, and treatment by lumbar puncture or venesection, according to the indications provided by the particular case, may abort or cut short the attack. (*Vide* Diagnosis.)

It may be concluded that some of the symptoms of renal uræmia are due to a toxæmia acting on the nervous system caused by the abnormal metabolic products resulting from inadequate excretion by a diseased kidney. An important part of the clinical syndrome is due to a failure of the kidneys to maintain the normal hydrogen-ion concentration of the blood. The acidæmia that results is in part due to a failure of the kidneys to excrete acid phosphates (Marriott and Howland). Other symptoms, such as increased nerve excitability and localised muscular twitchings, have been attributed to a fall in the blood calcium by de Wesselow, and Izod Bennett compares such twitchings with those of tetany. Lastly, the disturbance of cerebral circulation, whether due to cerebral œdema or vascular spasm, may play a part. On these several lines we are approaching an adequate explanation of the uræmic syndrome. Lastly, account must be taken of the possibility of the secretion of a pressor substance by ischæmic kidneys being a factor in the causation of the uræmic state.

Symptoms.—A convenient clinical classification of the types of uræmia is: (1) *Cerebral* in the fulminating and acute cases; (2) *Respiratory* where acidæmia is predominant; and (3) *Gastro-intestinal* in the chronic cases. The terms acute and chronic apply to the uræmia and not to the disease responsible for it. But each of these types is really nervous in origin. Usually the first

type begins with severe headache. Drowsiness and twitchings of the face and hands follow. The twitchings may become aggravated into epileptiform convulsions, and the drowsiness may deepen into coma, ending in death. But several important departures from this course may occur. Sudden loss of vision, amaurosis, is not infrequent, although the fundi may not show the changes characteristic of albuminuric retinitis. Local palsies, hemiplegia or monoplegia, may come on spontaneously or after a convulsion, and are frequently due to small vascular lesions. Intense itching of the skin, tingling and numbness of the extremities, muscular cramps or insomnia may usher in the more serious symptoms. Sudden mania or delusional insanity may be the first and a very misleading symptom. The cerebral type is often rapidly fatal, but convulsions and amaurosis, though more striking, are less grave than the other symptoms. In the epidemic of war nephritis we saw seven instances of uræmic convulsions with complete recovery from the nephritis.

The commonest respiratory symptom is dyspnœa, often paroxysmal, to which the name of uræmic asthma is given. It is associated with a fall in the CO_2 of the alveolar air from the normal 5 per cent. to 3 per cent. or lower. There is diminished alkalinity of the blood, from the presence of some non-volatile acid. Addison called attention to the hissing character of the respirations in this condition. In all types of uræmia there is a tendency to stomatitis, and this is perhaps particularly so in uræmic asthma. This combination of dyspnœa of a hissing character in a drowsy patient with bleeding gums often characterises the terminal phase of uræmia. At first there may be no signs in the chest except the ordinary cardiovascular signs of chronic nephritis, but as the attack proceeds there are usually abundant moist sounds from the onset of œdema of the lungs. The heart fails, the patient becomes steadily waterlogged, slipping down into the bed from the orthopnœic position as he becomes more and more drowsy. The fatal issue may not occur in this way, however, but from development of some of the more acute nervous symptoms.

Less common than this type of dyspnœa is Cheyne-Stokes' respiration. The whole of the cerebral functions may then show a curious periodicity; thus the pulse quickens during the noisy breathing, the pupil dilates, the patient becomes more conscious and restless. As the apnœic pause succeeds, the pulse slows down again, the pupil contracts and the patient becomes quieter or even comatose.

The gastro-intestinal symptoms are nausea, hiccough, vomiting and diarrhœa. The gastric part of these symptoms may be very chronic. Any practitioner who neglects systematic examination of the urine will sooner or later treat a case of uræmia as one of simple dyspepsia. Apart from the urine, there is, however, one significant point: the dyspepsia may improve under treatment while the vomiting persists. In simple dyspepsia vomiting is never the last symptom to clear up. It is stated that this vomiting has no relation to meals, but this is far from being invariably true. Vomiting may occur only then, and so the mistake is made. In severer cases the vomiting may be quite uncontrollable, when the prognosis becomes correspondingly grave.

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occurring by the bowel, when urinary elimination is inadequate, irritates the intestine and leads to the so-called albuminuric ulceration. Another explanation of this condition is that hæmorrhages which occur here as elsewhere in chronic nephritis are the precursors of the ulceration. There may also be an intense catarrhal or even "diphtheritic" colitis. Here, therefore, there are local lesions sufficient to account for symptoms usually referred to uræmia, for such lesions are conspicuously absent at least in the asthmatic and gastric syndromes. It is accordingly inadvisable to call these symptoms uræmic, as is generally done. At any rate the term should be confined to those violent choleraic attacks which are out of all proportion to the local lesions. Both the vomiting and diarrhœa are sometimes regarded as an attempt at vicarious elimination of toxins. The fact that the vomit may contain a higher percentage of amines than the blood certainly suggests this, but it must not be forgotten that either vomiting or diarrhœa may so alter the *p*H of the blood as to aggravate existing renal damage. It is this alteration which may actually determine the onset of uræmia.

Diagnosis.—This brief account of the symptoms of uræmia will indicate also some of the pitfalls besetting diagnosis. When the patient is known to have had Bright's disease, or indeed any disease or injury to the urinary system, the possibility of uræmia will arise. The finding of hæmaturia, albuminuria, cylindruria, low specific gravity urine, bacilluria or pyuria, will indicate urinary disease. The estimation of the blood urea and CO_2 combining power of the plasma will often be necessary to establish the diagnosis.

The first differential diagnosis to make is between extra-renal and renal uræmia. The causes of extra-renal uræmia must be inquired into, particularly as to whether the patient is taking alkali. Anæmia is a predisposing factor. The importance of vomiting and diarrhœa in causing extra-renal uræmia must be taken into account. In acute extra-renal uræmia, such as may be due to vomiting, the concentration of urinary urea is high. In chronic cases, however, secondary kidney damage may lead to polyuria, low specific gravity urine, and low urinary urea even in extra-renal uræmia.

Certain conditions which clinically resemble uræmia are separated from it under the term *pseudo-uræmia*, because they have a different pathology and belong to a different order of clinical events. The commonest cause of pseudo-uræmia is cardiovascular disease. Under this heading are to be included the convulsive seizures and varied evidence of cerebral disturbance in arterio-sclerotic subjects in whom the symptoms are due to vascular lesions, sometimes limited to capillary areas, in the brain. Heart failure, when responsible for cerebral disturbance, nocturnal dyspnœa, Cheynes-Stokes' breathing, and on occasion psychosis, belongs to the same order of events, and has to be distinguished from true uræmia. It may be a matter of considerable difficulty to distinguish between cardiovascular disease in which the right side of the heart is failing, and in which there is renal congestion with albuminuria, microscopic hæmaturia and cylindruria—a difficulty which may be increased by the fact that the blood urea may rise to 80 or 100 mgm. per cent. in congestive heart failure. Further, in true or renal uræmia cardiac failure may be an important complicating factor. In simple congestive heart failure the urine is loaded with urates, its specific gravity is raised, twitchings do not occur, and the blood urea is normal or inconsiderably raised. Disorder of the cerebral circulation, whether due to cerebral thrombosis, capillary

hæmorrhages, angio-spasm, or cerebral œdema, may be responsible for transient monoplegia or hemiplegia, convulsions and coma. In some cases these and other symptoms of central nervous origin are associated with a sudden rise in blood pressure and constitute hypertensive cerebral attacks. In other cases the intracranial disturbance is due to œdema of the brain, as was first suggested by Traube in 1860. In this type of attack the patient is usually under the age of 40. There is complaint of sudden severe headache. Drowsiness is common, and motor weakness with focal signs or loss of vision may be transient phenomena. Retinal hæmorrhages, exudates and papillœdema appear within a few hours. The blood pressure rises and the cerebro-spinal fluid pressure is also raised (McAlpine). The blood urea is normal unless the attack occurs as a complication of uræmia. Œdema of the brain is found post mortem.

Other diseases which may simulate uræmia are cerebral tumour and meningitis. Some cases of cerebral tumour without localising signs, but with the classical symptoms of headache, vomiting and optic neuritis, may be very difficult to distinguish from uræmia, if there is chronic nephritis as well —a not very uncommon complication in syphilitic tumours of the brain. But such cases are more chronic in their course than uræmia. If the cerebral type of uræmia be accompanied by pyrexia, as it sometimes is, the question of meningitis must be considered. Lumbar puncture may then throw light on the case by the cytology, bacteriology and urea content of the fluid. Lastly, when the uræmic state has reached the stage of coma the differential diagnosis from alcoholic poisoning, status epilepticus, trauma, opium, diabetic coma, the apoplectiform onset of general paralysis and cerebral hæmorrhage must be made. In all such cases a careful examination of the urine is essential, because comparatively slight renal inadequacy may lead to toxic symptoms by the retention of some poison which would otherwise have been promptly eliminated. Thus salicylates, iodides, opium and mercury are badly excreted by the nephritic.

Treatment.—As in the case of extra-renal uræmia the maintenance of the normal acid-base balance of the blood is of first importance. In most cases of renal uræmia there is acidæmia, and this is treated by the cautious administration of alkali by mouth, or by the intravenous injection of a 2 per cent. solution of sodium bicarbonate 200 to 400 c.c. Anæmia renders the acid-base balance unstable. It is treated by the administration of iron, and 60 to 90 grains of iron and ammonium citrate are given in divided doses daily, provided the salt does not upset the digestion. Vomiting and diarrhœa should be checked, because they weaken the patient, prevent assimilation of food and cause dehydration. Vomiting causes alkalosis, and diarrhœa may cause acidæmia. A bismuth mixture or 3 minims of dilute hydrocyanic acid and 10 minims of solution of adrenaline hydrochloride 1 in 1000 in half an ounce of water given every 3 or 4 hours may afford relief.

The retention of urea is treated by a low nitrogen diet. The diet advised for acute nephritis may be given with advantage for a week or 10 days, and after this for 1 or 2 days in each week. If a low nitrogen diet is continued it must at least be adequate in its protein content to retain nitrogenous equilibrium, for which purpose 1 G. per kilo body-weight is required. Elimination is promoted by maintaining bowel function, avoiding constipation on the one hand, and diarrhœa on the other. According to von Noorden, 8 G. of

nitrogen can be excreted by the bowel in the day and 3 G. by the skin. Strong aperients and mercurial preparations should not be employed. A good evacuation may be secured by magnesium sulphate 30 to 60 grains repeated as necessary, 60 to 90 grains of pulv. jalapæ co., 1 oz. of mist. sennæ co., or 60 to 90 grains of compound liquorice powder. The function of the skin is promoted by suitable clothing, wearing wool or flannel next to the skin, and sleeping between blankets. Much sweating may have disadvantages that it causes dehydration, and gives the kidneys a more concentrated and therefore a more irritating urine to secrete. The vapour bath or hot pack is more trying to the heart than the hot-air bath. None of these measures should be continued more than a quarter of an hour after sweating has begun, and a careful watch must be kept on the pulse ; the procedure should be stopped at once if there are any signs of collapse, and stimulants should be at hand. If the treatment is having a good effect, sweating will begin at a lower temperature with successive baths. A nightly hot bath, containing 4 tablespoonfuls of mustard, followed by wrapping in hot blankets until sweating has ceased, is useful in some chronic cases, even where there is no œdema. Pilocarpine is no longer advised to provoke sweating.

Headache and other symptoms of cerebral irritation may be relieved by lumbar puncture when accompanied by an increase in cerebro-spinal fluid pressure. It is safe to draw off 10 or 20 c.c. if the pressure is raised, but if with the drawing off of the fluid there is increase of headache the needle should be withdrawn immediately. If the headache is due to a hypertensive attack, particularly if there is evidence of congestive heart failure, venesection may give relief. The withdrawal by venesection of 10 to 20 oz. of blood may cure the headache, and it may stop convulsions in acute nephritis with an overburdened heart. Venesection is contra-indicated in chronic uræmia with anæmia. Bromide and chloral hydrate will often relieve headache. Twenty to 30 grains of sodium bromide with 15 to 20 grains of chloral hydrate are given by mouth. Aspirin, phenacetin and codeine are other useful drugs best prescribed in combination in severe cases. Morphine, papaveretum (omnopon) and dilaudid are reserved for intractable cases, and are to be used with caution.

LARDACEOUS DISEASE

Synonyms.—Amyloid or Waxy Kidney.

Definition.—A pathological condition in which the blood vessels of the kidney, in more advanced cases the tunica of the tubules and the interstitial tissue also, are the seat of waxy degeneration.

Ætiology.—This affection is now rarely met with. It attacks men more than women, and although occasionally seen in children it is more likely to occur in adolescence and earlier adult life, being uncommon after fifty years of age. It is usually due to chronic suppuration, especially in bone, chronic tuberculosis and syphilis. It rarely occurs in other chronic infections, but it has been described in severe rheumatic heart disease, and a certain amount of amyloid change has sometimes been found post mortem in patients suffering from chronic cardiovascular disease and chronic nephritis in the absence of chronic suppuration. As it is a degenerative change it has however more affinity with nephrosis than with nephritis.

Pathology.—Amyloid material or lardacein is a product of protein degeneration, and consists of protein linked with chondroitin-sulphuric acid. The latter substance is a normal constituent of elastic tissue and cartilage. In uncomplicated cases, the affected kidney has the appearance of a large white kidney with a smooth surface and a capsule that strips easily. The organ is firmer than it otherwise would be. On section, the cortex is thicker than normal and has a yellowish white appearance; the glomeruli may be visible as minute translucent spots. The pyramids are dark red, in contrast to the pale cortex. If a solution of iodine in potassium iodide is poured over the surface, some of the glomeruli stand out as mahogany-brown spots and the vasa recta as brown streaks. In histological preparations stained with methyl-violet, amyloid material takes a pink colour. The disease tends to appear first in the capillaries of some glomeruli, while others are normal, and its incidence is often partial within a single glomerulus. The afferent arterioles, vasa recta and capillary plexus are next affected; in more advanced cases there is amyloid degeneration of the tunica propria of the tubules with amyloid deposits in the interstitial tissue. In most cases there is an associated nephritis, interstitial rather than parenchymatous. The kidney lesion is generally the most striking part of a widespread lardaceous degeneration which also involves the liver, spleen and intestine; less commonly the blood vessels of the thyroid, suprarenals, pancreas, heart and brain may be affected as well. Occasionally only the kidney is implicated.

Symptoms.—The onset is insidious and the symptoms are not likely to occur unless chronic suppuration has existed for at least 3 months.

The urine is copious, of low specific gravity (1003 to 1010). The amount of albumin is variable; when abundant there is probably coincident nephritis. The amount of urine and its specific gravity may also be affected by the presence and degree of coincident nephritis, and the state of the heart. Hyaline and granular casts are present in the urine; casts staining brown with iodine are not evidence of amyloid disease, and may occur in other diseases of the kidneys. True waxy casts are not found. In later stages there is œdema, with diminished excretion of urine. The blood pressure is not raised, nor is the left ventricle hypertrophied, unless there is coexistent chronic nephritis.

Diagnosis.—The diagnosis is indicated by the nature of the urine. It is made (1) when there is a sufficient cause in the past history or present condition, namely, chronic suppuration or syphilis; (2) on the general condition of the patient, namely, a secondary anæmia, which may reach an extreme grade, with a pale or "alabaster" facies and cachexia; (3) on signs of lardaceous disease in other organs, such as enlargement of the liver or spleen and diarrhœa.

Course and Prognosis.—This depends on that of the primary cause. If the latter is unchecked, the disease is slowly progressive and death occurs from exhaustion due to the original disease, less often from uræmia. Where the original disease can be cured, recovery may occur. Complete recovery of the kidneys is less likely than is recovery of the liver, spleen and intestines.

Treatment.—The treatment is that of the original disease. In suppuration of the bones or joints, empyema, etc., it is surgical; but it must be recognised that in advanced cases surgical treatment may be too late, even though it is successful in eradicating the septic focus. In all cases fresh air

and sunlight and a nourishing diet are essential. Iron, arsenic and cod-liver oil should be given. Cases of syphilitic origin should be treated with bismuth and arsenic, while mercury and iodides should rarely be given, and then only with caution since even therapeutic doses have produced serious reactions.

PYELITIS

Definition.—Pyelitis is inflammation of the renal pelvis. The changes in the renal parenchyma are those described under Toxæmic Kidney. Pyelitis may be complicated by nephritis, and the condition is then termed pyelo-nephritis.

Ætiology.—Most cases are due to a blood-borne infection of the renal pelvis, and it may be noted in this connection that it is a normal function of the kidney to excrete micro-organisms present in the blood stream; whether the renal parenchyma is, or is not, of necessity damaged in the process is a point on which there is not as yet exact information. The pelvis may also be involved by ascending infections—(*a*) via the lumen of the ureter when there is ureteral obstruction; it is probable that infection does not spread by this channel when the lumen is normally patent. (*b*) By way of the peri-ureteral lymphatics from local foci in lower parts of the urinary tract, such as the bladder, urethra, prostate, seminal vesicles and epididymis. Lastly, there is the possibility of direct spread of infection from the bowel, and by cross lymphatic channels from one kidney to the other. In those cases in which a pyelitis occurs secondary to appendicitis, cholecystitis, ulcerative colitis, etc., the spread of infection may be by the lymphatics or the blood stream.

Pyelitis is more common in females than in males. Its age incidence depends on the determining cause. Thus, it is common in female infants, as a result perhaps of urethral infection, to which they are more liable than male infants. It is not an uncommon complication of pregnancy, occurring especially in the fifth month of gestation. It is common in males at a later age, associated with enlarged prostate and cystitis.

In general terms any injury or disease of the renal pelvis, or any condition which interferes with the normal flow of urine, may be the determining cause of pyelitis. Thus it is a common complication of hydronephrosis from whatever cause. It often complicates stone in a kidney, tuberculosis of the kidney and new-growths of the renal pelvis. The frequency of pyelitis as a complication of intestinal catarrh (whether due to infection or the habitual use of laxatives) and ulceration is probably due to the increased virulence and excessive numbers of bacteria that reach the kidney in such conditions.

Pathology.—The mucous membrane of the pelvis is swollen, œdematous and hyperæmic, and the submucous venules are engorged. Where there is obstruction, the pelvis is dilated and contains a slightly turbid or opalescent fluid. In these circumstances the ureter above the obstruction is dilated and tortuous and its walls are thickened. The kidney is swollen and pale, from cloudy swelling, and in severe cases there may be multiple small abscesses in the renal parenchyma.

Bacillus coli is by far the most common infecting micro-organism. Streptococci, staphylococci, gonococci and bacilli of the proteus and typhoid

groups may be found. The infecting micro-organism is readily recovered from the urine.

Symptoms.—The clinical types of pyelitis differ greatly from one another, and the condition may be responsible for an acute fulminating illness or for chronic malaise of indefinite nature.

LOCAL SYMPTOMS.—Pain is the most important, especially as a diagnostic indication in acute cases. It is a dull ache in the loin or flank, at first slight and intermittent, later, or in other cases at once, constant and sometimes intense. Occasionally it takes the form of renal colic. At its onset the pain may be diffuse and abdominal. Increased frequency of micturition is a common symptom. There may be strangury.

GENERAL SYMPTOMS.—In acute cases there may be sudden onset with rigors, vomiting, headache and the general constitutional disturbance of profound toxæmia. These cases may simulate septicæmia (in fact there may be septicæmia), appendicitis, or, when associated with abdominal distension, constipation and vomiting may even simulate intestinal obstruction. In other cases, with cerebral symptoms, meningitis may at first be difficult to exclude.

In subacute cases, without marked pain or rigors, there is general malaise, fever, anorexia, wasting and a secondary anæmia associated with some degree of polymorphonuclear leucocytosis (W.B.C. = 10 to 15,000).

In relapsing cases there are periods of exacerbation with acute symptoms, and intervening periods of fair health or general malaise. Fever is commonly present; in acute cases with rigors it may rise to 105° or 106° F. In general the temperature is irregular, remittent or intermittent, varying between 102° and 104° F. in acute cases, and 100° and 102° F. in subacute cases. The pulse is raised in proportion to the temperature, and there is a corresponding slight increase in the respiration rate. Of other general symptoms constipation or diarrhœa frequently precedes the disease, and constipation generally accompanies it. Toxæmia is often marked.

Deep tenderness on palpation of the renal region is the most important sign to determine. There is some degree of abdominal rigidity, and it may be possible to determine enlargement and tenderness of the kidney. The urine is passed in small quantities at frequent intervals. It has the usual characters of febrile urine and is turbid. The turbidity or an opalescence is still present after filtration. When an appreciable quantity of pus is present it settles at the bottom of a specimen glass in a thick whitish deposit. Examination of the deposit (catheter specimen in women) shows pus cells and epithelial cells from the urinary tract. There may be hæmaturia.

Bacteriuria.—In this condition bacteria are present in the urine in such quantity as to make it hazy to the naked eye, but there is little or no inflammatory reaction in any part of the urinary tract. Hence there are no localising symptoms and few pus cells. The urine when freshly passed has a hazy appearance. In a test-tube, when the tube is rotated, the urine has a "satiny" appearance or shimmer. It is not cleared by filtration. It often has a fishy smell in *B. coli* infection, and is ammoniacal in smell in *B. proteus* infection. Its reaction is acid, unless due to staphylococcal or *B. proteus* infection. It generally contains a trace of albumin, and often may contain a few white blood corpuscles and epithelial cells. A catheter specimen grown in broth, in dilutions of 1 c.c., $\frac{1}{10}$ c.c. and $\frac{1}{100}$ c.c. urine in

·10 c.c. broth, gives a growth in all dilutions, and in *B. coli* infections there is generally a growth in greater dilutions. Streptococcal and staphylococcal infections are less common.

There may be no other symptoms. On the other hand, there may be indefinite malaise, fever, gastro-intestinal disturbance, especially indigestion, constipation and abdominal pain ; in other cases headaches, rigors and even meningism may occur. There may be local symptoms, such as enuresis in children and frequency of micturition in adults. When the symptoms point to inflammatory reaction in one part of the genito-urinary tract, such as pyelitis, cystitis, prostatitis, urethritis, or epididymitis, the condition is better diagnosed accordingly.

The recognition of bacilluria may be of great importance, not only because of the ill-health, acute disease or complications for which it may be responsible, but also because it may be a valuable pointer to other disease. For instance, a patient may complain of loss of energy and indefinite malaise. On clinical examination the only clinical finding may be some degree of secondary anæmia or bacilluria. A further examination of the urine bacteriologically, or X-ray examination of the urinary tract, may reveal previously unsuspected tuberculous disease, stone or neoplasm, even in the absence of urinary symptoms.

Diagnosis.—When there is fever and constitutional disturbance without localising signs or symptoms, the differential diagnosis is from those diseases which come in their early phases under the category of indeterminate fever. The diagnosis is established by examination of the urine. Pyonephrosis is diagnosed by the presence of a tumour. Calculus is recognised by its clinical features and by X-ray photograph. Perinephric abscess in its early stages is not accompanied by pyuria or frequency of micturition. Cystitis is generally afebrile ; and it is accompanied by suprapubic discomfort and pain, particularly at the end of micturition ; the diagnosis can be established by cystoscopy. Urethritis is recognised by local tenderness, urethral discharge and urethroscopy, and prostatitis by swelling and tenderness on rectal examination.

Prognosis.—The natural course in the majority of cases is to recovery in a few weeks. With modern remedies the urine can generally be sterilised in 7 to 14 days unless the urinary infection is a complication of some other condition or disease. The prognosis depends very largely on this sterilisation of the urine, because the persistence of even a minimal infection is likely to lead to relapse, or apparent recovery may be followed by a recurrence after a variable length of time. The disease may progress to pyelo-nephritis, ascending suppurative nephritis, pyonephrosis or perinephric abscess. A fatal termination is rare, except when the condition complicates other disease, such as paraplegia, or in elderly persons with obstruction to the outflow of urine.

Treatment.—Prophylaxis is important in nurseries and children's hospitals, since there is evidence of spread of infection via the urethra, at any rate in females. Here it is a question of cleanliness. In general terms exposure to cold, over-fatigue, and loose stools are to be avoided when there is susceptibility to coli infection of the urinary tract.

The treatment of an acute attack consists of absolute rest in bed, flushing out the kidneys with large quantities of fluid, and regulation of bowel

function. It is important, especially when there is fever, to avoid exposure to cold and any possibility of chill. Particularly when there is fever the patient should wear wool next to the skin, lie between blankets and be nursed in bed. Five to 8 pints of fluid are given in every 24 hours in the form of water, barley water, imperial drink, lemon drink, weak tea and thin soups. Milk as such is unsuitable, but junket, buttermilk, whey and cream are good. As the temperature subsides the diet is increased by the addition of carbohydrates, fruit, vegetables and fat. Cooked milk in the form of milk puddings is allowed. Alcohol is withheld. The bowels are emptied with an initial laxative, followed by an enema if necessary. After this the action of the bowels is regulated with paraffin, salts or mild laxatives, such as liquorice powder, senna pods or rhubarb, so that constipation is avoided on the one hand and loose stools on the other.

In the initial febrile stage when there is bacterial toxæmia, sufficient alkali is given by mouth to make the urine alkaline. A mixture containing 30 grains each of potassium citrate and sodium bicarbonate is given 3-hourly until the urine is alkaline. Every specimen of urine passed is tested with litmus paper. When the urine is alkaline the quantity of alkali by mouth is reduced by giving it 4- or 6-hourly, but always in sufficient quantity to keep every specimen of urine alkaline, until the temperature is normal. One of the sulphanilamide group of drugs is then given 4-hourly. A full dose is sulphanilamide 1 gramme 4-hourly (6 grammes in 24 hours). This may be reduced to 4 grammes in 24 hours after 3 or 4 days, and later to 3 grammes (*i.e.* 0·5 gramme 4-hourly). Alternatively sulphapyridine (M. & B. 693) may be prescribed, or rubiazol (Roussel) 12 to 8 tablets in 24 hours (one tablet contains 0·2 gramme of the azo-compound). In some cases, especially if these drugs are not well tolerated, a mandelic acid salt may be given. The usual dose is 45 grains of ammonium or calcium mandelate thrice daily.

Flushing out the kidneys with large draughts of water must always dilute the antiseptic drug. Flushing and antisepsis should therefore be attempted consecutively and not simultaneously.

In uncomplicated cases a sterile urine may be expected in 7 to 10 days. In some cases the drug may have to be administered for a longer period, or the course of treatment may have to be repeated after an interval of a fortnight or 3 weeks. Occasionally in resistant cases, or in those which continually relapse as soon as the drug is withheld, good results have been obtained by giving ammonium mandelate for several weeks, provided that the patient is under good observation, so that the occurrence of kidney damage and acidæmia can be prevented. In acute cases with fever it may be better to initiate treatment with a sulphanilamide drug without the initial course of alkali therapy, provided that a close observation of the case can be maintained, including estimation of the blood urea as required. During the acute phase of the disease the kidneys are more susceptible to the toxic effects of these drugs.

It is important to remember that, like simple bacilluria, infections of the urinary tract are often a complication of organic disease of either the urinary tract or bowel. A urinary infection, which at first sight appears to be a simple coli infection of the urinary tract, may be only a complication of tuberculosis of the kidney calculus, hydronephrosis or neoplasm. Equally it may be a complication of organic disease of the digestive tract, such as chronic appendicitis,

especially if the right ureter is involved, diverticulosis, or even cholecystitis. In any case of urinary infection that is resistant to treatment or presents any unusual symptom, a detailed investigation of both urinary and digestive tracts is required in order to determine or exclude a change in structure which may be the underlying and determining cause of the urinary infection.

In the uncommon fulminating cases with unilateral suppurative nephritis, nephrectomy may save the patient's life.

Chronic cases.—An initial course of treatment such as that outlined for acute infection with rest in bed is advisable. In some cases, perhaps on account of long-standing infection, or some other disease of the urinary tract, such as calculus diverticulum of the bladder, enlargement of the prostate, etc., it may be impossible to sterilise the urinary tract. Every effort should then be made to build up the patient's resistance by living in fresh air, avoiding chill and over-fatigue, a generous and nourishing diet, and by so arranging the diet that the bowels are open regularly without taking purgatives other than a simple saline in the morning, paraffin and agar, or other laxative which determines the evacuation of a formed stool. It is important so far as is possible to restore integrity of structure to the body as a whole by the cure of anæmia, for instance, and by the eradication of obvious sepsis elsewhere in the body. In incurable cases the infection may be controlled to a greater or less extent by long-continued use of hexamine, which may often be given with advantage with methylene blue.

PERINEPHRITIS AND PERINEPHRIC ABSCESS

1. Perinephritis without suppuration is really a part of some cases of chronic nephritis. Its clinical importance is not generally recognised, but it may be a cause of lumbar pain in that disease. The capsule of the kidney is thickened and adherent to the perirenal tissues, many of the adhesions being vascular.

2. Perinephritis proceeding to suppuration may be primary or secondary.

Ætiology and Pathology.—The primary form may follow injury, but more frequently it results from boils, carbuncles and tonsillitis, or complicates an acute specific fever. Soon after the War of 1914-1918, cases were so common as to be described under the name of *epidemic perinephric suppuration.* The infecting organism is *Staphylococcus pyogenes.* J. Koch has shown experimentally that intravenous injection of staphylococci is followed by their excretion in the urine after an interval of 4 to 6 hours. In the process of excretion, according to Koch, they may give rise to multiple cortical abscesses, cylindrical medullary abscesses, or, passing along the cortical lymphatics, may gain access to the perinephric tissues and there cause abscess formation. In these circumstances perinephric abscess is an example of the mildest form of staphylococcal pyæmia with single metastatic abscess formation. The secondary form may complicate suppuration in the neighbouring organs, such as the kidney, liver, gall-bladder or appendix. It may be secondary to caries of the spine. In other cases the infection may be carried by lymphatics from a focus in or around the bladder, rectum or female pelvic organs.

Such is the ordinary terminology, but it will be observed that the "primary" form is really due to infection from a distant focus through the blood stream, while the "secondary" is due to direct extension or infection through the lymphatics from some focus in the neighbourhood of the kidney.

Symptoms.—The onset is generally gradual. It is characterised by fever and malaise as in typhoid fever. There may be no local symptoms for the first 7 to 14 days, and during this period there is increasing toxæmia, general abdominal discomfort or pain, slight fullness and resistance, with deep tenderness, in the affected loin. As the abscess forms, pain and tenderness increase, there is induration and, later, redness of the skin and œdema in the lumbar region. The tumour first tends to spread backwards, obliterating the normal hollow in the loin, and then as pus collects it may spread forwards, forming a tender tumour palpable from the front. In its relations to the colon it resembles a renal tumour, but does not move with respiration. There is resistance or rigidity of the abdominal wall on the affected side. There is an increasing polymorphonuclear leucocytosis up to 20,000 or even 40,000. The urine is febrile in character, containing a trace of albumin and perhaps a few white blood corpuscles; it does not contain pus, unless the kidney itself is involved, but hæmaturia may occur. In some cases the disease runs an acute course, and there may be rigors at an early stage.

Course.—When the condition is simply associated with chronic nephritis it has no separate significance. When it proceeds to suppuration the abscess may rupture into the peritoneum, colon or pleura, or on to the surface, unless the abscess is opened and drained.

Diagnosis.—Before localising signs appear the condition may be mistaken for typhoid fever, malaria or septic endocarditis. The blood examination is important for the purpose of excluding malarial parasites; leucocytosis is against typhoid fever, and when above 15,000 is in general against infective endocarditis. Absence of agglutination of micro-organisms of the typhoid group is further evidence.

When the tumour exists it has to be distinguished from a renal tumour or pyonephrosis. Renal and adrenal growths may be accompanied by fever, but do not usually give the general symptoms of suppuration; they tend to extend forwards rather than backwards, and induration of the tissues is absent. Pyonephrosis causes symptoms of suppuration and a tender swelling, but the tumour is circumscribed, moves with respiration, and does not cause any bulging in the lumbar region. Pyuria is usually present.

The diagnosis of caries of the spine, hip disease, and even of myositis as distinct from perinephritis may be difficult. Since perinephritis in itself induces lumbar rigidity and some degree of scoliosis, X-ray examination may be required to exclude caries of the spine. Hip-joint disease is excluded by absence of local tenderness and by the freedom of flexion and rotation of the thigh.

Treatment.—In the early stages, before there is evidence of suppuration, and when the chief symptom is lumbar pain, the treatment is that of a patient acutely ill with a general toxæmia. The bowels should be kept well open, and fomentations or poultices applied to the lumbar region. Aspirin

may be given to relieve pain. An operation should be performed and the abscess evacuated as soon as the diagnosis is definitely established.

TUBERCULOSIS OF THE KIDNEY

Small grey tubercles are frequently found scattered through the kidneys in persons who die of acute miliary tuberculosis; the kidney disease, however, scarcely affects the clinical aspect of the case, and this form of renal tuberculosis will not be considered here. Further, in patients who die of pulmonary tuberculosis it is not uncommon to find tuberculous foci in the kidneys post mortem, although there was no indication of their presence during life.

Clinical renal tuberculosis is either the fibro-caseating form of the disease, or it is tuberculous hydronephrosis. In either case, the tuberculous infection is generally primary in the kidney in so far as its clinical expression is concerned.

Ætiology.—It is more common in women than men. The maximum age incidence is in the third and fourth decades; the disease is uncommon in the young and rare in the old. At an early stage the disease is unilateral. In the majority of cases the tubercle bacilli are carried to the kidney by the blood stream from a tuberculous focus, such as a caseating lymph gland. Recent experimental work has shown that bacteria do not ascend in the lumen of the ureter unless it is diseased, when the infection may spread by direct extension in its walls. Infection may also reach the kidney via the lymphatics in a proportion of cases. The path of infection is by way of the ureteric lymphatics, and it is probable that in pelvic tuberculosis, for example, tuberculous prostatitis, may spread to the kidney by this route. There is also reason to think that tubercle bacilli from a diseased kidney may infect the opposite healthy kidney by the same lymphatic path, the bacilli first travelling in the urine and walls of the ureter from the diseased kidney and causing disease of the bladder, and then travelling from the bladder by way of the ureteric lymphatics to the sound kidney. On the other hand, there is a shorter path for infection from one kidney to another by the para-aortic lymphatic system. Since the disease in the other kidney takes the same anatomical form as it originally had in the kidney first affected, it is probable that, if the first is due to a blood-borne infection, so is the second. Vesical tuberculosis is, as a rule, secondary to infection elsewhere in the urino-genital system commonly in the kidneys.

Pathology.—The initial lesion is in the cortex, or one of the pyramids, and it consists of one or more tubercles. The morbid process spreads by destruction of kidney tissue; there is caseation in the centre of the lesion, inflammatory reaction, with intense small-cell infiltration, giant-cell formation and more or less fibrosis at the periphery. The lesion also spreads by the deposition of tubercles at a distance; these are scattered through the cortex, singly or in groups. Extension through the capsule is uncommon, but extension to the renal pelvis is frequent. Complete destruction of one or more pyramids may occur, or the disease may spread and involve one or more calices or the entire pelvis. The resulting infiltration and cicatricial contraction may lead to hydro- or pyo-nephrosis. The disease tends to extend

down the ureter, and the bladder is commonly infected at an early stage. Secondary infections may lead to metastatic abscesses in the kidneys and ultimately to destruction of the whole organ.

Symptoms.—Frequency of micturition is often the earliest symptom; it is first noticed by day and later at night. Urgency and painful micturition develop next. The urine may show no other abnormality than a trace of albumin at an early stage; characteristically it is pale and a little turbid from the presence of pus; it is acid in reaction, it may contain a few renal cells, and it is sterile on culture. By appropriate staining tubercle bacilli may be demonstrated in the centrifuged deposit. Hæmaturia may be the first symptom, or the disease may develop insidiously with lumbar pain. On examination, the kidney is sometimes enlarged, and it may be hard and irregular; it is often tender. Tenderness along the course of the ureter or thickening of the ureter, as determined by abdominal or rectal examination, is of great importance. The rest of the urino-genital system requires close examination; this should include cystoscopy and in some cases ureteral catheterisation. X-ray examination of the abdomen may reveal calcified tuberculosis of the kidneys or lymph glands, and it may be required in the differential diagnosis from renal calculus. Finally, a careful review of the patient's history and present condition for evidence of a chronic bacterial toxæmia or of tuberculous infection elsewhere must be made.

Diagnosis.—The presence of tubercle bacilli in the urine, whether determined by microscopic examination of the stained deposit or by guinea-pig inoculation, is not absolute proof of renal tuberculosis, because the bacilli may be excreted by a healthy kidney or they may come from some other part of the urinary tract. Nevertheless, the demonstration of tubercle bacilli in the urine is of the first importance in a doubtful case, and the diagnosis may be established by cystoscopy. The cases which require most careful examination are those with an atypical onset, such as massive hæmaturia, and those in which there is a gross secondary infection when first seen. The possibility of renal tuberculosis must always be borne in mind in hydro- and pyo-nephrosis. The differential diagnosis from simple albuminuria and the several forms of Bright's disease is made on the presence of pyuria and the absence of signs and symptoms of chronic nephritis. Patients with pulmonary tuberculosis are perhaps more prone than others to chronic nephritis on account of the secondary infections which complicate their disease.

Course and Prognosis.—The onset is insidious and the course progressive. Natural recovery is hardly known, though occasionally an unsuspected caseous kidney may be found at autopsy in patients dying of other diseases. The disease runs an uncertain course, having a duration of a few years up to ten or even twelve years from the date of diagnosis. Death results from tuberculous toxæmia, secondary infection, or failure of renal function.

Treatment.—When the disease is unilateral the kidney should be removed but nephrectomy is rarely justified if the other kidney is involved. In any case the patient's health and resistance should be raised to the utmost by rest, fresh air and good food, on the general lines of treatment of tuberculosis of the lungs. Cautious tuberculin treatment may be indicated when the disease cannot be treated surgically.

RENAL CALCULI (NEPHROLITHIASIS)

Renal calculi may be composed of calcium oxalate or carbonate, uric acid, urates, phosphates, cystin, or of a mixture of these.

Ætiology.—All these materials are sparingly soluble in water and their solubility in urine is dependent on (i) its *p*H. If this stands at 5 uric acid is precipitated, while phosphates and carbonates are deposited at *p*H about 8; the others at some intermediate point. (ii) On the presence of urea, which renders both uric acid and oxalates more soluble. (iii) The protective action of certain non-albuminous colloids. If these become coagulated their protective influence is lost. Thus two factors are required to form a renal calculus: crystals derived from the urine and some colloidal material to bind them together. Hence, as Benjamin Moore pointed out, the commonest nucleus of a stone is calcium oxalate, since oxaluria excites albuminuria and even hæmaturia, thus providing the necessary colloid. Prolonged recumbency, as after fracture of the femur, provides opportunity for calculus formation apparently from stagnation in the dorsal portion of the calices. Infection of the urinary tract such as pyelitis is not considered so important as formerly, and indeed may be merely secondary to the calculus; but it is a factor in cystinuria, which will not lead to a calculus unless the urine becomes infected. Pure uric-acid stones may occur in quite young children, but the definite deposit of uric-acid crystals in the pyramids and pelvis of the kidney which is almost a normal event does not seem to lead to calculus formation and milk is usually sufficiently diuretic to remove them. The most important single factor in the prophylaxis of stone is adequate diet. Lack of vitamin A is especially prone to excite stone. In a recent investigation 96 per cent. of cases of renal calculi showed evidence of its deficiency. It is necessary for the maintenance of the proper nutrition of epithelial linings everywhere. The former comparative frequency of uric-acid stones in the children of the poor in London was probably related to the scarcity of fresh vegetables in the diet. Such stones were also common in Norfolk and the neighbouring fens. Chalk in the soil or in the drinking water does not predispose to stone. The factors leading to the deposits of various crystals in the urine have already been discussed (see Abnormalities of the Urinary Secretion).

Calculi may occur at any age, but are very rare in the old. They are commoner in males than in females. Those of sedentary habit are more liable to them. Alcohol and lead are said to predispose to renal calculi. A high blood calcium, whether due to excess of parathormone (as in parathyroid tumours) or of vitamin D, can be an important factor in producing calculi of calcium phosphate.

Pathology.—The pure oxalate stone is very hard, mulberry-shaped, stained by altered blood, and varies in size from that of a mere granule to that of a walnut. If it is encrusted with uric acid it becomes brown, and in form a coral-shaped mass, representing a cast of the renal pelvis and calices. Phosphatic stones are generally smooth and white. A cystin stone is hard, oval, light amber or greenish in colour, with a glistening surface. Other forms are rare. If the stone remains in the renal pelvis it may (1) by gradually increasing in size lead to the atrophy of the renal tissue; (2) by eroding the

capsule of the kidney produce a fistula into the perinephric tissues, resulting in a perinephric abscess; (3) by obstructing the outflow of urine cause hydronephrosis or, more frequently, pyonephrosis. If it passes into the ureter it may become impacted, in this way again exciting hydronephrosis or pyonephrosis, or if it obstructs the ureter completely, may produce atrophy of the kidney. If it causes ulceration of the ureter, this may be followed by stenosis. If it passes into the bladder it is very likely to excite ammoniacal decomposition, and thus become encrusted with phosphates.

Symptoms.—A stone may remain latent in the kidney without causing any symptoms. More usually it causes pain, particularly on any jolting movement. This is occasionally referred to the opposite side, a point to be borne in mind when considering operation. A bout of pain may be accompanied by hæmaturia, and there may be albuminuria for some days afterwards. A small oxalate stone may produce more pain than a large uratic stone, because of its hardness and roughness. A large, branched uratic stone occasionally causes profuse hæmaturia without any pain. The results of renal calculi may be classified as (*a*) mechanical, (*b*) septic. Under the first heading come colic, hæmaturia, anuria, hydronephrosis; under the second, pyelitis, perinephric abscess, pyonephrosis.

Renal colic is the most severe and distressing manifestation of calculus. It is particularly likely to be started by riding on a horse or in a train or omnibus, which causes the calculus to engage in the entrance to the ureter. Violent paroxysms of pain then occur, radiating along the course of the genito-crural nerve down into the groin and testis, which becomes retracted in the scrotum. The pain is also felt in the loin, and the muscles overlying the kidney become rigid. Vomiting and sweating are common. The patient is unable to keep still, and rolls about or gets on to his hands and knees, calling out with each paroxysm. He becomes pale and his pulse increases in frequency, and the temperature is apt to rise. During or after the attack there is usually some hæmaturia, and crystals may be found in the urine. The attack may last several hours and then end as abruptly as it began. Anuria is a serious symptom and implies that the ureter is completely blocked, and the other kidney is either diseased or its secretion reflexly inhibited. Occasionally both ureters may be blocked by calculi. Symptoms referred to the bladder, prostate or seminal vesicles do not occur until the stone reaches the bladder or the lower end of the ureter.

Diagnosis.—The occurrence of renal colic and hæmaturia suggests stone, but these symptoms may be produced by the passage of a blood clot from renal neoplasm or by acute pyelitis, especially in a movable kidney. Ordinary examination of the abdomen reveals nothing beyond lumbar tenderness in uncomplicated cases. X-ray examination is of great value. Oxalate stones are the easiest to detect by that method, as even when small they throw a dense shadow. This is fortunate, since oxalate stones are the commonest. Pure uratic stones may not be detected unless they are large. Cystin stones throw very little shadow. Calcareous abdominal glands and phleboliths may be mistaken for calculi on X-ray examination. In doubtful cases, pyelography, intravenous or instrumental, should be done. A skiagram of the pelvis should never be omitted, since a stone may have passed down to this region. Attacks of pain and hæmaturia with the presence of calcium oxalate crystals in the urine, but with a negative X-ray examination, are probably

due to crises of oxaluria (see p. 1296). Appendicular colic may simulate renal colic, but the point of maximum tenderness is different.

Prognosis.—As long as there is no serious destruction of kidney substance or septic complication the outlook as to life is good, if treatment be adequate. Attacks of renal colic may occur from time to time, with great suffering, and even after stones have been removed by operation they may form again, though this is exceptional. Occasionally stones may be followed by a true chronic nephritis with its usual consequences.

Treatment.—The methods which should be employed when crystals likely to form stones are found in the urine have been described under urinary deposits. Carsful attention must be given to the diet, especially to its vitamin content. Disinfection of the urine should be carried out as described under bacilluria and pyelitis. It is well, however, not to render the urine alkaline when a stone is suspected, since this would lead to a deposit of phosphates upon it. A book of litmus papers should be given to the patient with instructions to place blue and red strips in the morning urine, which is likely to be the most acid. Enough citrate of potash should be given to render the urine amphoteric but not alkaline. Probably 20 grains at night will be sufficient for this purpose. The urine should be kept dilute by taking water freely. Mineral waters, such as Contrexéville and Evian, are helpful, the former particularly for uric acid, the latter for oxalates. Whey is also helpful when uric acid crystals are present. If a renal calculus is present, and this is confirmed by X-rays, removal by operation is indicated. The following points, however, are generally contra-indications for operation: (i) large bilateral stones; (ii) stones which are only the size of a pea or smaller, unless there is severe pain, extensive absorption of renal substance causing toxic symptoms, or obstruction to the outflow of urine. If a small stone is not passed as a result of medical treatment, its removal by operation should be seriously considered; (iii) in some patients small calculi are repeatedly formed and passed. In these cases operation is better postponed because of the likelihood of recurrence. If the diagnosis is uncertain, or operation is refused or postponed or considered inadvisable because of the patient's general condition, the treatment appropriate to the deposit found in the urine should be continued. Violent exercise and jolting movements should be avoided. Small stones can often be got rid of by giving the patient 5 to 10 minims of tincture of belladonna with 10 grains of potassium citrate every 4 hours for a few days, and directing that 5 pints of water should be taken in the 24 hours. For the symptomatic relief of pain, aspirin in 10-grain doses, hot baths and kaolin poultice (antiphlogistine) may be of service. Morphine should be avoided in the treatment of chronic renal pain, on account of the danger of establishing a habit.

For an attack of renal colic, $\frac{1}{8}$th to $\frac{1}{3}$rd of a grain of morphine tartrate, together with $\frac{1}{100}$th of a grain of atropine sulphate, should be given hypodermically. The anti-spasmodic effect of the atropine aids the onward passage of the stone, while the morphine relieves the pain. If morphine be given alone, the pain is apt to recur as soon as its anodyne effect passes off. Ten minims of tincture of belladonna should then be given in an ounce of water every 3 or 4 hours, with abundant fluids, as described above, until the pupils are dilated and the face rather flushed. Inhalations of chloroform may be necessary at the onset, until the drugs have had time to act. Hot applications

to the loins or hot baths may help to relax spasm. Inversion of the patient has been advised, to attempt to disengage the stone from the ureter. After the paroxysm is over, the aid of X-rays should again be invoked to locate the stone if it has not been passed.

HYDRONEPHROSIS

Definition.—A condition in which the pelvis and calices of the kidney are distended by the accumulation of non-infected urine due to ureteral or urethral obstruction.

Ætiology.—CONGENITAL.—The condition may be congenital, due to an abnormality of the ureter or urethra; other congenital defects may be present. The ureteral stricture is commonly found at the exit of the ureter from the pelvis of the kidney, or near its entrance into the bladder. Other congenital causes are a faulty connection of the ureter to the pelvis of the kidney, or an aberrant renal artery. Hydronephrosis is sometimes found post mortem in infants and children without evidence of obstruction to the outflow of urine. In these cases the condition is presumed to be due to a neuro-muscular inco-ordination comparable to congenital hypertrophic stenosis of the pylorus.

ACQUIRED.—It is more common in females than in males, and the maximum age incidence in 74 cases collected by Herringham was between the third and sixth decade.

(*a*) *Bilateral* hydronephrosis results from stricture of the urethra, phimosis, enlarged prostate, obstruction within the bladder, or from a pelvic tumour; the last named is the commonest cause.

(*b*) *Unilateral* hydronephrosis is due to ureteral obstruction from—

1. Obstruction of the lumen by a stone, growth or blood clot.
2. Stricture of the ureter following ureteritis.
3. Pressure from without due to growths.
4. Torsion of the ureter by displacement of a movable kidney. It is also thought that chronic prostatitis or cervicitis may cause sufficient inflammation to produce some dilatation of the kidney pelvis and upper ureter which lengthens and thus kinks the latter.

Pathology.—Two types of hydronephrosis are recognised, namely, the pelvic type due to upper urinary tract obstruction and the renal type from obstruction to the lower tract. In the former the pelvis of the kidney is dilated and there is less absorption of renal parcachyma in the calices. In the latter the calices are more dilated and there is considerable destruction of kidney substance.

It is generally held that hydronephrosis results from intermittent obstruction. It has been produced experimentally, however, by ligature of the ureter causing complete obstruction. But complete obstruction is more usually followed by atrophy of the kidney.

Symptoms.—Many cases are latent, and give rise to no symptoms. The tumour may be discovered accidentally, or there may be complaint of pain in the flank or back. The onset is insidious.

The symptoms by which a hydronephrosis is indicated are the presence of a renal tumour and complaint of an aching pain in the flank or back, and

sometimes polyuria or hæmaturia. In intermittent hydronephrosis, the tumour suddenly disappears with the passage of a large quantity of watery fluid; after an interval the tumour gradually reappears and finally empties suddenly as before. This sequence may be repeated at intervals. Where true polyuria or hæmaturia occurs it is due to a coincident nephritis or pyelitis. There may be acute exacerbations of the chronic pain, with vomiting and collapse; such attacks may accompany emptying of the hydronephrotic sac.

Course.—When unilateral, hydronephrosis may never cause serious trouble, and intermittent cases may persist for years and finally disappear. In bilateral cases uræmia may supervene. Infection of the kidney is not uncommon, and may lead to acute pyonephrosis. The sac may discharge spontaneously through the ureter, and the fluid never reaccumulate. The sac may rupture into the peritoneum, or rarely through the diaphragm into the lung. Cases have occurred in which the ureter of the sound kidney has been blocked by a calculus.

Diagnosis.—The condition, especially when bilateral and unaccompanied by symptoms, is generally overlooked. In its most characteristic form, where the hydronephrosis is intermittent, the diagnosis is readily made. When the condition is apparent simply as a renal tumour the diagnosis from renal neoplasm (or retro-peritoneal glands in a child) is difficult. When the tumour is large it may be mistaken for an ovarian tumour. The diagnosis can be established by intravenous pyelography supplemented, if necessary, by instrumental pyelography. Aspiration of the sac has been occasionally done for diagnostic purposes; but surgical exploration is a safer measure. Fluid from a hydronephrotic kidney is clear or slightly turbid; it contains albumin, and traces of urea and other urinary constituents; in the deposits are epithelial cells.

Prognosis.—This depends on the cause of the hydronephrosis and the condition of the opposite kidney.

Treatment.—The first indication is to remove the cause. Cases of intermittent hydronephrosis that do not cause serious symptoms should be treated on general lines. An abdominal belt to support a hydronephrotic mobile kidney may be of service.

In unilateral hydronephrosis causing serious symptoms, or of large size, von Lichtenberg's plastic operation or nephrectomy is advisable. Since the state and function of the opposite kidney can be fairly accurately ascertained by pyelography and examination of a sample of urine obtained by ureteral catheterisation, nephrectomy is a less serious risk than it was before these exact methods of diagnosis were available. Sympathectomy has been recommended, but it is not clear how this can produce the desired effect.

In bilateral hydronephrosis the main indication is to remove the cause when possible, and to adopt every measure that may aid in preventing infection of the urinary tract.

PYONEPHROSIS

Definition.—Distension of the renal pelvis with pus, to an extent sufficient to cause a renal tumour.

Ætiology.—The affection is a sequela of pyelitis or hydronephrosis.

There are two main types, namely, tuberculous and pyogenic pyonephrosis. The latter, which is the commoner, is most frequently due to an impacted calculus.

Symptoms.—The patient is wasted, toxic and febrile. Rigors are common. There is a renal tumour, which is tender on palpation, and moves to some extent with respiration. Pyuria is present, unless the ureter is completely obstructed.

Diagnosis.—The differential diagnosis from hydronephrosis is made from the presence of pyuria and of local and general symptoms of bacterial infection. Perinephric abscess gives signs of a more diffuse swelling, usually with œdema and redness of the surrounding skin, and does not move with respiration.

Treatment.—In bilateral cases the treatment is palliative. In unilateral cases nephrectomy is indicated, if tests show that the other kidney is adequate.

TUMOURS OF THE KIDNEY

Benign Growths

These are of relatively slight importance.

Adenomata are the most common, occurring in the cortex or under the capsule. They may be single or multiple; multiple nodules commonly occur in sclerotic kidneys in old age. They seldom attain any size.

Fibromata are not uncommon as nodules, sometimes multiple, in the cortex or medulla. Lipomata and angiomata are rare.

Malignant Tumours

Dysembryomata.—These tumours are found most commonly in children under 3 years, and almost always under the age of 11 (Hadfield). They are more often bilateral than carcinoma. They consist of cells remaining at the embryonic level and failing to differentiate in any direction ("Round-celled Sarcoma"). There is a stroma of undifferentiated fœtal connective tissue which resembles spindle-celled sarcoma. In some tumours some degree of differentiation may take place. Thus these tumours may contain embryonic striped muscle, primitive cartilage or nervous tissue, and primitive poorly-formed tubules can usually be found. They are yellow and homogeneous on section.

Adenocarcinoma of Renal Tubules.—As a result of an examination of the 74 specimens of tumours of the kidney in the St. Bartholomew's Hospital Museum, Hadfield has come to the conclusion that renal tumours previously known as Hypernephromata are in fact Adenocarcinomata. These tumours are single, large, well circumscribed, and often surrounded by a capsule of compressed kidney tissue which is destroyed by pressure rather than by infiltration. These tumours consist of anastomosing columns of cells. Their blood supply consists of irregularly dilated, lake-like sinusoids which lie between the tubules of the growth in contradistinction to adenomata, which are composed of well-formed tubules having well-defined lumina and a simple capillary circulation. Both in adenomata and

adenocarcinomata, and especially in the latter, the cells are infiltrated with a lipoid-fat-glycogen complex ("lipoid infiltration"), which gives these tumours their peculiar yellow colour. Recent and old hæmorrhage is commonly seen. Cystic degeneration often occurs. On section there is fine and coarse lobulation. These tumours may spread along the renal veins into the inferior vena cava, and to the pelvis of the kidney and perinephric tissues.

Symptoms.—1. Hæmaturia is the first symptom in more than 70 per cent. of the cases. It is much less frequent in children. The blood is fluid or clotted, and moulds of the pelvis or ureter may be passed. The hæmaturia is spontaneous, profuse and intermittent; it is little influenced by rest, nor is it provoked by exertion. It may be the only evidence of a neoplasm, and after lasting for a week or 14 days may cease, leaving no further evidence of the growth until at some later date a tumour is felt. The urine frequently contains albumin at intervals.

2. Pain is uncertain. It may be a dragging feeling, or a constant ache. The passage of clots may give rise to renal colic; otherwise the hæmaturia is not accompanied by pain.

3. The presence of a tumour is a most important sign. It is felt on deep palpation bimanually. It is first palpable below the ribs, outside the rectus muscle, as a solid swelling, with rounded borders, that moves with respiration. It may be possible to define its upper border. As the tumour increases, it tends to go forward. It may fill the hollow below the twelfth rib behind, but does not cause a swelling in the back. Large renal tumours cause asymmetry and bulging of the abdominal wall and marked displacement of neighbouring abdominal viscera. On the right side, the ascending colon lies in front, on the left the last part of the transverse colon and the upper part of the descending colon; the tumour is, therefore, resonant on percussion in front. When the tumour is highly vascular, pulsation is felt in it, and a systolic bruit may be heard over it. In later stages, the tumour is liable to become fixed by adhesions.

4. Progressive emaciation is generally late. It may be absent although the tumour is large.

5. Metastases are sometimes the first sign of a renal neoplasm, occurring in the lungs, bones or brain. Secondary deposits in the para-aortic lymph glands may cause obstruction to the inferior vena cava, or this may result from pressure of the tumour itself.

Diagnosis.—Diagnosis is made on the presence of hæmaturia, with a tumour. When hæmaturia occurs alone, and other causes have been excluded by careful clinical, bacteriological and X-ray examination, then a more detailed investigation of the urinary tract must be undertaken immediately. This entails cystoscopy, intravenous pyelography and on occasion retrograde pyelography. When a tumour is the only sign an exploratory laparotomy is advised. The tumour requires to be distinguished from splenomegaly, hepatomegaly and Riedel's lobe. A renal tumour has not the definite edge characteristic of splenomegaly and enlargement of the liver. Enlargement of the liver is also often a source of difficulty. A Riedel's lobe is continuous with the liver, does not extend back into the loin, and is dull on percussion. Splenic tumours are recognised by the fact that they tend to occupy an oblique position in the abdominal wall, by the presence of a notch and of a

sharp inner margin, free movement with respiration, and dullness to percussion.

A differential diagnosis from retroperitoneal tumours, including those of the suprarenal, is not always possible, though the suprarenal growths may sometimes be recognised by certain characteristic features. Thus, there is the medullary sarcoma type described by Hutchison, generally occurring in children, characterised by metastases in the skull, ecchymotic swelling of the eyelids, papilloedema and severe anæmia, and the " infant Hercules " type of tumour of the adrenal cortex.

Prognosis.—The disease is almost invariably fatal. Many die within 2 years, and the majority within 4 years, though exceptional cases of survival for 5 to 10 years after operation have been recorded.

Treatment.—Surgical treatment alone holds out a prospect of cure. Symptomatic treatment includes the use of drugs for the relief of pain and the control of hæmaturia.

CYSTS OF THE KIDNEY

Solitary Cysts

These may occur in an otherwise normal organ. They vary in size from very small cysts to tumours of considerable bulk. They result from dilatation of an obstructed tubule, and they may be congenital.

Multiple Cysts

Multiple cysts of small size are commonly met with in sclerotic kidneys. They result from chronic inflammatory changes that lead to obstruction of the tubules with subsequent dilatation. There are also rare cases of multiple cysts, of large size, whose ætiology and course are little known.

Polycystic Disease of the Kidneys

Definition.—Polycystic kidneys appear as a massive conglomeration of cysts, varying in size from a pin's head to a marble, separated by dense strands of fibrous tissue, in which little or no renal tissue is evident on naked-eye examination.

Ætiology and Pathology.—The commonest age incidence is between 40 and 50 years; they are relatively common in the decades preceding and following; they may occur in infancy and childhood, and of these a large proportion are in still-born infants. Those occurring in infants are congenital, and other congenital abnormalities may be present. The disease in adults is probably also congenital in origin. In this case it must be progressive, because the renal damage in the later stages is too severe to have been compatible with many years of active life. In this connection it is noted that the disease is often found in more than one member of a family and in successive generations. Its familial incidence, congenital origin, and association with cysts in other organs, especially the liver, all suggest that this disease belongs to the group of congenital-developmental errors.

The organs are enlarged in size, and weigh 20 to 30 ounces each, or even 3 to 4 lb. They have been compared to a bunch of grapes in appearance. The cysts project from the surface and form the mass of the organ. They are lined by a layer of flattened cells, and are filled with fluid. This fluid is clear or turbid, limpid or viscid, colourless or yellowish; it is sometimes blood-stained, giving it a red, purple or green colour. Urea has been found in the fluid, which may also contain fat globules, cellular débris, cholesterol and triple phosphate crystals. On microscopic examination more or less renal parenchyma is found in the septa between the cysts; the tubules are distorted, and exhibit varying degrees of atrophy, degeneration and dilatation, while the glomeruli show changes characteristic of chronic interstitial nephritis. The blood vessels of the kidney undergo sclerotic changes; there is increased fibrous connective tissue and small cell infiltration. In some cases cysts are also found in the liver, ovaries, broad ligament, uterus, pancreas and spleen; but they are rare in any other organ than the liver.

Symptoms.—The affection is nearly always bilateral. When the tumours develop to large size in the fœtus, difficulty in labour may result. In the adult there may be no symptoms, or any of the symptoms of chronic nephritis may develop and may terminate in uræmia, cerebral hæmorrhage or cardiac failure. General arterial disease, with raised blood pressure and cardiac hypertrophy, is commonly present; on the other hand, the condition may reach an advanced stage and fatal termination without appreciable cardiac hypertrophy. In a third group the bilateral renal tumours are the most striking features, associated with general malaise, dull aching pain in the loins, and recurrent hæmaturia. The tumours are not tender, and present the ordinary signs of renal tumours (*q.v.*). The urine is of low specific gravity, and commonly contains a trace of albumin; there may be polyuria.

Course.—This usually follows that of "chronic interstitial nephritis."

Diagnosis.—A condition of "chronic interstitial nephritis" with large palpable kidneys should suggest polycystic disease. Renal neoplasms other than sarcomata are nearly always unilateral. The absence of fever and pyuria excludes bilateral pyonephrosis.

Treatment.—The treatment is that of chronic nephritis. Operation is contra-indicated, since both kidneys are nearly always equally affected.

Other Forms of Cystic Disease

Echinococcus cysts may occur in the kidney, and the discharge of the daughter cysts has produced attacks of renal colic. *Cystic degeneration of renal neoplasms* is described elsewhere.

MOVABLE KIDNEY

The kidney is normally held in place by the perirenal fat, the renal vessels and the peritoneum stretched over it. But this does not prevent a certain amount of respiratory excursion, as may be seen either by X-ray examination or in the operating theatre. The range of movement varies between 1 and 2 inches, and is more marked on the right than the left side. The term movable kidney should therefore only be applied to cases where there

is an excessive respiratory descent, so that the upper as well as the lower pole can be felt, or where the kidney can be moved about by external manipulation. As the kidney slips downwards, the lower pole gradually passes towards the middle line, while the organ rotates slightly, causing the hilum to look somewhat upwards.

Ætiology.—Movable kidney is about seven times more common on the right than on the left side. The ascending colon and the hepatic flexure lie on the inner aspect of the right kidney, thus tending to drag it down when the bowel is loaded or dropped. On the left side, on the other hand, the strong costo-colic fold suspends the splenic flexure much more securely, while the descending colon lies to the outer side of the left kidney.

The condition is much commoner in women than in men. In men the kidney pouches are deep, narrow and rapidly diminish in breadth from above downwards, while in women they are much shallower and broader, and diminish only slightly in breadth from above downwards. This natural difference is accentuated in the spare long-waisted women with narrow loins, who are recognised as specially liable to floating kidney. The greater liability of women to chronic constipation further helps to induce dropping on the right side.

Pathology.—Many reasons have been given for the occurrence of movable kidney; but few will stand investigation. Wasting with loss of perirenal fat, or loss of tone in the muscles of the abdominal wall, have been held responsible, but movable kidney is so common apart from such conditions that their importance is doubtful. Glénard emphasised the frequency with which movable kidney is associated with a general visceroptosis; indeed it is rare to find a movable kidney without coloptosis. Naturally, if there is general visceroptosis, the kidney is its most obvious sign. It is a firm organ which can be readily grasped, while the other dropped viscera would elude palpation. As Landau says, "Pleased with his discovery, the physician may impute all subsequent symptoms to the movable kidney." Most of these are really due to visceroptosis.

A serious sequel is the occasional occurrence of hydronephrosis produced by torsion of the ureter during the forward rotation of the organ or by its becoming kinked over the renal vessels. If hydronephrosis occurs, a subsequent infection may convert it into a pyonephrosis.

Symptoms.—There may be no symptoms at all and, if the movable kidney is only discovered in the course of routine examination, it is better not to tell the patient of its existence. It may be well, however, to inform a reliable relation, if such can be found, in order to protect oneself against a less discreet medical attendant subsequently revealing the fact to the patient. The commonest symptom is a constant dragging pain owing to traction on the renal plexus. This most frequently first declares itself between 25 and 35 years of age. A zone of hyperæsthesia corresponding to the distribution of the tenth thoracic segment may also be present. More serious symptoms directly due to movable kidney are Dietl's crises; but these are not common. The attacks are characterised by intense pain radiating down the ureter and through the back, shivering, nausea, vomiting, fever and collapse. The urine is scanty, and may contain blood. Sometimes the pelvis of the kidney may become distended, giving rise to an obvious increase in the size of the organ. This may pass off later, with abundant

discharge of urine, showing that the crises are due to kinking and consequent partial obstruction of the ureter. If repeated, they may lead to hydronephrosis.

The other symptoms which have been attributed to floating kidney are really due to the associated visceroptosis (*q.v.*). But there is no reason to attribute far-reaching nervous consequences to movable kidney, yet, for some enthusiasts, hysteria in women, hypochondriasis in men, and even insanity, are common outcomes. There is little doubt that far too much stress has been laid upon this condition as a cause of manifold complaints.

To detect a movable kidney on the right side, the left hand should be placed under the loin while the patient is recumbent, though some authorities prefer a semi-recumbent posture. The patient should then be told to take a deep breath while the right hand is placed just under the edge of the liver in the nipple line. The kidney may then be felt to slip between the fingers. Usually, this does not cause the patient a definite pain, but a dull, sickening sensation. In the more advanced degree of the condition, the organ may be felt far from its normal position, even to the left of the middle line or nearly down to Poupart's ligament. In examining on the left side, the observer should stand on the patient's left, placing his right hand behind the loin and palpating in front with his left.

A movable kidney usually feels larger than the normal excised organ. This is because of the surrounding investments through which it is felt.

Diagnosis.—Usually this is obvious, as the shape and mobility of the organ are so characteristic. Occasionally, a Riedel's lobe has been taken for movable kidney; but the continuity of the former with the liver should prevent this mistake being made. In the same way, a distended gall-bladder is continuous with the liver, and cannot be separated from it. Moreover, it is not nearly so movable, and curves characteristically towards the umbilicus. Carcinoma of the pylorus has offered difficulties in some cases; examination of the stools for occult blood, a test-meal and X-ray examination would clear up the diagnosis. Scybala near the flexures of the colon may be mistaken for floating kidney; but their indefinite shape and inelasticity generally help to distinguish them. Their disappearance after a series of enemata would settle the question. In one case a mesenteric cyst appeared closely to resemble a floating kidney.

Prognosis.—Apart from the development of hydronephrosis, movable kidney does not tend to shorten life in any way. It is doubtful whether a kidney once prolapsed can ever maintain the normal position unaided.

Treatment.—Some cases call for no local treatment, though the associated visceroptosis and neurasthenia will require attention. If pain is felt, the adoption, for a short time, of the knee-elbow position will help to replace the kidney and relieve the tension on the renal plexus. If pain is at all frequent, some form of abdominal support, such as a specially designed corset, should be worn. Hurst has urged that the support should be designed to increase the general intra-abdominal pressure, and not to replace any one viscus. We are convinced that this is sound and that, in many cases, a "kidney belt" is worse than useless, while the addition of ingeniously placed pads only increases the discomfort. Whatever the form of the support, it need only be worn while the patient is in the erect posture, and it is best fitted while she is recumbent, preferably with the pelvis raised on a pillow so as to

aid the replacement of the kidney. Often, when a support of this kind has been worn for a year or two, it is possible to give it up without recurrence of symptoms. Breathing exercises to develop the expansion of the lower thorax, with exercises to improve the tone of the abdominal wall have in many cases proved more efficacious than a passive support. Operation should not be advised except for recurrent Dietl's crises or when there is evidence of hydronephrosis, when nephropexy may be done. But even this may not be successful, and ultimately nephrectomy may be required for the hydronephrosis.

Treatment of Dietl's crises.—The patient must be put to bed and hot fomentations or antiphlogistine applied to the affected side. A hypodermic injection of a quarter to one-third of a grain of morphine may be required if the pain is severe. Usually this is sufficient but, should the attack last more than a few hours, an attempt must be made, under an anæsthetic, to rectify the position of the kidney by manipulation. Naturally, conditions are unfavourable for nephropexy during or immediately after a crisis, because of the congested state of the organ.

W. Langdon-Brown.
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SECTION XVII

DISEASES OF THE JOINTS AND INFLAMMATORY DISEASES OF THE FIBROUS TISSUES AND MUSCLES

ARTHRITIS

The diagnosis of " arthritis " should be reserved for cases in which there are pathological changes at the surface of a joint. In the past there has been a tendency to employ this term too loosely.

The clinical conception of arthritis is much simplified by modern classification, which divides it into two clear-cut *clinical* types, each of which presents distinctive features. These are the rheumatoid arthritic type and the osteo-arthritic type. Consequently such terms as " arthritis deformans " should no longer be used.

The features of the rheumatoid and osteo-arthritic types of arthritis will be found under their respective headings below, and since the criteria of these types are clinical, this terminology can be correctly employed in those cases in which the ætiology remains obscure.

The most basic difference between these two types is that rheumatoid arthritis is a generalized disease in which the most obvious local effects fall upon the locomotor system ; while osteo-arthritis is a degenerative type of condition, which, without affecting the patient's general health, for various reasons becomes localised in certain joints.

There are, in addition, certain cases which are referred to as " Mixed arthritis," in which the degenerative lesions of osteo-arthritis become superimposed upon those of an inflammatory arthritis of the rheumatoid type.

1. RHEUMATOID ARTHRITIS

Synonyms.—Atrophic Arthritis ; Infective Polyarthritis.

Rheumatoid arthritis has generally been described as being of two types, namely, the " classical " or idiopathic type, of which the causation is unknown ; and the infective type, in which a discoverable infective agent is causative. It was the opinion of the committee appointed by the Royal College of Physicians (1934) that the term " rheumatoid arthritis " is best reserved for the first type, and " infective arthritis " for the second. It is, however, generally impossible to distinguish between the two types on purely clinical grounds, and the distinction should therefore depend on the pathological findings. Either type may, however, be correctly referred to as the " rheumatoid type " of arthritis.

Rheumatoid arthritis is a generalised progressive disease affecting principally the joints, which are swollen and painful. If unchecked great destruction and deformity results.

Ætiology.—The malady is said to occur at least five times as frequently among females. The type of patient most commonly affected by the classical form of the disease is a young woman between 20–40 years of age, and of slender delicate build, with a somewhat narrow back and acute costal angle. The affection seldom commences after the menopause. Predisposing factors exist in many cases and include the climateric, chronic gout, malnutrition, emotional shock, and minor focal infection which is not in itself causative of the condition.

Pathology.—The pathological processes are inflammatory in nature. The soft tissues and the white fibrous structures around the joints are the first to be affected. The inflammation then spreads to the capsule and synovium, and granulation tissue forms in the angle made by the articular cartilage with the synovium. The latter then gradually extends inwards as a ring of "pannus," covering and eventually replacing the articular cartilage. As this happens on both articular surfaces the tendency is for them to adhere, especially if the joint is immobilised, and so fibrous ankylosis occurs, which in some cases progresses to a bony ankylosis.

There are atrophic changes affecting the skin, subcutaneous tissues, muscles, ligaments, joints and bones. This latter condition of generalised osteoporosis shows as the first *X-ray* evidence of the disease. The peri-articular swelling can also be seen in outline, but actual joint changes do not occur until considerably later. Some degree of patchy recalcification may be observed when the progress of the disease is checked. Osteophytes are never found in rheumatoid arthritis, but in late cases very considerable disorganisation of the joints take place, and in these areas the bone sometimes gives the appearance of having been dissolved away.

The chief pathological change in the blood is an increase in the sedimentation rate of the red blood cells. This is an important index of activity, and the response of a patient to treatment over a considerable period can be estimated with some accuracy by means of this together with clinical observation. A secondary anæmia is usually present in the pre-arthritic phase. The glucose tolerance of the patient is generally found to be reduced in the active stages of the disease.

Symptoms.—There is in most cases a prodromal period, during which the patient loses a considerable amount of weight; and fatigue, both mental and physical, is a marked feature in nearly all cases. There may be other symptoms, such as paræsthesia, Raynaud-like phenomena, irregular menstruation, tachycardia, sweating, and a secondary anæmia.

The onset of the arthritic phase is often announced by a swelling of the mid-phalangeal joints of the second and third fingers of both hands. It is usually insidious, but is acute in about 10 per cent. of cases. In the case of the former, it is not uncommon for the disease to be marked by long periods of low and intermittent fever. The cause of this is not known. The thyroid gland is also sometimes enlarged, and fibrositic pains may be complained of.

Wasting of the small muscles of the hands is generally the next event, while the uncompensated pull of the interossei muscles, which appear to be affected a little later in the disease, tends, in combination with trauma, to drag the fingers into the typical position of ulnar flexion, in which they often become ultimately fixed. The affection then spreads centripetally

towards the trunk, involving in turn the wrists (which often become the seat of ankylosis), ankles, elbows, knees, shoulders, hips and jaw. The bilateral and symmetrical way in which all the joints are affected is a striking feature of the disease. This point, however, is not so well marked in cases of infective arthritis as in the idiopathic type of rheumatoid arthritis. In some cases the spine itself in due course becomes affected. (See p. 1362).

Whenever a joint becomes involved it will be noticed that the muscles which control it, particularly the extensors, waste rapidly, giving rise to the varying flexion deformities seen in the later stages. These may be perpetuated by a fibrous ankylosis of the affected joints, and contraction of the joint capsule. Bony ankylosis may follow this stage, and when it does so it generally occurs in the wrists and the bones of the carpus in the first place.

In certain cases enlargement of the lymphatic glands occurs, and even the spleen may become palpable. Sufferers with rheumatoid arthritis generally experience considerable pain which interferes with their sleep, and this adds progressively to the severity of the condition.

Symptoms often clear up during pregnancy occurring during the course of the disease, but in most cases they return with renewed vigour after parturition. It should not be forgotten that periodical intermissions are a well-observed occasional feature of the disease, which sometimes results in undeserved credit to any treatment which is being undertaken at the time.

Prognosis.—Under properly planned and supervised treatment, about 20 per cent. of patients should prove completely amenable to therapy, a further 50 per cent. should show great or moderate improvement, and an additional 20 per cent. are improved to some extent; leaving 5–10 per cent. of cases which appear to be entirely resistant to treatment of all kinds. With modern methods of splintage, gross deformity should very seldom occur, even when ankylosis takes place. It should be remembered, however, that in many cases treatment of some sort for months or even years is required, and that relapse may occur after apparent cure. Enlargement of the lymphatic glands has often seemed to be of bad prognostic significance, especially when the white cell count is profoundly altered in addition, and subcutaneous nodules appear. If the disease is not checked, the end-result is complete and painful crippledom. This often takes place within a very short period, particularly when the patient is young. Cases which occur later in life tend on the whole to be less virulent in their course.

Treatment.—As yet there is no specific form of therapy. It is by a careful and intelligent selection and combination of methods suited to the individual patient that success will be achieved.

Diet.—This should be rich in vitamins, especially B and C, and should be of the high caloric type, except in the rare cases in which the patient is overweight. When the sufferer is much underweight and does not return to normal by dietetic means alone, a small dose of insulin (5–10 units) may be administered 15 to 20 minutes before two meals in the day, which should be rich in carbohydrates.

Physical Therapy.—In the acute phase, most methods of external treatment will prove too exhausting and are therefore undesirable. An exception is progressively graded ultra-violet rays, which stimulate the skin, and to some extent the patient's powers of resistance. Later, massage and heat

will help to relax the muscle spasm, which is often a cause of pain and ultimate deformity.

Drug Therapy.—This has only a limited scope in arthritis of all types, and should never be the sole method of treatment employed. On general principles such patients need iron for anæmia, laxatives for constipation, and analgesics—especially aspirin, phenacetin, and, when necessary, in addition Dover's powder (gr. 10–15), or codeine phosphate (gr. ¼–½)—for pain and sleeplessness. A valuable remedy is guaiacol carbonate, which is an intestinal antiseptic and analgesic. It may be given in doses of 5 to 10 grs. three times daily after food. A useful combination is guaiacol carbonate, grs. 8, aspirin, grs. 4, in cachet form, three times daily after food. Guaiacol carbonate is free from any danger of toxic symptoms. Arsenic is of considerable tonic value, especially if combined with nux vomica and taken before meals. Cod-liver oil also has great value and, if preferred, may be combined with malt extract. It should be given in full doses of one ounce two or three times daily if such can be tolerated. Thyroid is useful in cases occurring about the menopause. Iodine in the form of liquor iodi simplex once daily is useful in some cases.

Injections of gold salts have recently been found helpful in many cases suffering from the idiopathic type of the disease, especially when the onset is fairly recent and the blood sedimentation is high. When the malady is known definitely to be the result of an infection their employment is inadvisable until this has been eradicated.

This method of treatment is contra-indicated with renal or hepatic damage, diabetes mellitus, eczema, severe anæmia, colitis, pregnancy, hæmophilia, or a history of having suffered from any severe alteration in the white-cell count in the past, or purpura. With regard to other cases, the dangers of reaction, complications and mortality should be taken into consideration. There should be a complete blood count, blood sedimentation test, and an examination of the urine for albumin. The chief complications are purpura, rashes, boils, exfoliative dermatitis, gastro-enteritis and colitis, nephritis, jaundice, aplastic anæmia and stomatitis. There is a mortality of about 1 per cent. attendant upon this form of therapy. The patient herself should decide after being informed of the danger of reaction, complications and mortality. She should not be allowed to expose herself to strong sunshine or ultra-violet light, for fear of pigmentation.

It is well not to administer gold near the period of the menses, as skin eruptions are said to be more liable to occur then. There are several preparations of gold salts on the market. It is wise always to employ those which are administered intramuscularly. Whether they are suspended in an oily or in an aqueous solution appears to be immaterial. The initial dose should be 0·01 gm., and subsequent doses may be 0·05 and 0·1. This latter dose should not be exceeded, nor should the injections generally be given more frequently than once weekly. The total amount in a complete course should in most cases be limited to 1–1·5 gm. An interval of at least six weeks should then elapse before a further course is commenced. The dosage should be adjusted according to the patient's condition and response to previous injections. Patients of very light weight probably require smaller initial doses and more careful subsequent grading. A complete blood count, blood sedimentation rate test, and urine examination for albumin should be

repeated at regular intervals during the treatment. Great care should be exercised in watching for the first signs of reaction, or any other complication. In the first instance, no further injections should be given until 48 hours after the reaction has entirely subsided. In the second, the injections should be stopped immediately, and not resumed, if at all, until the patient has been free for two to three weeks. If complications appear treatment is palliative, while if the skin is involved also, calamine lotion, with 1 per cent. phenol, should be applied, and a mixture containing bromide and phenobarbitone (gr. ¼) should be administered thrice daily until the complication has disappeared. Patients with jaundice should be put to bed and treated as if suffering with catarrhal jaundice. For the other complications 10 c.c. of a freshly prepared 20 per cent. solution of sodium thiosulphate should be given intravenously every day, and 10 c.c. of 10 per cent. calcium gluconate may be administered intramuscularly at the same time.

Vaccine Treatment.—In infective arthritis a course of vaccine injections is a rational form of therapy. In certain cases it is very successful in reducing the activity of the disease. But it should, however, not be expected to take the place of the simple orthopædic and other measures necessary to prevent contracture of the joints. When the patient is suffering from idiopathic rheumatoid arthritis the results of vaccine therapy are less certain. But it is often worth a trial, either previous to the employment of gold therapy or in the interval between the courses. In cases in which gold is contra-indicated or is not well tolerated, it may be the method of choice, except in those who are febrile and much exhausted, when the powers of reaction are very low and harm may result. The right dose is the lowest which is found to provoke a favourable reaction, and not the highest which can be tolerated, as is believed by some.

Protein shock may be given in the form of intravenous T.A.B. vaccine injections. This is a non-specific procedure designed to raise the patient's temperature temporarily in the hope of benefiting him subsequently. Such treatment should never be undertaken when the patient is in an active phase of the disease. Once improvement has started, however, it may be justifiable to endeavour to speed its tempo by this means. Three to five injections should be administered, the dose varying according to the age and weight of the patient. At least 24 hours of normal temperature should be allowed between the injections, which should not in any case be given more frequently than twice weekly.

Additional methods of treatment useful in certain cases include blood transfusions in those in which improvement by other means is long delayed; colonic lavage when there is reason to believe that the lower bowel is implicated; and sulphur injections, which have a similar object to protein shock.

Finally, certain considerations regarding *focal sepsis*: It is a safe rule in such a disease such as rheumatoid arthritis, in which the exact ætiology is often obscure, that "whatever is found wrong—put it right!" This should extend to the discovery of foci of infection. It is, however, unwise to embark upon operative procedures while the patient is in a condition of debility, or while the disease is running an acute febrile course, with marked joint pain and swelling. In such patients an endeavour should previously be made to build up the general health. If after 4–8 weeks no improvement has occurred and the focus is still believed to be of importance, cautious

measures for its removal may be initiated. The patient should in such cases be warned that it is unlikely that the removal of such a focus will cure the arthritis, but that his general health, and the powers of active resistance will be stimulated thereby. The foci of infection which are of particular importance and should always be investigated are situated in the tonsils, the sinuses, and teeth—in that order. Less important foci include the colon, the appendix, gall-bladder, cervix, tubes, prostate and bladder. If more than one focus of infection is found the most apparently active should be treated first. If this cannot be determined the matter should be dealt with in the order mentioned above. In cases in which the sinuses and the tonsils both require surgical attention it is important to allow a period of several weeks to elapse between the two operations.

2. SPECIFIC INFECTIVE ARTHRITIS (OF RHEUMATOID TYPE)

Gonococcal Arthritis

From 1 to 5 per cent. of those infected with gonorrhœa develop gonococcal arthritis. The latter is also found in babies, whose infection occurs at birth. In view of the fact that infection due to this cause frequently ends in great crippling and bony ankylosis of the joints, it is important to make the diagnosis at the earliest possible stage. If this is done the prognosis is now good.

The clinical appearance and course of gonococcal arthritis is similar to that of the idiopathic type of rheumatoid arthritis when the onset of the latter is acute. A differential diagnosis may be made from the following points: (1) A recent history of gonococcal infection or urethritis. Unless specifically questioned, patients often omit to mention this. (2) The onset of joint symptoms within three weeks of such an infection. (3) There is a predominance of 3 : 1 in males, unlike true rheumatoid arthritis. As in the latter disease, however, the malady is usually a polyarthritis from the onset. (4) The knees, wrists and ankles are generally the seat of the most virulent attack; while a painful teno-synovitis around the wrists and ankles is a common forerunner of actual arthritis. (5) Conjunctivitis and irido-cyclitis is not uncommonly associated with gonococcal arthritis.

If pathological aid is available the complement fixation test of the blood is found to be positive in about 80 per cent. of cases after the first month. Gonococci may in many cases also be grown by special methods from samples of the joint fluid, which affords an immediate confirmation of the diagnosis.

The main points in treatment are (1) that of the primary focus and prostate; (2) the sulphanilamide group of drugs; and (3) artificial fever therapy (hyperpyrexia). The last, whenever it is available, is considered by American observers to be " specific " for gonorrhœal polyarthritis.

In the chronic stages cases should be treated on the same lines as rheumatoid arthritis, except that gold salts are contra-indicated. (See also p. 23).

Pneumococcal Arthritis

A polyarthritis clinically of the rheumatoid type is a rare sequel of lobar pneumonia. It affects children more commonly than adults. An arthritis

affecting one or more of the larger joints is somewhat commoner. These conditions will generally occur subsequent to the stage of pneumonic resolution. Primary pneumococcal arthritis of either type is uncommon.

Pathology.—The joint fluid is in most cases purulent, and pneumococci can be found in it, except in cases which have received sulphapyridine in large doses.

Prognosis.—If the patient survives the pulmonary infection his resistance to the organism should be good, and joint function is in most cases preserved provided erosion of the cartilage has not taken place.

Treatment.—Joints affected in this way should be aspirated early and irrigated with isotonic saline solution, although drainage is not advisable. They should be immobilised in light plaster splints, which should be removed daily to permit of gentle movement. Sulphapyridine should be given in full doses.

Acute Suppurative Arthritis

This is often polyarticular in its distribution, and may be mistaken at first for acute rheumatic fever or rheumatoid arthritis. It is commoner in children than in adults.

Ætiology.—The condition may be a blood-borne infection (metastatic), or may arise as an extension from neighbouring areas of osteomyelitis, or other infection. The former is the more common and may be secondary to a focus of infection in the middle ear, throat, sinuses or prostate. It may also follow the acute specific fevers, particularly scarlet fever and septic tonsillitis. It has also been reported as following meningitis, septic endocarditis, infected varicosities and burns, pyelitis and furunculosis. An arthritis following typhoid fever is not generally suppurative, but may become so.

The organisms which are chiefly responsible are the hæmolytic streptococcus, the staphylococcus, the pneumococcus and the gonococcus.

Symptoms.—These include an acute onset of chills and sweats, pyrexia, local pain and tenderness in the joints, with redness, swelling and limitation of movement. There is in most cases a high degree of polymorphonuclear leucocytosis.

Course.—The joint fluid rapidly becomes purulent and extensive damage to the joints will occur if treatment is not instituted rapidly. Badly damaged joints generally ankylose ultimately. The mortality amongst such cases is in the neighbourhood of 20 per cent.

Treatment.—This should be directed towards the primary source of the infection as well as the affected joints. If the organism is known to be a streptococcus, pneumococcus, gonococcus or meningococcus, drugs of the sulphonamide or sulphapyridine group will be of value. But they are ineffective in cases of staphylococcal arthritis, in which condition sulphathiazole may be of benefit.

Immediate aspiration of the affected joints is essential, both for diagnosis and therapeutically, and lavage with normal saline should be done. In some cases it is necessary to open the joint for this purpose. Blood transfusion is valuable in these cases; and orthopædic care is required if ankylosis appears probable. Hyperpyrexia treatment is useless in the majority of cases.

Tuberculous Arthritis

Tuberculous arthritis usually occurs in young patients, and is an infection from a primary tuberculous focus elsewhere in the body, and frequently signs of tuberculosis in other parts of the body are present. The possibility of an arthritis in a young subject being tuberculous should always be borne in mind, and an X-ray examination is of great value in differentiating this type from other varieties. The subject is dealt with fully in surgical books, to which the reader is referred.

Dysenteric Arthritis

A polyarthritis of the rheumatoid type follows bacillary dysentery in about 3 per cent. of cases, at an interval varying from three weeks to several months after the cessation of acute symptoms. It may also occur in the course of a chronic ulcerative colitis. In some cases the process will only affect one joint, but in either event the process commences as an inflammation of the periarticular tissues and progressively invades the joint surfaces. Suppuration is very rare.

Treatment will be directed to the dysenteric condition, and should be palliative so far as the joints are concerned.

Undulant Fever or Brucelliasis

A mild polyarthritis due to the organism of this disease is probably more frequent than is usually believed. It is generally associated with myalgia, and sometimes with intermittent hydrarthrosis. The onset may be acute or chronic, and the clinical picture may closely resemble rheumatoid arthritis or rheumatic fever. Cases have also been confused with pulmonary tuberculosis and "neurasthenia."

The general symptoms are indefinite and multiple, and include malaise, long-continued low-grade pyrexia, which "undulates," loss of weight, sweating and depression. The blood may show a secondary anæmia and a leucopenia with relative lymphocytosis. The agglutination tests will probably also be positive if the disease is of some weeks duration.

Dengue

This disease gives rise to a very acute form of peri-arthritis. Intense pain and sometimes swelling occur in the tendons and muscles around the joints. These usually disappear when the fever subsides, but in the stage of convalescence may recur and last for weeks or months. The condition should be differentiated from rheumatic fever, from which it differs in being epidemic and in not responding to salicylates.

Meningococcal Arthritis

This is not uncommon in the second week of cerebro-spinal fever, and may be polyarticular or monarticular. It sometimes becomes purulent. It resembles gonococcal arthritis closely, except that it is generally less severe. There is also a sporadic form—chronic meningococcal septicæmia—

which occurs in the absence of meningitis. The diagnosis in these cases rests upon the presence of intermittent fever, a rash, which may be purpuric, and a positive blood culture. The fluid from the joints affected may contain the organism. The patients often seem surprisingly well, and complain of little except joint pains. Both these types respond well and rapidly to sulphapyridine therapy.

3. OSTEO-ARTHRITIS

Synonyms.—Hypertrophic Arthritis; Arthrosis; Arthritis Deformans; Morbus Coxæ Senilis (of hip).

Osteo-arthritis is a degenerative condition which affects the articular cartilages and weight-bearing surfaces of the larger joints.

Ætiology.—The known factors include trauma, certain disorders of metabolism, and nervous diseases, *e.g.* Charcot's joints. Senility is also a cause, as may occasionally be prolonged toxæmia. There is, however, no evidence that focal sepsis is primarily concerned in the ætiology of this type of arthritis.

The malady tends to occur principally in men over middle life who have led a strenuous existence; while in women it mainly affects the knees and is secondary to the proliferative synovitis which is often a distressing feature of the menopausal period.

Pathology.—The changes which occur in the joints affect primarily the articular cartilage, which in the early stages will show grooving and "fibrillation," starting at the points where the pressure of the opposing surfaces is greatest. Later, the cartilage may actually wear through at these points, and the two bony surfaces will come into contact. When this happens, the constant rubbing of bone on bone will gradually polish and "eburnate" these areas. At the same time a gradually progressive enlargement of the articular surfaces will occur, which culminates in the production of "lipping" and of bony outgrowths from the joint margins called osteophytes. These excrescences may be easily palpable at the joint margins, and are the typical lesions of osteo-arthritis. No constant changes are found in the synovium.

Symptoms.—The onset of the disease is insidious. The first symptom to be complained of is usually stiffness, often accompanied by some pain after exertion. The site is generally one or more of the larger joints; or it may be any joint which is subjected to particular stresses as the result of the patient's occupation or sport. In the course of time considerable wasting of the muscles controlling the affected joints supervenes. These therefore tend to become unstable and so liable to further trauma. The coarse grating which can be elicited in joints affected with the disease is due to an accompanying teno-synovitis, and is no measure of the actual damage to joints. When extrinsic joint changes have occurred, the patient usually experiences considerable pain, particularly on bearing weight. The movements of the joint also become much limited on account of spasm of the surrounding muscles, which may in itself be a cause of pain. There is generally not much effusion present. Occasionally new bone formation may limit the movements of the joint, although this is not very common. Small rounded bony swellings on the terminal phalanges of the fingers and thumbs, termed

Heberden's nodes, not infrequently develop during the course of the disease. These may be the cause of considerable pain in their early stages.

The examination of a hip joint affected with early osteo-arthritis will reveal some limitation and pain on rotation and often also of abduction of the joint, long before the movements of flexion and extension are appreciably interfered with. In addition, it may be found that such a patient when standing will not support his weight equally on both hips, in order to avoid pain. Some wasting of the gluteus muscle on the affected side will also be evident fairly early; while in advanced cases actual shortening of the affected limb will occur, either the result of absorption of the femoral head or from its dislocation upwards. Another point to remember is the possibility that even severe pain complained of in the knee may in reality be referred from a diseased hip; and in such cases if a full examination of the patient is omitted treatment may be directed to the wrong joint. "Sciatica" is often found to be the result of osteo-arthritis of the hip, or of the lumbar spine, and is sometimes the initial symptom.

Osteo-arthritis of the lumbar spine is frequently present without giving rise to symptoms. Such cases are often discovered radiologically in the course of an examination for another purpose. This sometimes gives rise to difficulty in compensation cases when existing symptoms may be attributed to this cause *post hoc*. The sacro-iliac joints are in the same way frequently reported as being the seat of osteo-arthritis. In many cases, however, there is an absence of symptoms and so no treatment is required, unless low backache or sciatica supervenes.

The osteo-arthritic joint does not ankylose, but may become locked as the result of excessive osteophyte formation. In other cases it becomes unstable, owing to continued use in the presence of insufficient muscular support, due to muscular wasting; in these cases the joint surfaces may ultimately become very disorganised.

When a weight-bearing joint is affected, the patient suffers great pain on standing, and a certain amount of absorption of articular bone may occur, resulting in some shortening of the limb.

In some cases the articular cartilage may become fragmented, or osteophytes may break off into the joint cavity. In both these circumstances they form loose bodies which give rise to all the symptoms usual in that condition, in addition to those of the arthritis.

The results of radiological examination and blood sedimentation rate and glucose tolerance are described under Diagnosis.

The general health is not affected, unless the result of unaccustomed inactivity necessitated by the affection.

Diagnosis.—Osteo-arthritis should never be confused with rheumatoid arthritis, the two conditions being entirely different. The former is a degenerative condition affecting one or two joints, usually the larger ones. There is generally a history of trauma in the past, or of continued trauma of a minor nature, such as some occupational or sporting stress or strain; or a postural defect; or in some cases a sudden increase of weight, with resultant strain on the ankles, knees, or hips, as may occur at the menopause. Apart from the menopausal group of cases, the patient is more often a male, and his general health is not directly affected by the disease. Again, the pain is generally relieved by rest.

In rheumatoid arthritis, on the other hand, the joint changes are inflammatory in nature, and trauma is not a marked feature. The onset is in the smaller joints, many of which are generally affected, symmetrically and bilaterally. Finally, the patient is usually a woman, and there are indications of general ill-health and also loss of weight, which often preceded the joint manifestations.

The *radiographic* appearance of a joint affected with osteo-arthritis is generally typical. The bone density is unaffected and the joint space is narrowed; this depends upon the amount of erosion which has occurred in the cartilage. Osteophytes will be seen at the joint margins, and there is frequently also a deposition of calcium in the attached ends of certain tendons, such as those of the patella and ligaments, *e.g.* the cruciates, which result in an appearance of "spiking." Such, however, should not be confused with osteophyte formation, as it will sometimes be found independently of the existence of osteo-arthritis. In osteo-arthritis of the hip considerable deformity, both of the head of the femur and of the acetabulum, may be seen, and, in addition, small degenerative cystic areas adjacent to the joint are not infrequently noticed.

The blood sedimentation rate and the glucose tolerance are normal.

Differential Diagnosis.—Conditions which are liable to be confused with osteo-arthritis are Paget's disease, osteochrondrosis dessicans, and occasionally neoplastic growths of the articular ends of bones.

Prognosis.—If not treated the course of osteo-arthritis is progressive and generally ends in disablement. Much, however, can be done in the early stage to prevent this, by relieving the affected joint of all possible strain, and by support and correct treatment. The outlook is perhaps best in that form known as "menopausal arthritis," provided full and adequate measures are taken before the malady becomes established. In such cases a return to the normal may be anticipated in the course of time.

Treatment.—As in osteo-arthritis there is an absence of general symptoms, there is no indication for general treatment other than seeing that the patients receive an adequate supply of vitamins and that their bowels act regularly, while definite periods of rest are advisable. If the patient is obese, a diet low in fats and carbohydrates should be insisted upon if success from other measures is to be achieved. The caloric value should not exceed 900–1600 calories, and fluids should not be taken at the same time as food. The patients should be reassured that they will not become extensively and hopelessly crippled, as may occur in rheumatoid arthritis.

It is the experience of most observers that little benefit is to be anticipated as the result of removing foci of infection. If, however, these are found they should be dealt with on their merits. If varicose veins are present, as is often the case when the malady is situated in the knees, treatment directed towards these will frequently result in improvement in the joints.

The drugs chiefly valuable in this condition are those of the analgesic group, such as aspirin, guaiacol carbonate, phenacetin and occasionally codeine. They should not be prescribed as a routine and should only be used when pain is severe. The iodides are also employed on general principles, and appear to be of value in some cases, as are sulphur (by mouth) and guaiacum. Gold salts should not be used in this type of arthritis.

In cases which arise about the time of the menopause small doses of thyroid are often of value, but should be combined with the other measures outlined, particularly those for reduction in weight, muscular re-education and joint support by means of elastoplast.

Physical therapy of some sort is essential in treatment of osteo-arthritis. The desiderata are: heat, to stimulate the failing circulation locally and to relieve muscle spasm and consequently pain; massage, to maintain and stimulate the nutrition and drainage of the skin and underlying tissues; and movement, in order to maintain the mobility of the joint, to prevent or repair muscle wasting, and discourage the formation of adhesions.

Movement should, if possible, be active, *i.e.* special exercises, or if this is not feasible at the outset, electrical stimulation by means of the surging faradic current, or hydrotherapy, if available, may be substituted. Movement of the affected joint should, however, as far as possible be disassociated from weight-bearing through the affected joint, in order to allow of repair in the cartilage.

A further method of stimulating the circulation reflexly is by means of histamine ionisation. Sufficient current should be used to produce a temporary urticarial reaction in the skin under the pad. When dealing with the extremities, paraffin wax applied at a high temperature is also useful as a means of applying heat.

The question of posture, or "body mechanics," is an important and neglected aspect of many cases of osteo-arthritis. For instance, pronated feet may cause strain and, later, arthritis in both knees and lumbar spine; as may a pendulous abdomen. Proper postural exercises should be taught, which the patient should continue until the correct posture is maintained reflexly.

When after a period of rest the patient begins to put weight on to the affected joint again, the latter should always be adequately supported. For this purpose a crêpe bandage, or better still elastoplast, is of great value. In some cases special appliances, such as the Howard-Marsh splint for the knees, or a back support when the spine is affected, may be needed for a period in order to protect the joint. For the feet proper arch supports may be necessary, while in cases of severe arthritis of the hip or knee, when weight-bearing continues to give great pain, some form of walking caliper, whereby the weight of the body is "by-passed" from the ischium down to the heel of the shoe by a light metal rod, is indicated.

In very advanced cases operative procedures will sometimes prove necessary. Chief amongst these are synovectomy; in those cases in which soft tissue proliferation is not responsive to other treatment. When in the hip-joint a small degree of painful movement is all that remains possible of achievement, arthrodesis, either by open operation or by means of the Smith-Petersen pin, will often be the best method of treatment. Multiple bone puncture has recently been advocated (empirically), but no controlled series of the effects of this has yet appeared.

Recently X-ray treatment has been considerably employed as an anæsthetic procedure in painful osteo-arthritis. The effects are very variable but on the whole appear to be more successful when it is the superficially placed joints which are to be treated.

Finally, the question of climate should be considered. If the economic

status of the patient will allow him to live in a warm climate, this will in most cases prove to be very beneficial.

4. HYPERTROPHIC PULMONARY OSTEO-ARTHROPATHY (see p. 1375)

5. ARTHRITIS DUE TO GOUT (see pp. 432, 434)

6. SPONDYLITIS

Spondylitis is arthritis of the spine. Most cases fall into one of three types: (1) the ankylosing type—spondylitis ankylopoietica; (2) rheumatoid arthritis, in which the spine is involved as a secondary spondylitis; and (3) osteo-arthritic type of spondylitis.

1. Ankylosing Type of Spondylitis

Synonyms. — Ankylosing Spondylitis; Spondylitis Ankylopoietica; Atrophic type of Spondylitis; Spondylose Rhizomélique; Von Bechterew's Disease; Marie-Strumpell Disease. It is now realised that all these terms apply to the rheumatoid type of spondylitis or sub-varieties of this.

Ætiology.—As the condition is a form of rheumatoid arthritis with a special localisation to the spine, the predisposing and exciting factors are the same as in that disease (*q.v.*). The age of onset is also similar, occurring chiefly in the young. The malady differs, however, in chiefly affecting males. It is considerably less common than the classical form of rheumatoid arthritis.

Pathology.—The only true joints in the spinal column are those which permit of movement between the intervertebral articular facets and the costo-vertebral joints. This type of arthritis commences as a synovitis of these joints, together with some osteoporosis of the vertebral bodies. In the vast majority of cases radiological evidence of an infective process will be found in the sacro-iliac joints, concurrently with these changes. The nature of this is unknown. The ligaments surrounding the affected joints subsequently calcify, and those portions of the spinal column become rigid. When this process is complete the lateral borders of the intervertebral discs also calcify, as do the anterior and lateral longitudinal ligaments, the whole process resulting in a bamboo-like appearance which is typical of the condition.

Symptoms.—The early symptoms of the rheumatoid type of spondylitis are usually of a diffuse and insignificant nature, and are therefore generally overlooked until they are localised in the spinal region, which may be comparatively late in the disease. The principal complaint will often be of a diffuse fibrositis which chiefly affects the upper part of the body. This syndrome, if it persists, should always arouse a suspicion of spondylitis in the case of a young male. In others pain may be referred directly from the affected spinal segment, and may simulate that of renal calculus, pleurisy or even of tabes. Sometimes neuritis or numbness and loss of power in the limbs, or severe spasm of the muscles of the back may be complained of. All these symptoms are usually intensified on forced movement of the spine,

and in addition pain is often elicited by firmly tapping the spinous processes involved.

There is also increasing stiffness in the back, and ultimately this may become completely rigid (" poker back "), generally in a position of kyphosis and slight forward flexion of the spine. In untreated cases this position becomes very exaggerated, the chin sinks into the chest wall, and the patient is unable to stand erect or move. Those who are not bedridden move with a characteristic slow, bent, shuffling gait. As the costo-vertebral joints ankylose, so does the respiratory expansion of the chest diminish.

For the results of radiological examination, see later.

Complications.—Those who die with this disease generally do so from an intercurrent respiratory infection, the result of the diminished or absent expansion permitted by the ankylosed costo-vertebral joints. The disease in itself usually does not shorten life.

Diagnosis.—All patients, especially young and athletic males, who complain of vague pains affecting the limbs and upper part of the body which do not respond to treatment should be suspect. The presence of detectable rigidity of the spine is unusual at this stage. If the blood sedimentation rate test is high this increases the suspicion and should lead to the patient being X-rayed. The radiological appearances at this stage are loss of definition (" wooliness "). of the sacro-iliac joints, osteoporosis of the neighbouring bones and lumbar vertebral bodies. Later, the sacro-iliac joints become obliterated, and the intervertebral joints, if they can be shown, are hazy and later on ankylosed. The edges of the intervertebral discs and the spinal ligaments are calcified. The vertebræ primarily affected are usually those of the lumbar and lower cervical portions of the spine. Osteophytes are not found. At this later stage the diagnosis becomes obvious as the whole spine is rigid, and the hip and shoulder joints are also sometimes ankylosed. Hysterical contracture of the spine should be differentiated.

Course and Prognosis.—In cases in which the onset is acute, ankylosis of the spine may occur within a few months. The younger the patient the more likely is this to happen. An associated swelling of other joints in the body develops at some period of the disease in about 25 per cent. of all cases, while the hips and shoulder joints are liable to be permanently involved in about the same proportion of cases. Iritis will occur in a small proportion, and is of bad prognosis.

Treatment.—It should be remembered that spondylitis of this type is a systemic disease and thus needs general treatment, as well as more specialised attention to the spine. Treatment will be more successful if it can be started at an early stage of the disease. The general treatment is similar to that advised for rheumatoid arthritis: rest, high caloric and vitamin diet. Vitamin C is particularly important in this malady. Any definite foci of infection should be cautiously removed and anæmia counteracted. Ultra-violet light is a useful general tonic, but gold salts do not appear to be useful in this condition.

The special treatment needed in the active stage includes rest in bed and mobilisation of the chest by means of breathing exercises. Fracture boards should be placed under the mattress, to prevent sagging, and the patient should be as flat as possible, the pillows being removed several times daily to hyperextend the spine. Breathing exercises done in this position

should aim at keeping the chest wall mobile by restricting abdominal breathing. Physical treatment is chiefly of value in the form of radiant heat or infra-red rays to the back, in order to relax spasm and relieve pain. Gentle massage is useful for the same purpose, and later on active movements should be performed under supervision. If there is already some deformity of the spine a plaster cast of the back should be made, and the patient should lie in this night and day to relax completely all spasm. The shell should be altered frequently so as to take advantage of the gradual postural improvement, and when the patient first assumes the upright position he should be fitted with a light spinal brace to relieve the back from all strain.

Recently X-ray treatment has been advocated in the treatment of this disease, but the results so far are variable.

Even with the greatest care it is sometimes impossible to avoid ankylosis of the spine supervening. But if it does occur it is almost always possible to ensure that it does so in the optimum position and thus the patient will ultimately be able to lead his life in an erect posture.

2. Rheumatoid Arthritic Type of Spondylitis (see p. 1352)

3. Osteo-arthritic Type of Spondylitis

Synonyms.—Osteo-arthritis of Spine; Hypertrophic Spondylitis; Degenerative Spondylitis.

Some degree of osteo-arthritis of the spine is said to be demonstrable by means of the X-rays of nearly all those over 50 years of age; but it is rare for these changes to cause symptoms. Its incidence is rather higher in men than women, and it seldom occurs before middle life.

Pathology.—The changes are not inflammatory in nature and are identical with those of osteo-arthritis met with elsewhere in the body. Bony ankylosis does not occur in this type of arthritis, but osteophyte formation is always seen, together with narrowing of the intervertebral spaces. The areas most commonly involved are the cervical and lumbar regions.

Symptoms.—When symptoms are present they may include the following: root pains, of which sciatica is the most frequent example; increasing stiffness of the back, which, however, never becomes completely rigid. Headache and pains in the neck, shoulders, and arms are common, sometimes in conjunction with areas of paræsthesia or anæsthesia in the skin. Pains are generally aggravated by movement of the spine, as the nerve roots are liable to pressure in or around their exit from the spinal foramina.

Diagnosis.—This should be confirmed radiologically. The lesion typical of osteo-arthritis is the osteophyte; while marginal exostosis and shrinking of the vertebral margins, with narrowing of the intervertebral spaces, are also seen. The sacro-iliac joints are generally normal. In all cases the possibility of malignant growths in the spine should be borne in mind, as the symptomatology is the same.

Treatment.—This is similar to that of osteo-arthritis elsewhere in the body, and includes the correction of body posture and flat feet. The frequent application of heat in some form, followed by rest and muscular relaxation, is important. Massage and faradism at a later stage will tone up muscular support of the back. Sometimes it will be necessary to supplement the

support of the back mechanically by a plaster shell or a brace for a time. Deep X-ray treatment will sometimes relieve intractable pain which proves resistant to analgesic drugs, such as aspirin, pyramidon, or codein.

7. STILLS' DISEASE

This disease is believed by some observers to represent true rheumatoid arthritis in childhood. But although the articular changes are of an inflammatory nature their effects are more often confined to the periarticular tissues. Again, even in cases of long standing, it is not unusual to find little or no radiological evidence of destruction at the actual joint surfaces.

Ætiology.—The sexes are affected in about equal proportion, while the age incidence resembles that of rheumatic fever, namely, that the malady is seldom met with before the age of three years and the average age at onset is between six and seven years. The cause remains unknown, although the factors held to be responsible for rheumatoid arthritis are usually invoked to account also for Stills' disease. These are focal infection, such as in the teeth, tonsils, sinuses or bowel; metabolic or endocrine disorder; or, in some cases, unsuspected or attenuated infection with the bacillus tuberculosis. A hæmolytic streptococcus is commonly present in the nasopharynx and other foci. In the majority of cases it is very difficult to assign any one cause. It is certain, however, that once the disease has commenced a cold damp environment will exacerbate it considerably.

Symptoms.—If a careful inquiry of the history of the patient's illness be made it will very often be found that a considerable period of prodromal ill-health preceded the onset of the joint symptoms.

The onset of the joint condition is not infrequently rapid, with pyrexia, and pain and swelling of several joints. This often leads to an initial diagnosis of rheumatic fever, but it is soon found that sodium salicylate has no beneficial effect and that the joint swellings, far from being transient, increase in number and intensity. When the onset is gradual there is little pyrexia but a slowly progressive degree of swelling and limitation in movement of the knees, wrists, elbows, fingers and ankles—usually in that order. Later, the cervical spine and also the hips may become affected and the patient will be completely crippled. The foregoing joints are usually attacked symmetrically, and their appearance is characteristic in that the periarticular swelling renders the joint fusiform in shape. The skin over this swelling is rather stretched and often slightly bluish. The muscles adjacent to the affected joints waste, which further exaggerates the fusiform appearance. In the case of the wrists, ankles and elbows the bony contours are often completely obscured. The affected joints are generally tender on pressure, but usually are not painful except on movement. This leads to further voluntary limitation of movement and so intensifies the muscle wasting already present.

In many cases of this disease the joint swelling and muscular wasting is accompanied by a lymphatic reaction which will show as enlargement of the superficial lymphatic glands, especially those around the elbows and in the axillæ. In about half the cases seen there is also enlargement of the spleen. These changes were present in the cases originally described by Still

in 1897. The enlarged glands are not tender, and are generally discrete and "rubbery." Subcutaneous nodules are sometimes found in addition.

There is generally a secondary anæmia, and quite often patches of light-brown pigmentation on the skin. When the disease is established, the extremities are always cold and clammy, and there is an increase in the temperature before other joints are affected. In long-standing cases normal growth is considerably interfered with.

In the late stages the type of deformity seen in adult rheumatoid arthritis develops. There is flexion of the fingers and ulnar deviation of the hands, and also flexion of the knees and elbows.

The X-ray picture is chiefly remarkable for the advanced degree of the osteoporosis which always occurs. There is often little or no actual joint changes, and osteophytes are never found in this type of disease.

The end result, so far as the joints are concerned, is a fibrous ankylosis, or a fibrosis of the joint capsule, which is sufficiently complete to resist all attempts at movement of the joint.

It is stated that at post-mortem examination diffuse pericardial adhesions and adhesive mediastinitis are often discovered, although unsuspected during life, and evidence of valvular disease of the heart has occasionally been reported.

Prognosis.—Until recently there was considerable doubt as to what was the ultimate fate of these patients. Some authorities held that they recovered while others explained the rarity of the affection seen in Adult Out-patient Departments by assuming that the patients either died or became rapidly bedridden after leaving the children's departments. A recent "follow-up" at Great Ormond Street Hospital showed that the mortality in those under five years of age is about 25 per cent. (due to intercurrent infections); that complete recovery occurred in a small proportion; while in the majority, the disease remains apparently arrested, often for several years at a time, only to resume its ravages at increasing intervals until the patients are entirely crippled and bedridden.

Treatment.—When the presence of an infective focus is established, this should be dealt with at an early stage of the disease. In all cases the child's resistance should be built up by all available means. A nourishing diet, an open-air life and a dry sunny climate are indicated. In addition, cod-liver oil and malt, syrup of iodide of iron, and courses of an arsenic-containing tonic are important.

Vaccine treatment with autogenous very weak vaccine is worthy of trial if a hæmolytic streptococcus is found.

Salicylates have little or no beneficial effect. Non-specific protein therapy is often recommended, but is possibly too drastic and temporary a measure to employ except in the later stages. Recently good results have been reported from small doses of gold salts administered intramuscularly in short courses. But in some cases these salts provoke unfavourable reactions, and so should be used very cautiously. No case should receive a larger dose than 0·1 gm. and a total course of 0·75 gm. should rarely be exceeded. The injections should be given at weekly intervals. At least six weeks should elapse before any subsequent injections are administered, and the onset of toxic nephritis, stomatitis, diarrhœa and dermatitis should be especially looked for.

All swollen joints should be bandaged and lightly splinted, or put into thin plaster-of-paris casts, to avoid the contraction deformities which will otherwise inevitably occur. The child should always sleep in these, and will soon become accustomed to them. They should be removed daily, however, for a short period, during which the joint must be given passive movement, to prevent fixation. Dry heat from a radiant heat or infra-red ray lamp is comfortable and renders the performance of these daily active movements easier. These movements are also essential to remedy the muscular atrophy present. Massage is generally unnecessary in these cases.

In the very late stages, and the patient is bedridden owing to extensive contraction deformity, minor surgical procedures, such as tenotomy, are sometimes justifiable to remedy the deformity.

PSEUDO-ARTHRITIS (JOINT EFFUSIONS)

Effusion of fluid into the joints may be associated with various conditions, and is often of a temporary or intermittent nature. If not followed by damage to the joint surface, it should not be strictly referred to as an arthritis.

Apart from the various forms of arthritis already described, the following may give rise to joint effusion :

(i) *The specific fevers*, especially scarlet fever, meningococcal fever, puerperal fever, influenza, syphilis, subacute bacterial endocarditis, typhoid or paratyphoid fever, measles and malaria. In the United States a form of pseudo-arthritis associated with lympho-granuloma venereum is not uncommon.

(ii) *Abnormal blood conditions*, such as purpura simplex or purpura rheumatica (Schönlein's disease), scurvy and hæmophilia will give rise to swelling of the joints due to an effusion of blood. The knees are most frequently affected.

(iii) *Growths affecting the bones*, in near proximity to a joint. An X-ray examination will elucidate the ætiology in such cases.

(iv) *Injection of animal sera.*

(v) *Trauma* will cause synovitis of the affected joint. It should be noted that the strain imposed on certain joints due to faulty body posture will often result in a chronic form of hydrarthrosis.

(vi) *Intermittent Hydrarthrosis.* A periodic recurrence of joint effusion of unknown ætiology which persists for several days and usually affects the knees. Attacks tend to recur at regular intervals ; they show no local evidence of inflammation ; and they are refractory to most forms of treatment. Some authorities consider this condition is the result of an allergic sensitisation, and advocate treatment directed along these lines.

NON-ARTICULAR RHEUMATISM ; FIBROSITIS

Fibrositis may be defined as a condition in which acute or chronic inflammatory changes involve the fibrous tissues of the body, such as the subcutaneous tissues, the superficial and deep fascia, the muscle sheaths and tendons, the fibrous portions of the joint capsules and ligaments, the bursæ,

and the fibrous sheaths of the nerves. The affection gives rise to pain and impairment of movement. It may be subdivided broadly into three types according to the nature of the structures primarily attacked:

1. Panniculitis: Inflammation of the subcutaneous tissue and fat.

2. Inflammation of the muscle sheath and the fibrous tissue between the muscle fibres, the aponeuroses, the tendons and the superficial and deep fascia.

3. Peri-arthritis: Inflammation affecting principally the fibrous portions of the joint capsules, ligaments and bursæ (bursitis).

4. Peri-neuritis: Inflammation affecting primarily the nerve sheath (perineurum) and the fibrous tissue between the nerve fibres.

Ætiology.—A large group of cases can be traced to the presence of focal infection, and both the teeth and the tonsils are generally suspect. This is perhaps more particularly so in cases in which the upper part of the body, including the arms, are chiefly affected. In this connection it is to be remembered that negative X-ray evidence of apical infection of the teeth should not be accepted as conclusive evidence, since changes which can be demonstrated by this means are necessarily of a chronic and advanced nature. Further foci of infection should be sought in the sinuses. Occasionally the bowel, particularly the colon, may be thought of as a focus of infection, but when considering the question of vaccine treatment the old aphorism that it is " a poor bowel which does not grow something " may be remembered with advantage. Another focus of infection, which is sometimes overlooked, is the prostate, and in the absence of other infection it is worth while to perform prostatic massage and culture the " bead " so obtained.

A further group of cases would appear not to be of a primarily infective nature but to be allied to gout or to a special sensitivity to certain types of food.

Finally, a certain proportion of cases of fibrositis can be traced to chronic strain, often secondary to faulty posture. A common example of this will be found in those cases in which the fascia lata of the thighs is tender and painful in conjunction with a flattened plantar arch. Such patients are usually cured when the distribution of the body weight is readjusted by raising the inner edges of the shoes. Some cases of low backache seem also to be attributable to the same cause. Other causes of this chronic strain will arise out of the occupation, or sometimes the sports of the patient, while any unaccustomed muscular exercise should be inquired into, especially if in conjunction it has been associated with exposure to cold and wet, *e.g.* the frequent occurrence of sciatica in doctors who drive a car in wet clothes for a long period.

Morbid Anatomy.—The morbid anatomy of this affection was investigated originally by Stockman, who found that the results of injury to fibrous tissue, whether bacterial or traumatic, had the effect of producing in the acute stage an exudate and inflammatory œdema. This is followed by organisation of the exudate, and the growth of new fibroblasts and new blood vessels with thickened walls. There is no migration of polymorphonuclear leucocytes and no pus formation, a few lymphocytes alone being attracted to the inflamed area. As the condition becomes chronic there is a production of dense connective tissue in nodules or strands, which differ from normal fibrous tissue in having more fibroblasts, in having arteries

with thickened walls, and in leaving the sheaths of the nerves passing through it in a state of interstitial inflammation. The pain of fibrositis is apparently due to the swelling of the tissue through the inflamed exudate, and subsequently to the involvement of nerve fibres in the new fibrosis, apart from the interstitial inflammation of the nerve twigs themselves.

Symptoms.—It is to be noted that the pain complained of in fibrositis is not always at the real seat of the lesion but may be referred to other areas and therefore careful location of the actual seat of the inflammation is essential. Again, the symptoms will vary according to the area of the body affected. As examples, the predominant effect of involvement of the muscles of the neck will often be headache; of those of the limbs, numbness and tingling; and of the fibrous tissue surrounding joints, stiffness and pain on moving these, which is often wrongly attributed to true arthritis.

Panniculitis is met with most typically in the early stages of "menopausal arthritis" in which tender pads of thickened tissue are found over the internal aspects of the knees, the back of the neck, the extensor surfaces of the arms, the outer aspects of the thighs and elsewhere. It occurs most frequently in stout people, and Dercum's disease or adiposis dolorosa is a progression of this process. In some cases this syndrome appears to be associated with moderate hypothyroidism.

In the case of inflammation of the muscle sheaths and the intramuscular fibrous tissue, the local effect is to keep the muscles in a state of spasm during the acute period. Subsequently the spasm will relax, but localised patches of nodular induration may be palpable in the muscles. Occasionally, also, thin fibrous cords may be felt running through the subcutaneous tissues. These "nodules" will generally, but not invariably, prove tender on palpation. Lumbago is perhaps the most common manifestation. Its onset may often be very acute. It should be distinguished from arthritis or caries of the spine, sacro-iliac disease, perinephric abscess and renal disease, all of which may simulate it. Pleurodynia is a rheumatic inflammation of the intercostal muscles which gives rise to severe pain when the affected muscles are brought into action, as on coughing or deep breathing. Usually local tenderness can be elicited on palpation; but careful examination is needed to exclude such sources of pain as pleurisy or intercostal neuralgia. The muscles of the abdomen are sometimes the site of a local lesion, and this will occasionally simulate intra-abdominal disease. They are also affected in epidemic myalgia (Bornholm disease). The extensor muscles of the thighs, when they are the seat of rheumatic inflammation, give the clinical appearance of sciatica, and this possibility should always be considered before making a diagnosis.

One of the commonest causes of pain, generally diagnosed as brachial neuritis, is the presence of a degenerative lesion in the tendon of the supraspinatus muscle. This lesion will sometimes calcify and may then be seen in an X-ray, if the shoulder be externally rotated. This type of lesion is often the cause of inflammation of the subacromial bursa through which this tendon passes. "Tennis elbow" is the term applied to the painful fibrositis affecting the origin of the extensor tendons of the forearm from the external condyle of the humerus.

Bursitis may occur in any of the large bursæ. The most commonly affected is the subacromial bursa, referred to above. The chief clinical

manifestations of "deltoid bursitis" are great pain on actively abducting the affected arm to an angle of 90° with the body. Above this point abduction can generally be completed without pain; the pain returning, however, at the same point when the arm is again lowered. Passive movement through this range is not painful. Pain of this type will encourage the sufferer to immobilise the affected arm, and this will allow the inflammation to spread to the joint capsule, which will contract, and so ultimately limit, or even entirely prevent, movement taking place in the joint subsequently. The patient is often unaware of the full degree of limitation of the movement which has occurred in such cases, as a considerable degree of movement is possible by virtue of the mobility of the scapula. This condition is the severest type of peri-arthritis, and the apparent ankylosis of the joint must be differentiated from a true arthritis by means of radiology, as peri-arthritis of this type may be cured by the employment of diathermy, gentle manipulation, and remedial exercises. The next most commonly affected bursæ are those over the olecranon process, around the knee joint, over the ischium and over the great trochanter. Inflammation of any of these should be differentiated from a true arthritis of the neighbouring joint. Another form of peri-arthritis depends on inflammation of the tendon sheaths of muscles surrounding joints. This may occur as part of a chronic rheumatic process unassociated with trauma or gout. Its association with gonorrhœal and dysenteric infections has been mentioned. The flexor tendons of the wrists and knees are the most commonly attacked. Pain, swelling or crepitus results and sometimes synovial effusion. The palmar fascia is sometimes the site of a chronic fibrositic process, and the resulting thickening and contracture is known as Dupuytren's contracture. This is seldom painful, but can give rise to considerable disablement of a somewhat intractable nature. The condition, which is commoner in males, is often found to be familial. A somewhat similar condition, which, however, does not cause so much contracture, is known as "painful heel." In some cases a small spur of bone is found radiographically at the insertion of the plantar fascia into the os calcis. But in the majority of cases, no cause for the pain can be found.

In the case of peri-neuritis, the sciatic nerve is the most commonly affected, next in order are the nerves of the brachial plexus, and then the intercostal nerves. Some forms of Bell's "palsy" are thought to be of similar origin. The symptoms in a fully developed case do not differ from those of a true neuritis, but the distinction can generally be made from a history of an initial fibrositis of neighbouring structures which later spreads to the nerve sheath. Since the introduction of radium therapy for carcinoma of the lung, cases of axillary fibrosis, followed by severe and sometimes permanent brachial neuritis, have been seen.

The subjects of fibrositis are usually found to have some degree of defective skin circulation, as evidenced by abnormal sensitivity to cold weather or to local draughts, spontaneous bruising, or the fact that they perspire in the hottest weather only with difficulty. Attacks of fibrositis will occur in many people without apparent detriment to their general health, and in such persons the suspicion should arise that the cause may not be primarily an infective one.

The group of cases which appear to be allied to gout or to a special sensitivity to certain types of food may be suspected by the excellent general

health, even during attacks, the periodic or seasonal nature of the attacks, a history of familial gout or of being "unable to digest" certain foods or drinks, and finally by the fact that the fibrositis tends to affect the lower limbs and other lower parts of the body. Such patients, in addition, often exhibit the symptom-complex described by the French as "hépatisme." This is shown principally by morning headache, furred tongue, and a tendency to incomplete bowel emptying, with light-coloured and offensive stools; often, too, there is slight tenderness on palpation in the neighbourhood of the liver.

Prognosis.—Provided sufficient care be taken and the value of external as well as internal remedies is remembered, the outlook is good. An exception, however, is in the case of very old patients, for the senile form of fibrositis is sometimes intractable to all the usual remedies.

Treatment.—When symptoms do not call for urgent treatment, the first indication is to investigate the ætiology. In the great majority of cases in which the malady is believed to be allied to gout or to a special sensitivity to certain types of food, appropriate treatment should be adopted.

At the outset, a mercurial purgative, such as calomel (gr. ½–2), followed next morning by a saline, should be prescribed.

In the acute stage rest in bed is desirable. The internal administration of analgesic drugs is indicated. Aspirin and calcium acetylsalicylate (5–15 grs.) are in the majority of cases the most efficient for this purpose. If necessary, potassium iodide (2–5 grs.) may be added, as may phenacetin (5–10 grs.) or caffeine (5 grs.) at four-hourly intervals. A useful addition to aspirin and phenacetin is codeine phosphate (⅛th gr.) or Dover's powder (5–15 grs.). Amidopyrine (3–10 grs.), a centrally acting drug, is sometimes effective when the salicylates fail. It should be borne in mind, however, that if this drug is used there is a danger of agranulocytosis in susceptible individuals and therefore frequent blood counts are required. An ointment designed to act either as a rubefacient or as a counter-irritant should also be prescribed. A hot linseed poultice containing opium will also often give considerable relief if applied every few hours; as may a hot cloth wrung out in a solution of ordinary mustard in water. Massage is undesirable in the acute stage.

In certain cases benefit will result from a short course of colonic lavage twice a week for 2 to 3 weeks.

When it is desired to immobilise the muscles of the back during the acute stage of lumbago, the most effective method is by means of a perforated belladonna plaster, which should be made to cross the mid-line behind and come round to the front. Ordinary wide strapping is a good substitute.

When the condition is less acute and the patient is able to get up, the application of both heat and massage to the affected regions is indicated. The former may be applied in a dry or a moist form, the one often succeeding when the other has failed. Dry heat may be given by means of a portable lamp, an electric heating pad, exposure to a gas-fire (which gives out infra-red rays), the application of a hot iron through brown paper applied to the skin, a hot-water bottle, or a bag of salt or sand which has been heated thoroughly in the oven. When the condition is deep-seated, diathermy will be the best form in which to apply it.

Moist heat may be applied in the form of kaolin, bread or linseed poultices, kaolin poultice (antiphlogistine), mud packs, or applications of hot paraffin wax of a special melting-point (which is sold for this purpose), or, if the patient is in a condition to have such, a Turkish bath. In the course of the last, the patient should be instructed to drink fluids copiously during and after it, as otherwise the temporary concentration of the blood is likely to provoke a further acute attack. Perhaps the simplest method of moist heat is an ordinary bath, to which 4 lb. of Epsom salts (or common salt) have been added. This should be taken as hot as possible, and, contrary to the general belief, the patient should not "soak in it" but should get out after only 5 to 10 minutes' immersion and be briskly rubbed down, after which some analgesic ointment should be rubbed rapidly into the affected areas, and he should be wrapped in a blanket and put to bed for several hours. After this, deep massage should be ordered for the affected areas, although painful at first.

Hydrotherapy and Counter-irritation.—When the patient is near a Spa or an Institution equipped for hydrotherapy, "Vichy" douche massage, followed by "contrast douching" (alternate hot and cold water directed on to the painful areas under pressure from a hose-pipe), is probably the best follow-up treatment; it stimulates the skin to resume its normal function.

In certain cases, particularly when the complaint is that of lumbago, counter-irritation by means of a small cautery may be of great value. A small blister should result from each application, and the whole area may then be covered over with a gauze dressing. Another method is to produce blisters by means of "blistering fluid," or cantharidin plasters, but these are not of such value as the actual cautery. Dry-cupping is a somewhat obsolete method of treatment, but is occasionally effective; as is full exposure to a mercury vapour lamp at a distance of 18 to 24 inches from the affected area.

In the chronic stage massage is essential if an attack is to be terminated in the minimum time and also if recurrence is to be avoided. To be effective, the indurated areas (nodules) should be carefully sought for in the muscles, and at these points the massage should be very deep. It will be found that following deep kneading with the finger-tips or thumbs, after an initial period during which they may be increasingly painful, they will gradually become insensible to palpation, and ultimately disappear. This process will be considerably facilitated if it be preceded on each occasion by 20 to 30 minutes' application of heat in one of the forms mentioned above. In certain cases a "nodule" will prove to be too painful for deep massage treatment, which will then induce protective spasm in the surrounding muscles, and so render further "kneading" impossible. In such cases a dose of aspirin or some other analgesic may usefully be administered before beginning the treatment. When one or more discrete nodules can be felt and when the pain is found to be chiefly localised in these sites, the effect of injecting a few cubic centimetres of a local anæsthetic, such as procaine hydrochloride (½ per cent. in saline) or "A.B.A." compound, is sometimes dramatic. When there is more diffuse pain and tenderness, this method of treatment is not of much use, and unless the injection is made with great accuracy into the nodule the trouble may even be exacerbated.

Diet and After-care.—If there is obesity, this should be treated (see

p. 438). In cases in which a gouty origin is suspected, this should be corrected (see pp. 435, 436).

After an attack of fibrositis, it is important that the patient should be taught to contract the affected muscles daily by means of appropriate exercises. He should also make a point of obtaining some regular exercise in the open air, even at the cost of rising somewhat earlier in order to walk part of the way to the office. The obese subject must not be allowed to regain his lost weight once the attack recedes. The question of the localisation of attacks, as the result of the occupation or hobbies of those predisposed to suffer, should not be omitted.

MYOSITIS OR INFLAMMATION OF THE VOLUNTARY MUSCLES

Three forms occur—(1) the suppurative type; (2) the non-suppurative type: and (3) myositis ossificans progressiva.

1. Suppurative Myositis.—In this condition there is a primary inflammation of the affected muscles associated with the local signs of inflammation and the general symptoms of a septic infection. Abscesses form in the affected muscles, which require incision, and in the pus obtained pyogenic organisms, such as staphylococci, or less commonly streptococci, are usually found.

2. Non-Suppurative Myositis.—It must be remembered that the voluntary muscles are affected in the course of other diseases. Thus, degeneration of the striped muscle, known as Zenker's degeneration, may occur in any acute infection of long duration, and it was first observed in typhoid fever. In scurvy, intra-muscular hæmorrhages are very common, and these are followed by a chronic inflammation, which usually clears up; but in a few of such cases we have seen suppuration occur. Trichinosis is accompanied by a myositis, set up by the encapsulated larvæ of the trichina spiralis deposited in the voluntary muscles.

Dermato-myositis is an acute or subacute inflammation of the muscles of unknown origin, which is associated with dermatitis and œdema. The onset is usually gradual, and ultimately all the muscles of the body may be involved. Pain is an early symptom, and fever of a mild intermittent type occurs. Œdema develops over the affected muscles, and is accompanied by a dermatitis of erythematous or urticarial type. Sweating is common, and enlargement of the spleen usually develops. Owing to involvement of the respiratory muscles broncho-pneumonia is a late complication. The disease is usually progressive, and generally fatal, though some recoveries have been recorded. The treatment adopted has been for the relief of symptoms, and no specific treatment is known at present.

A type of the disease in which hæmorrhages occur in and between the muscles is known as "polymyositis hæmorrhagica."

3. Myositis Ossificans Progressiva.—This is a progressive inflammatory affection of the locomotor system of unknown origin, characterised by the deposition of bony substance in the fasciæ, muscles, aponeuroses, tendons, ligaments and bones, with resulting ankylosis of most of the articulations. The disease is rare. It usually commences in early life, and is commoner in males. Three stages occur in the muscle changes. In the first stage, swelling

and infiltration of the affected muscle with embryonic connective tissue occurs. In the second stage, the embryonic connective tissue becomes organised and forms ordinary connective tissue, which retracts to a hard fibrous mass. In the third stage, calcification of the fibrous mass occurs, and this becomes replaced by bone.

The muscles of the back and neck are usually the first involved, and the vertebral ligaments become ossified, so that irregular bony swelling occurs and deformity and fixation of the spine result. The upper and lower limb are later involved, the muscles contracting and causing fixation of the joints. The muscles of mastication become finally involved and prevent movement of the lower jaw. Ultimately the patient becomes helpless and bedridden, and usually dies from some intercurrent affection, such as pneumonia, or pyæmia resulting from bedsores. The disease is always progressive, but is usually of long duration, and there may be a cessation in its progress for several years. No specific treatment of value is known.

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SECTION XVIII

DISEASES OF THE SKELETON

Diseases of the skeleton will be considered under three headings, according to whether bone, endochondral ossification, or bone marrow is primarily affected.

DISEASES OF BONE

HYPERTROPHIC PULMONARY OSTEO-ARTHROPATHY

Synonyms.—Hippocratic Fingers; Marie's Disease; Acropachy.

Definition.—A symmetrical enlargement of the bones of the hands and feet, and of the distal ends of the long bones, accompanied by clubbing of the fingers and toes, occurring in association with certain chronic diseases, especially of the lungs.

Ætiology.—The primary diseases in the course of which hypertrophic osteo-arthropathy may develop are:

1. Diseases of the lungs, such as (*a*) chronic cavitating tuberculosis and fibroid phthisis; (*b*) empyema and bronchiectasis; (*c*) malignant disease of the lung, pleura or mediastinum; and (*d*) fibrosis of the lung, non-tuberculous in nature.
2. Congenital heart disease, and infective endocarditis.
3. Chronic diseases such as dysentery, pyelonephritis, alcoholism, Raynaud's disease, and jaundice, as in hypertrophic cirrhosis of the liver.
4. Rarely a neuritis may lead to clubbing of the fingers and osteo-arthropathy. Pressure on the brachial plexus by a subclavian aneurysm has given rise to clubbing of the fingers on the affected side.

It appears that in the majority of cases a chronic infection leads to the development of osteo-arthropathy. This is the case in the lung diseases above mentioned. In congenital heart disease, the circulatory defect itself will lead to marked clubbing of the fingers; in this condition, however, the long bones are not appreciably affected, and the changes are limited to the soft parts of the terminal phalanges, the hypertrophy of which leads to clubbing.

The disease is eight times more common in males than females. All ages may be affected. The most striking examples are seen from 30 to 50; but in congenital heart disease and in chronic lung disease in children, such as bronchiectasis and fibroid phthisis, signs of the disease often appear in early life.

Pathology.—The bones most frequently affected are the metacarpal bones and the first two rows of phalanges. The radius and ulna may be

affected, and more rarely the lower end of the humerus and the scapula. In the lower extremities the corresponding bones are affected. X-ray examination shows a thin layer of newly formed bone spread over the shaft. The periosteum is raised unevenly, so that the outline appears serrated and the deposits beneath it are unevenly calcified giving a lace-work effect. The bony changes are the result of a chronic inflammation, and the thickening of the periosteum and new formation of bone beneath it may be accompanied by atrophy and rarefaction of the pre-existing bone. There are no bony changes in the terminal phalanges, the soft tissues and nails alone being affected.

Symptoms.—The onset is usually gradual, and little local pain is experienced, though stiffness and clumsiness of movements occur. Sometimes marked clubbing of the fingers develops in a few weeks; but usually several months or more elapse before the condition is characteristic. There is a remarkable symmetry in the pathological changes. The ends of the fingers and toes may be cyanosed. The nails are large, broad and curved, both longitudinally and transversely—the so-called parrot-beak. They show longitudinal striation and are brittle and easily split. The root of the nail is raised above its bed, and if pressure is applied at the root a distinct space between them can be made out. Sometimes the joints in the neighbourhood of the affected bones show swelling, from effusion and thickening of the synovial membrane. Osteo-arthritic changes in the joints are only present in the severe osteo-arthritic type.

Three types of cases are seen, but these may be only grades in the development of the extreme form of the disease.

1. *Cases showing only clubbing of the fingers, in addition to the signs of the general primary disease.*—This symptom may disappear if the primary disease is cured, as, for example, empyema.

2. *Cases showing clubbing of the fingers and painful thickening of the bones of the hands and feet, forearms and legs, in addition to symptoms of the primary disease.*

3. *The "osteo-arthritis hypertrophica" type.*—The hands and feet become greatly enlarged, owing to the bony changes and thickening of the soft parts. The forearms and legs are thickened. The pelvis, sternum, ribs and clavicles may be thickened, and the vertebræ may show changes resulting in kyphosis. Osteo-arthritis occurs in the parts involved, so that movement of the joints is painful and difficult. In this type of case the very remarkable changes in the bones and joints overshadow the symptoms of the primary disease.

Diagnosis.—The disease is recognised by the presence of the characteristic changes in the extremities, and by the presence of signs of one of the primary diseases already mentioned.

Infective arthritis is distinguished by the absence of clubbing of the fingers, and by the characteristic changes shown by X-ray examination.

Acromegaly is to be distinguished by the spade-like hand, the spatulate fingers, enlarged knuckles, and the characteristic facial appearance. The kyphosis is more often cervico-dorsal, whereas in hypertrophic pulmonary osteo-arthropathy it is more often dorso-lumbar.

Osteitis deformans shows irregular enlargement of the bones but there is a good deal of bowing, the hands are normal, and the X-ray appearances are pathognomonic.

Prognosis.—The prognosis appears to depend on the primary disease. If that can be arrested or cured, there is hope of arrest or improvement in the hypertrophic osteo-arthropathy.

Treatment.—This should be directed towards the cure or improvement of the primary disease. Other treatment is symptomatic and similar to that adopted in the treatment of infective arthritis.

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OSTEITIS DEFORMANS

Synonym.—Paget's Disease of Bone.

Definition.—A chronic and somewhat rare disorder causing enlargement and deformity of many bones. It is not a generalised disease of the skeleton. The bones are affected in the following order of frequency: pelvis, spine, femur, tibia, skull, fibula, clavicle, humerus, radius, and rib. In a few cases the disease is confined to one bone or to part of one bone: tibia, femur, clavicle, a vertebra, the ilium, or half the pelvis.

Ætiology.—This is unknown. The disease is sometimes familial. It rarely begins before the age of 40, and the commonest age of onset is 55. The sexes are affected in the proportion of three men to two women. Osteitis deformans is not inflammatory in origin. It seems likely that it is a disorder of mineral metabolism. Syphilis is not an ætiological factor. No alteration in the parathyroid glands nor in any other endocrine gland has been demonstrated. Both histological and chemical investigations have proved beyond doubt that generalised osteitis fibrosa (hyperparathyroidism) is unrelated to osteitis deformans.

Pathology.—There is a great alteration in the architecture of the bones affected. They become enlarged, irregularly thickened, and sometimes bowed. The skull is very thick, the sutures and foramina being narrowed in consequence. The cortex of the long bones ceases to be pure ivory bone but looks coarse and spongy with red streaks and dots. Histologically there is continuous excessive resorption of bone associated with an increased new bone formation that more than compensates for the bone lost. The excessive erosion disturbs the skeletal architecture, the compact bone being replaced by irregular angular trabeculæ, which also form the cancellous bone. There is still an attempt at structural adaptation to stresses, but this is very imperfectly achieved because the material is not used to the best mechanical advantage.

Biochemistry.—The serum calcium and plasma phosphorus are normal. The plasma phosphatase is constantly high, as in many other diseases of bone. In more than 80 per cent. of cases the calcium output in the urine is increased and sometimes reaches four or five times the normal figure. There seems to be a complete absence of correlation between the length of history, the density of bone shadows in radiographs, and the calcium output. A case showing increased density of bone trabeculæ throughout pelvis, lumbar spine, and femora is just as likely to reveal a high output of calcium in the urine as a low output.

Symptoms.—The disease may remain symptomless for ten years or more. It is very slow in progress and rarely influences the general health, giving rise in most cases to few symptoms other than those which are due

to changes in the shape of the bones. In 80 per cent. of cases there is pain, and the patient usually recognises its origin in the bones. It varies widely in severity from a dull ache to a severe shooting or stabbing like a knife. The back and lower limbs are the parts usually affected but headache is fairly common. When the skull is involved the patient may have to take a larger size in hats. The enlargement in the circumference of the head leads to the forehead being prominent and the face small in proportion. In the later stages the head is held forward and the back is so bent that the arms appear too long and an ape-like attitude results. There may be considerable reduction in total height. The lower limbs especially are bowed, the knees being widely separated and held slightly flexed. The bones are enlarged, and bowing usually takes place in such a manner as to accentuate the normal curve of the bone. The enlargement is particularly noticeable in the case of the tibia. The changes in the vertebræ may cause encroachment on the spinal canal, resulting in compression paraplegia. Bony compression of the optic nerve may lead to optic atrophy, and of the oculomotor nerves to diplopia. Otosclerotic deafness is common in advanced cases. Spontaneous fracture is rare but when it takes place there is no delay in union. Osteogenic sarcoma may occur, but is much less common than Paget thought and is not seen until the changes in the bones have been present for ten years or more. Osteo-arthritis of the hip, knee, ankle, or spine is an occasional complication. Arterial degeneration, sometimes with hypertension, is found in most cases over the age of 50. It is possible that the excess of phosphoric esterase in the blood accelerates and intensifies the deposition of calcium salts in degenerate vessels. Retinal arteriosclerosis is a frequent finding, and it may be associated both with retinal hæmorrhages and extensive choroidal changes.

Radiological appearances.—The altered bone appears in radiographs in two forms, which may be called the spongy and the amorphous, the former being the more common. The two types are often found in the same patient. The spongy form consists of coarse irregular striæ arranged either as parallel trabeculæ or running in the direction of normal lamellæ of cancellous bone. The amorphous form is a generalised deposit producing an opaque finely granular appearance. The diameter of the bone is increased, sometimes to a marked degree, and in the medullary cavity the trabeculæ are accentuated and too widely separated, giving a streaky appearance. The corticalis is partly or entirely replaced by bone similar to that seen in the medullary cavity, and in an extreme case the impression is that the whole bone consists of cancellous tissue highly magnified. Irregular cyst-like areas are sometimes observed. Widening and bowing of bones are important points in the radiological diagnosis. The vault of the skull is thickened, and the differentiation between the inner and outer tables is lost. Small islands of dense bone are evident alongside pale cyst-like areas. A large clean cut area called *osteoporosis circumscripta* may sometimes be noted. In those cases in which part of one bone is affected there is a definite line of demarcation where the abnormal ends and the normal begins. Thus there may be definite changes in the upper two thirds of the tibia, while the lower third is normal. The average rate of progress of such a lesion is about 1 cm. in two years. Radiographs reveal the shadows of arterial calcification in more than 40 per cent. of cases. Such calcified arteries are best seen in the lower limbs. There

is no evidence of a higher incidence of renal or vesical calculus in osteitis deformans than in the normal.

Diagnosis.—When advanced the condition is unmistakable. In the early stages muscular rheumatism or osteo-arthritis may be wrongly diagnosed. Pulmonary osteo-arthropathy is distinguished by the clubbed fingers. In radiographs the amorphous type of osteitis deformans is sometimes mistaken for secondary carcinomatosis of the osteoplastic type. The difference is distinct and important, namely, that in carcinomatosis the bones are neither enlarged nor bowed. Syphilis of bones is now very rare, but when only one or two bones are involved in a supposed case of Paget's disease the Wassermann reaction should be performed.

Prognosis.—Because the disease is uncommon there is a tendency to regard its effects as dreadful. To announce the diagnosis as though it were a profound mystery may alarm both patient and relatives unnecessarily. Paget's disease is slowly progressive but does not usually shorten life. Thus, one patient though much deformed, continued to drive a crane in a dock-yard 15 years after the onset of the disease. Another was quite happy to have somebody hold him on a rock while he fished a stream, long after he was unable to walk unaided. Death usually results from the effects of arteriosclerosis or intercurrent infection, and only rarely from compression paraplegia or sarcoma of bone.

Treatment.—No known treatment alters the course of osteitis deformans in the slightest degree. Since the bones at one stage are sufficiently decalcified to bend, methods have been used which aim at increasing the calcium intake. The patient is given a high calcium diet, that is a diet containing three pints of milk or milk products daily, together with butter, cheese, and eggs. If milk is not tolerated in these quantities calcium caseinate or calcium lactate (10 grammes a day) may be prescribed. Vitamin D may be conveniently given in the form of tab. calciferol. (3000 units) one or two daily. The claim that prolonged exposure to general ultra-violet irradiation has resulted in increased density of the shadows of bones in radiographs has not been confirmed. Such treatment can be carried out, starting with short exposures to the mercury vapour or carbon arc lamp. Paget treated his patients with potassium iodide, but was not enthusiastic over the results. When there is pain in the bones Lugol's solution (of iodine in potassium iodide) may be given in milk, beginning with a dose of three minims three times a day, and increasing to ten times this amount. If iodine fails to relieve the pain, aspirin, amidopyrine, or allonal should be tried. Exploration of the neck for a parathyroid tumour is never justified. Osteotomy is rarely necessary, but it is interesting that when portions of bone have been removed for histological section relief of pain has sometimes occurred. Occasionally, and especially in those cases with secondary osteo-arthritis of the hip joint or knee joint, an ambulatory splint supporting the weight of the body on the tuber ischii is of value. A cork sole is often necessary, and when kyphosis causes pain a spinal jacket is useful.

LEONTIASIS OSSEA

Synonyms.—General Hyperostosis of the Skull; Cranio-sclerosis; Megalocephaly.

Definition.—The term leontiasis ossea is now used in two senses, specifically for a progressive sclerosing hyperostosis of the skull, and symptomatically when osteitis deformans and the various types of osteitis fibrosa happen to involve the bones of the calvaria and face.

Ætiology.—This is unknown. The fact that the disease commonly arises in the region of the nasal sinuses has led to an erroneous view that it is infective in origin.

Pathology.—When Virchow suggested the use of the term "leontiasis ossea" in cases of hyperostosis of the skull he had in mind fibroma molluscum in which masses of new connective tissue develop in the skin. He believed that the overgrowth of bone in hyperostosis corresponded exactly to elephantiasis of the soft parts, and he decided to call these cases leontiasis ossea, not because the bone disease produced a leonine appearance, but because he considered it to be analogous to the disease of the soft parts which did. The disease is very rare. It occurs in either sex, arising usually in early adult life. In most instances it begins in the nasal fossæ and sinuses, though in some cases the origin is near the orbit or in the base of the skull. Dense ivory bone appears and spreads slowly under the periosteum, being held up sometimes in the region of the suture lines but ultimately breaking through and spreading in many directions across the skull. The serum calcium and plasma phosphorus are normal.

Symptoms.—The early clinical features include nasal obstruction, blocking of the lachrymal ducts, and alteration in the shape of the face and jaws. Ultimately large masses of bone, increasing in various directions, give rise to terrible disfigurement. The cavities of the mouth, nose, and orbit may be greatly lessened. The eyeballs may protrude even beyond the lids, and blindness may occur from optic atrophy. There may be loss of the sense of smell, and interference with the mobility of the lower jaw. Except in the later stages pain is unusual.

Diagnosis.—Paget's disease usually begins at 55, and the pelvis, spine, and lower limbs are nearly always affected. Generalised osteitis fibrosa leads to decalcification of the whole skeleton, with a high blood calcium and low blood phosphorus. Focal osteitis fibrosa often shows multiple lesions scattered throughout the skeleton.

Treatment.—No treatment has any permanent effect though it may be possible to remove some of the more disfiguring masses of bone.

HYPERPARATHYROIDISM (GENERALISED OSTEITIS FIBROSA CYSTICA (see p. 498)

FOCAL OSTEITIS FIBROSA

Synonyms.—Osteitis Fibrosa Circumscripta (Schmidt); Local Fibrocystic Disease; Benign Giant-celled Tumour; Osteoclastoma; Osteogenetic Myeloma; Myeloid Sarcoma.

Definition.—A focal or multifocal disease of bone unassociated with constitutional symptoms or with any known endocrine disturbance.

Ætiology.—This is unknown. The disease occurs chiefly in adolescence,

and is much more common than is generalised osteitis fibrosa (hyperparathyroidism).

Pathology.—The lesions are benign, firm, grey or brown tumours. Histologically they show osteogenetic fibrous tissue and giant cells which, of course, are osteoclasts. This explains the numerous synonyms which are used. The tumours sometimes expand the corticalis and may give rise to cysts lined by osteoclasts. Even when the lesions are multiple the rest of the skeleton consists of normal bone. The figures for serum calcium and plasma phosphorus are invariably normal, a finding in striking contrast to that of the generalised disease. The calcium balance is usually normal, and, taken in conjunction with the normal blood chemistry, this finding is strong evidence against hyperparathyroidism.

Symptoms.—The malady affects one or more bones, is usually not disabling, is of slow progress, and shows a tendency to become arrested. Pain is unusual and the disease is often symptomless until spontaneous fracture occurs. Severe cases of the multifocal type may show considerable deformity, especially of the pelvis, femora and skull.

Radiological appearances.—In radiographs the principal changes are found in the ends of the long bones. Usually more than one-third of the shaft is affected by a fusiform enlargement composed of a pale cyst-like area divided by a few coarse trabecular strands. The cortex is thin and may be expanded. The periosteum and adjacent bone are normal. Radiographs taken with controls show that the whole skeleton apart from the lesions is normally calcified. The floor of the skull and the lower jaw may be affected.

Diagnosis.—The normal blood chemistry serves to distinguish the focal from the generalised disease. In adult cases it is sometimes difficult to differentiate between focal osteitis fibrosa and osteitis deformans, and it may then be necessary to follow the progress of the condition over a period of time before a definite conclusion is reached.

Treatment.—Fractures are treated in the usual way. If spontaneous fracture occurs in a long bone through one of the lesions, union is usually strong, and radiographs subsequently show that the pale cyst-like area of osteitis fibrosa becomes filled with bone. Exploration of the neck for a parathyroid tumour is quite unjustified.

THYROTOXIC OSTEOPOROSIS (see Hyperthyroidism, p. 488)

OSTEOMALACIA

Synonym.—Mollities Ossium ; Adult Rickets.

Definition.—A generalised disease of the skeleton due to vitamin D deficiency. Two types are found. The first is due to a diet deficient in vitamin D and calcium salts and may be referred to as dietetic osteomalacia. The second is a conditioned dietary deficiency disease, arising from deficient absorption of vitamin D and calcium salts ; it is seen in idiopathic steatorrhœa.

Ætiology.—Osteomalacia is rare in England. It is endemic over wide areas in Northern India, Japan and Northern China, and occurs sporadically in the Rhine Valley, Danube Valley, Vienna, and certain parts of Italy, Switzerland, Flanders and the Balkans. Heredity plays no part. The

disease pre-eminently affects women, and is likely to recur earlier and with greater severity with each successive pregnancy. But it is a mistake to suppose that pregnancy is essential in the ætiology. The malady is sometimes seen at puberty and is quite well known to occur, though rarely, in boys and men. In the majority of cases the symptoms begin between the twentieth and thirtieth year.

Pathology.—Rickets and osteomalacia are essentially identical. What difference exists is merely that of age incidence. Osteomalacia is adult rickets. Morbid anatomists agree that in rickets and osteomalacia the essential abnormality is a deficient calcification of osteoid tissue. This deficiency is generalised throughout the skeleton. The broad osteoid seams in both diseases are due to deficiency of the calcifying mechanism, which should convert osteoid tissue into true bone. In osteomalacia the bones throughout the skeleton are so soft that they readily bend and cut with a knife like rotten wood. Spontaneous fractures are common. The blood chemistry is comparable in experimental rickets of rats, in children with rickets, and in women with osteomalacia. The plasma phosphorus and sometimes also the serum calcium are diminished. The occurrence of fœtal rickets has been proved in babies born of osteomalacic mothers.

Symptoms.—Pain is a prominent symptom. It occurs especially in the back and thighs, is aching in character and is worse in the winter months. The pelvis, thorax, or long bones exhibit deformity in a haphazard way; one woman suffers in the pelvis, another in the ribs, and a third in both. Besides the changes in the pelvis, marked deformities occur in the chest and spine. Severe kypho-scoliosis may reduce the height by several inches and cause the head and neck to sink downwards and forwards on to the chest. Deformities of the sternum and ribs give rise to marked prominences and depressions in the chest wall. Coxa vara and irregularly curved long bones are less common. The bones are soft and flexible, rather than fragile, so that bending is much more common than is spontaneous fracture, though both are well recognised. The patient develops a characteristic waddling gait, and muscular weakness may add to her incapacity. In many cases the pelvic deformities interfere with marital relations or with labour, Cæsarean section frequently being necessary. Tetany is common. The teeth are normal. The course of the disease may be fairly rapid, lasting several months, but untreated cases extend over many years. The patient then becomes bedridden, spontaneous fractures, anæmia, cachexia, and bedsores adding to her discomfort and to the difficulties of nursing.

Radiological appearances.—The degree of lack of calcification in radiographs will vary with the severity of the disease, and it is therefore important to take radiographs with controls. In the slight cases the bones of the patient will be slightly more translucent than those of the control. The cortex will be less dense than normal but the bone pattern, especially the trabeculation, will be accentuated by contrast. In the severe examples there will be little or no difference between the density of the bone and surrounding soft tissues, and the cortex will appear as a mere pencilled outline. The bone pattern will have disappeared, the long bones will bend, and occasionally show fracture. All deformities apart from fracture are the result of weight stress or muscular action. The pelvis is tri-foliate, owing to the thrusts of the heads of the femora and sacrum. Lordosis is marked and kyphosis may

be present. In severe cases the chest and ribs are usually deformed. The vertebræ are biconcave, having the appearance of fish vertebræ. In severe cases the vault of the skull may show numerous areas of uneven translucence, varying in size and shape but all fairly clean cut. The spontaneous fractures are usually subperiosteal, and radiographs sometimes show pseudo-fractures. These appear as areas of complete translucence, running across the bone, the edges being quite clean cut, and separated from each other by one or two millimetres.

Diagnosis.—The occurrence of pregnancy and the examination consequent upon this lead commonly to the recognition of the pelvic deformity and of the disease which has given rise to it. Differential diagnosis from other generalised diseases of the skeleton usually produces no difficulty. In hyperparathyroidism there is a high serum calcium, a low plasma phosphorus, and an increased calcium excretion in the urine. In senile osteoporosis the patient suffers from kyphosis and a tendency to fractures particularly of the neck of the femur, and the blood chemistry is normal. In thyrotoxic osteoporosis, the usual signs of hyperthyroidism are present, and the blood chemistry is normal. In myelomatosis the Bence Jones protein is found in the urine in 75 per cent. of cases, the serum globulin is usually increased, and the albumin : globulin ratio diminished. The serum calcium is usually normal, but sometimes raised. The plasma phosphorus is normal, but it rises in cases showing renal insufficiency. In radiographs the condition may closely resemble osteomalacia.

Treatment.—Pure vitamin D is called calciferol because of its power to induce calcification in tissues, especially in osteoid tissue. It is 300,000 times as potent as cod-liver oil, weight for weight. The good effects not only of calciferol but also of cod-liver oil and ultra-violet irradiation have been noted both clinically and chemically, since they are capable of raising the serum calcium to normal. In cases where tetany is present calcium salts should be administered in addition. The diet of a woman suffering from osteomalacia should contain 3 pints of milk a day, with plenty of milk puddings, eggs, butter, cheese, green vegetables, and even nuts and raisins. The dose of cod-liver oil should be large, up to 2 or 4 oz. daily. This treatment relieves the pain in 3 to 4 weeks. Some cases are refractory, and it is then necessary to add 0·5 mg. of calciferol to the cod-liver oil daily. Tetany is rapidly removed by treatment with cod-liver oil and calcium lactate. A powder containing at least 10 grammes of the latter should be used daily, and is best administered fasting with a glass of milk. The patient should be exposed to sunlight when this is possible; otherwise treatment by ultra-violet irradiation may be used, starting with a short exposure to a carbon arc lamp and increasing gradually up to 30 minutes. There is no evidence that phosphorus is of any value in the treatment of osteomalacia. Where the disease exists in great endemic areas, questions of diet, and social and religious customs are proving very difficult. In large areas of China and India the diet is often deficient in quantity, and inadequate in calcium and vitamin D. In the high mountain valleys of these countries and in areas of India where purdah is practised, darkness adds to the danger by causing further deprivation of vitamin D. With regard to China, Maxwell states: "We want flocks and herds, milk and meat, with security of life and property." The suggestion has been made that it might be practicable

in India and China to dispense calciferol freely at a low price just as quinine is dispensed in malarial districts. The relation of ovarian function to calcium metabolism has not yet been settled. Osteomalacia gets worse during lactation, no doubt because of the great drain of calcium from the body. Improvement has been observed after ovariectomy. This operation may act merely by preventing pregnancy, and it is presumably just as reasonable to ligate the Fallopian tubes. When pelvic deformity demands it Cæsarean section is necessary.

Osteomalacia in Idiopathic Steatorrhœa

When osteomalacia occurs in the course of idiopathic steatorrhœa (Gee's disease), the following features may be present: fatty stools, dilatation of the colon, tetany, anæmia, skin lesions, and infantilism (see p. 476). The disease occurs in both sexes and the history nearly always goes back to early childhood. The symptoms develop in spite of an adequate diet. We must, therefore, suppose that there is some disturbance of gastro-intestinal function resulting in deficient production, absorption or utilisation of one or more essential factors. The serum calcium is low and the plasma phosphorus is low or normal. The total fat in the stools may reach 40 per cent. or more, and the bulk of this is unsplit fat. The clinical and radiological features are exactly the same as in dietetic osteomalacia. An opaque enema will reveal dilatation of the colon. In treatment the fat in the diet must be cut down to a minimum, and the calcium salts and vitamins kept high. Vitamin D must be given in a solid and not in an oily medium. The prognosis of this type of osteomalacia is good especially in young people. Splinting or even osteotomy may be necessary to correct deformities such as genu valgum. The pelvic deformity may necessitate Cæsarean section.

OSTEOGENESIS IMPERFECTA

Synonyms.—Fragilitas Ossium Congenita; Osteoporosis Congenita; Congenital Osteopsathyrosis; Osteopsathyrosis Idiopathica.

Definition.—A generalised disease of the skeleton, congenital, and in some 25 per cent. of cases hereditary, in which the bones are so fragile that repeated fractures occur. Multiple fractures may occur in utero (pre-natal type of Vrolik, 1849), or fractures may not occur until after birth (post-natal type of Lobstein, 1833). Both sexes are affected equally.

Ætiology.—This is unknown.

Pathology.—In both types the basic defect appears to be defective osteoblastic activity. The cortex of the bones may be scarcely thicker than paper, and the trabeculæ of spongy bone are extremely thin. In the pre-natal type many fractures are seen; in some cases practically every bone in the body has been fractured. The older fractures exhibit good callus formation. In extreme cases, especially in the pre-natal type, the cranial ossification is so disorganised that the vault of the skull consists of a mosaic of small Wormian bones. Congenital hypoplasia occurs in other mesenchymal tissues, notably the ligaments and the sclerotics. There is no evidence whatever of vitamin deficiency. No abnormality in the serum calcium,

plasma phosphorus, or calcium output has been demonstrated. The plasma phosphatase tends to show a raised value but this is not constant.

Symptoms.—The general health of the patient is good but fractures occur from the most trivial violence or even normal muscle action. In the course of time, 20, 30, or even 100 spontaneous fractures may occur. They are often subperiosteal and cause little pain. The patient tends to be short in stature and slender in build. As a result of anomalous cranial ossification, the shape of the head is often striking. A bitemporal protuberance so marked as to turn the ears outwards is frequently observed, but protuberances in the occipital and frontal regions are also seen. Every bone in the body may be deformed. The limbs are often bowed and of unequal length. Kypho-scoliosis, distortion of the ribs and sternum, and asymmetry of the pelvis all occur. Three other defects are commonly found in association with the fragile bones, namely, leaden blue sclerotics, a tendency to dislocation of joints, and after the age of 20 years otosclerotic deafness. Amongst the adult population affected with blue sclerotics approximately 60 per cent. have an associated liability to fracture, approximately 60 per cent. an associated otosclerosis, and 44 per cent. suffer from all three defects. Osteogenesis imperfecta sometimes occurs in an hereditary form without blue sclerotics.

Diagnosis.—Severe cases and all those with blue sclerotics are unmistakable. In the new born great shortening of the limbs may suggest achondroplasia, but the skull is quite different. Cases of spontaneous fracture in the adult occurring in hyperparathyroidism, hyperthyroidism, myelomatosis, osteoclastic carcinomatosis, and neuropathic atrophy of bones really cause no difficulty.

Prognosis.—Severe cases of the pre-natal type are either stillborn or live only for a short time. In post-natal cases the condition proves more severe the earlier the first fracture appears. Multiple fractures in the first few years of life may lead to such deformities that the patient can never walk and may die before puberty. In those who survive, the liability to fractures tends to become less before puberty. In general the longer the patient lives the greater will be the improvement, and in many of the adult cases the disability is slight only.

Treatment.—The utmost care must be taken to avoid the occurrence of fractures. Treatment consists in gentle handling and careful splinting. Union usually occurs without delay and is firm. Dislocations are reduced without difficulty. Vitamin D, calcium salts, and a high calcium diet have no effect on the course of the illness.

OXYCEPHALY

Synonyms.—Tower Skull; Steeple Head; Sugar Loaf Head; Acrocephaly; Craniostenosis.

Definition.—A congenital deformity of the skull due to premature synostosis of the cranial sutures. The skull is short from front to back and its vertical diameter is increased. Allied forms of craniostenosis are scaphocephaly, the boat-shaped head, and plagiocephaly, the obliquely flattened head.

Ætiology.—This is unknown. The disease is more common in males than females. It is sometimes hereditary and familial. It is usually present at birth but it may develop subsequently up to the age of six.

Symptoms.—In its slightest form it attracts attention, while in its grosser forms there is no passer-by but is shocked by the disfigurement and repelled by its hideousness. The forehead is much increased in height, sloping gradually upwards to the vertex with feebly marked superciliary arches. The vertex of the skull appears pointed instead of flattened or rounded, and a thin bony prominence is sometimes felt in the region of the bregma. The hairy scalp may be raised above the normal level and present the appearance of being perched on the top of a cone. Viewed laterally, the ears appear placed on a lower level than normal. Proptosis is present in most cases, and it may be so considerable that the eyeballs become dislocated in front of the lids. Failure of closure of the eyes, especially during sleep, may lead to lachrymation and conjunctivitis. Divergent squint is common and nystagmus is present in some cases. Symptoms arise from insufficient room within the skull for the developing brain. There is increased intracranial pressure with headache and sometimes vertigo. The condition is compatible with normal intelligence, but not infrequently optic atrophy supervenes. This is secondary to papillœdema in some 85 per cent. of cases. In the remainder it is brought about by narrowing of the optic foramen and is of the primary type. The sense of smell is often completely lost, but taste is affected very rarely. Hearing is unaffected. The following associated congenital malformations have been described in a few cases: webbing of the fingers and toes; malformation of ears, elbow and shoulder joints, and fingers.

Radiological appearances.—Radiographs show an increased vertical diameter of the skull with its highest point either at the bregma or somewhere between it and the lambda. The anterior fontanelle closes late, and its site is marked by a slight protuberance over which the bone is thinned. The sutures of the vault are partly or entirely absent, but the basal suture between the sphenoid and the occipital bone may be widely open. The air sinuses are rudimentary, and the middle fossa bulges forward. The most characteristic feature is the presence of numerous deep convolutional markings.

Prognosis.—The optic atrophy, whether primary or secondary, may advance to complete blindness. There is nothing to show that oxycephaly shortens life.

Treatment.—Anodynes should be used in the relief of headache. If the symptoms of increased intracranial pressure become marked, and the changes in the optic discs progress, decompression may be necessary.

DISEASES OF ENDOCHONDRAL OSSIFICATION

ACHONDROPLASIA

Synonyms.—Chondrodystrophia fœtalis (Kaufmann); Micromelia fœtalis.

Definition.—A disease of fœtal life in which defective endochondral

ossification makes the bones preformed in cartilage short, but stout and strong.

Ætiology.—This is unknown. Both sexes are affected equally. It is hereditary and has been recorded in six generations. Several members of the same family may be affected. The condition is unrelated to rickets, cretinism, syphilis, or tuberculosis.

Pathology.—The essential abnormality is found in the cartilaginous epiphyses. The cartilage does not prepare itself for ossification, which is in consequence so slow that the long bones are too short. Since, however, the periosteum goes on laying down bone normally, the bones are stout and strong. The membrane bones of the skull are unaffected, so that the calvaria is of normal size. Premature synostosis of the cartilaginous bones at the base of the skull leads to shortening, and consequent depression of the bridge of the nose. The clavicles are not affected. The pelvis is distorted and contracted, the sacrum being tilted forwards. Extreme lordosis may be present. The costo-chondral junctions are enlarged to form a rosary. The scapula is so small that the glenoid fossa scarcely holds the head of the humerus.

Symptoms.—The patient is dwarfed but of normal intelligence. The usual height of the adult is about four feet. The vault of the head is large and the frontal and parietal eminences prominent. The face is small and the nose has a depressed and flattened bridge. The nostrils are large, the lips thick, and the lower jaw and chin well developed. The teeth are normal. The trunk is of normal size but the extremities are much shortened, and with the arms at the sides the fingers reach no farther than the great trochanter of the femur. The humerus and femur are relatively more shortened than the other bones of the extremities, so that the proximal segments of the limbs show the most marked shortening. The arms are muscular and are held a little abducted from the trunk. The hands are short, thick, and trident-shaped, the fingers being almost equal in length. The lower limbs are thick and often show deep transverse furrows as if there were redundancy of the soft parts. This appearance is due to the packing of well-developed muscles into the restricted long axis of the limb. This muscular development enables the achondroplasic to perform feats which are surprising in one so small. He rises from the lying-down position by a characteristic springing movement from the legs without any assistance from the arms. The curving and enlargement of the ends of certain bones gives rise to bow legs and beading of the ribs. The lumbar curve is increased owing to tilting forward of the sacrum and excessive development of the buttocks. In consequence the gait has a peculiar duck-like waddling character. The genital organs are normal. The fact that the female may become pregnant makes the pelvic deformity of great importance. The conjugate diameter is greatly narrowed, and it is almost impossible for an achondroplasic woman to give birth to a living child except by Cæsarean section. That the disease has existed for something like five thousand years is known from models found in mummies of two achondroplasic gods of ancient Egypt, namely Ptah-Sokar and Bes. In the Middle Ages the attractive antics of achondroplasics made them much sought after as court jesters or dwarfs. To-day not infrequently they play the parts of clowns at fairs, circuses and music-halls, and sometimes break chains on the stage.

Diagnosis.—In the new born the great shortening of the limbs may suggest osteogenesis imperfecta, but the skull is quite different. In childhood the malady is readily distinguished from rickets and congenital syphilis by careful attention to the physical signs. Achondroplasia differs from cretinism in that the patient is of average intelligence, and has normal skin, hair and voice. The pituitary dwarf presents no difficulty because the limbs and trunk are in perfect proportion.

Prognosis.—The majority of infants suffering from achondroplasia are either still-born or die shortly after birth. If the child does survive, the expectation of life is normal. The female achondroplasic faces greater risks in parturition than a normal woman.

Treatment.—No treatment is of any avail. Orthopædic treatment for bow legs is unnecessary. The pelvic deformity may necessitate Cæsarean section.

DYSCHONDROPLASIA

Three clinical conditions are included under this heading. In all of them islands of ectopic cartilage are found giving rise to multiple ecchondromata or enchondromata. The three conditions are grouped together because of one feature they have in common, namely arrest or perversion of the normal process of endochondral ossification in certain bones. This change differs from that seen in achondroplasia only because it is neither symmetrical nor universal. Different manifestations of dyschondroplasia may occur in various members of the same family.

(i) *Hereditary multiple ossifying ecchondromata (hereditary deforming chondrodysplasia, diaphysial aclasis, or multiple cartilaginous exostoses).* This is a fairly common disease in which multiple bony tumours are found in association with certain other skeletal deformities. It is hereditary and may affect several individuals of the same family. It is more common in males than in females in the proportion of 3 to 1. It is usually discovered in childhood. Palpable bony tumours up to 2 cm. or more across are found more or less symmetrically placed near the knee, shoulder, hip, ankle and wrist. The scapula, ribs and pelvic bones may sometimes be affected. The stature is shortened and the limbs may be unequal in length. In the majority of cases the ulna and fibula are disproportionately short in relation to the radius and tibia. Bowing of the radius, ulnar deviation of the hand, irregular length of the fingers, and valgus deformity of the foot all may occur. Sarcoma supervenes in 5 per cent. of cases. Local exacerbation of symptoms in a patient over 30 years of age may be the first indication of its onset. Rarely pressure of an exostosis upon the spinal cord may cause paraplegia, or upon a nerve trunk pain or local paralysis. Aneurysm has been recorded from pressure upon an artery. The radiological appearances are characteristic. The metaphysis of the bone affected is broadened and distorted, and ossifying ecchondromata with broad bases and pointed tips project from it. The cartilaginous cap of the tumour is not seen unless it is calcified. The earlier the ecchondroma occurs the nearer to the centre of the shaft will it be. Where ecchondromata protrude between adjacent bones such as the tibia and fibula, local fusion may occur. The ulna is

likely to be short and to end in a point, articulating with the radius on its mesial aspect but not partaking in the carpal articulation. Usually no treatment is required but should it be necessary to remove any particular swelling this is easily carried out.

(ii) *Multiple chondromata* (*Enchondromatosis*). This is a rare disease affecting the bones of the hands and feet. Cartilaginous swellings in the fingers and toes begin in childhood and increase in size up to the age of 30 years. The swellings are firm, elastic, rounded and slightly translucent. The skin over the larger ones may be tightly stretched and shiny and show prominent veins. The hands and feet may become hideously deformed. Sometimes a rib near the costal cartilage, the sternum, the pelvis, and the scapula are affected. In certain cases the ulna and fibula are disproportionately short as in diaphysial aclasis. Spontaneous fractures may occur, and sarcoma may supervene after years. Radiologically chondromata are seen as rounded, eccentric translucent areas expanding the corticalis, interrupting its outline, and projecting into the soft tissues. Sometimes the swellings are trabeculated and they may contain dense, punctate, calcified areas. Where operation is undertaken to excise some of the chondromata care must be exercised to avoid spontaneous fracture of the phalanges or metacarpals.

(iii) *Unilateral chondrodysplasia* (*Ollier's disease*). This is a very rare type of chondrodysplasia occurring in children and sometimes familial. It usually has a completely unilateral distribution, but some cases have only one bone or one limb affected, and others are bilateral. Some abnormality is often first noticed between the first and second years of life, when as a rule one limb is found to be shorter than its fellow. The difference in length becomes progressively greater as growth proceeds. Deformity may occur either because weight bearing causes bending of the bone, or because of the different rate of growth where only one of the paired bones is affected. Most patients seem to reach adult life, when their symptoms are mainly those of their deformities and sometimes of a secondary arthritis. In a small proportion of cases sarcoma supervenes. The diagnosis largely depends upon examination of radiographs. The ends of the long bones show translucent longitudinal striæ interrupted by small pale mottled areas and dark punctate spots. In the areas affected there is extensive alteration in the pattern of the corticalis and spongiosa, but the centre of the shaft remains normal. As the child grows older the typical striped appearance disappears and is replaced by dense punctate speckling due to areas of calcification. The disease has occasionally been mistaken for osteitis fibrosa, but the radiological appearances are pathognomonic. Treatment is concerned with the prevention and relief of deformities, and proceeds along the usual orthopædic lines. Osteotomy is sometimes necessary. Fractures are of fairly common occurrence, and like the osteotomies appear to unite well.

DONALD HUNTER.

DISEASES OF THE BONE MARROW

MULTIPLE MYELOMA

Synonyms. — Myelomatosis; Kahler's Disease; Plasmacytoma; Hæmatogenous Myeloma.

Definition.—A fatal disease characterised by the development of multiple tumours in the skeleton, which arise from cells of the bone marrow. It is very rare. The bones are affected in the following order of frequency: spine, ribs, sternum, skull, scapula, pelvis, clavicle, humerus and femur.

Ætiology.—Multiple myeloma is of unknown origin. It is a malignant neoplasm of the hæmatogenous marrow occurring in multiple foci. The disease is related to leukæmia, but differs from it in the sharper localisation of the neoplasia, the absence of enlargement of the spleen or lymph-glands, the much smaller tendency for the abnormal cells to enter the blood stream and the frequent appearance of Bence Jones protein in the urine. Intermediate forms occur with features of both diseases. It is associated with interesting alterations of protein metabolism. The disease is sometimes familial. It begins most commonly at the age of 55, and only 10 per cent. of cases occur before 40. The sexes are affected in the proportion of three men to two women.

Pathology.—Multiple deep red or reddish-grey sharply defined tumours are found distributed throughout the red bone marrow. They are usually a few millimetres in diameter and very numerous. Occasionally a tumour may reach a diameter as great as 5 cm. They are composed of blood-forming cells, either myelocytes, myeloblasts, erythroblasts, or cells resembling plasma cells. They erode bone, sometimes expand the cortex, and cause deformities and spontaneous fractures. Rarely a diffuse hyperplasia of the marrow is associated with foci of tumour formation. Tumours may also be found outside the skeleton in the tonsils, liver, spleen, kidneys, or sex-glands, and these lesions may even precede those in the bones. The marrow tumours give rise in the urine to the Bence Jones protein which appears as a cloud when the urine is heated to 55° C., redissolves at 85° but reappears on cooling. It is found in 75 per cent. of cases, from a trace to a large amount. In some cases it appears early in the disease, in others late. Its occurrence may be continuous or periodic. Sometimes a substance allied to amyloid material is deposited in the muscles and in nodules connected with the periosteum, bursæ, tendon sheaths and joints. It is possible that both the Bence Jones protein and the amyloid substance are produced from the breakdown of myelomata. The serum globulin is usually increased even as much as 8 per cent. (normal 2 per cent.). The albumin-globulin ratio may drop from the normal 2·2 to a figure as low as 0·5. The formol-gel reaction is positive (see p. 253), and there is a very rapid rate of sedimentation of the blood. Metastatic calcification while by no means constant has been frequently observed in the kidney, lung, stomach, myocardium and uterine mucosa. The serum calcium is usually normal, but, taking into account the bone destruction which occurs as the result of erosion by the marrow tumours and also the metastatic calcification, it is not surprising

that high serum calcium values have sometimes been recorded. Figures from 13 to 16 mg. per 100 c.c. have been found. Those cases with a normal serum calcium have a normal calcium output, while those with a high serum calcium have an output up to double the normal. Where renal insufficiency complicates multiple myeloma the plasma phosphorus is found to be high and may rise as the kidney condition becomes worse. The parathyroids are not enlarged in multiple myeloma.

Symptoms.—The initial symptom is pain, often bilateral, in the thoracic, abdominal and lumbar regions, and sometimes in the neighbourhood of the joints. Progressive kyphosis or angular curvature of the spine with loss of total height follows. The spine, sternum and ribs may be tender on percussion. It is unusual for any of the myelomata to be palpable. In 60 per cent. of all cases spontaneous fracture occurs in the ribs, sternum, or later in the long bones. In no other type of bone tumour does pathological fracture occur so frequently. In some cases amyloid masses may be palpable as firm, rounded, slightly tender, subcutaneous nodules more than a centimetre in diameter. They are felt especially in the scalp, along the spine, near the joints, and in the musculature, particularly that of the pelvic and shoulder girdles. There is usually a hypochromic anæmia, which becomes aggravated in the terminal stages. In a few instances cells of the type which constitutes the tumour enter the blood stream in larger or smaller numbers, and it is probable that they can be found in the majority of cases if a sufficiently careful search is made. In rare instances the anæmia is of the leucoerythroblastic type (p. 783). Nephritis without hypertension is fairly common. The temperature is usually normal but recurring fever has been observed. The patient ultimately becomes bedridden and cachectic. It seems justifiable on clinical grounds to consider separately what may be called the vertebral form of the disease. Here the growth is confined for some time to the vertebral and extradural tissues. Moreover, death may occur before the growths become widespread, and sometimes without the Bence Jones protein having appeared in the urine. In this variety the patient rapidly develops signs of a transverse spinal lesion with blockage of the spinal canal. The thoracic cord is usually the site of compression and there is focal spinal tenderness. Radiographs show destruction of the corresponding vertebral body.

Radiological Appearances.—In radiographs the marrow tumours are found mainly in the spine, ribs, sternum and skull. They are seen as clean-cut elliptical or circular areas of complete translucence, set closely together and varying from 1 mm. to 5 cm. in diameter. The larger tumours may expand the cortex of the bone affected. There is a good deal of generalised osteoporosis throughout the affected bones. The spine shows collapse of the bodies of one or more vertebræ. The skull is not thickened. Pathological fractures, especially in the ribs, are very common.

Diagnosis.—Once the lesions have appeared in many bones the diagnosis is easily made. The age of the patient, multiple involvement of the bones of the thoracic cage, spontaneous fracture of a rib, Bence Jones protein in the urine, progressive anæmia, cachexia and characteristic radiographs make an unmistakable clinical picture. Biopsy of a portion of bone or examination of a bone-marrow smear from a sternal puncture may reveal the characteristic myeloma cells. Secondary carcinomatosis of bones may

cause difficulty, especially in cases in which the primary growth is symptomless. It is essential to differentiate the disease from generalised osteitis fibrosa (hyperparathyroidism). There is some resemblance in the clinical picture as it affects the skeleton, but the presence of the Bence Jones protein and the blood chemistry are characteristic. In multiple myeloma the serum calcium is usually normal. If it is high it is associated with a high plasma phosphorus, whereas the characteristic effect produced by parathyroid hyperfunction is a high serum calcium with a low plasma phosphorus. In osteomalacia the patient is usually a woman in the child-bearing period of life, and a good deal of bending occurs in the bones. The blood chemistry is characteristic. Sometimes in the early stages of multiple myeloma widespread pain in the thoracic, abdominal and lumbar regions may lead to a mistaken diagnosis of fibro-myositis. In tuberculous caries of the spine neither the ribs nor the sternum are involved. The fact that the Bence Jones protein is found in the urine in an occasional case of leukæmia need cause no mistake. In those cases in which nephritis complicates multiple myeloma the albuminuria may cause difficulty. The Bence Jones protein may be detected in the presence of albumin by making the urine slightly acid with acetic acid, boiling it and filtering while hot, using a funnel with a hot-water jacket. If Bence Jones protein is present the filtrate will become cloudy as it cools.

Prognosis.—The prognosis is hopeless. Death often occurs within six months of the onset of symptoms, but occasionally a patient survives for two years or more. Broncho-pneumonia, cachexia, or compression paraplegia with ascending pyelo-nephritis are the usual terminal events.

Treatment.—The patient should be treated by rest in bed, anodynes and suitable splinting when necessary. Occasionally deep X-irradiation can be used with good effect. It alleviates pain and reduces the size of the tumours, but it does not retard the progress of the disease. It is clearly unjustifiable to explore the neck in search of a parathyroid tumour. When the symptoms and signs point to compression of the spinal cord surgical intervention may be worth while. Laminectomy reveals a grey or reddish-grey extradural mass either pushing the cord backward or encircling it. Removal of the mass decompresses the cord and is followed by improvement. Deep X-irradiation and the wearing of a spinal brace are advised after laminectomy.

DONALD HUNTER.
LESLIE J. WITTS.

GAUCHER'S DISEASE

In 1922 Pick discovered a gross osseous form of Gaucher's disease. It is exceedingly rare. The symptoms are pain in the bones, pathological fractures and sometimes angular curvature of the spine. In radiographs the bones show patchy osteoporosis. A characteristic feature is that the ends of the femora are widened evenly. Both skull and pelvis may be involved. Sometimes scattered through the bones there are focal pale rounded areas which expand the cortex. These areas are deposits of kerasin, a galactolipin. The usual characteristics of Gaucher's disease are, of course, present (see pp. 834, 835).

HAND-SCHÜLLER-CHRISTIAN'S DISEASE

The lesions of Hand-Schüller-Christian's syndrome (lipoid granulomatosis or xanthomatosis of bones) are not confined to the calvaria, the orbit or the sella turcica (see p. 836). Erosions of the maxilla and mandible have been described, resulting in loosening or falling out of the teeth. Erosion of the petrous bones may lead to a syndrome simulating otitis media, and bilateral deafness has been observed. Large areas of rarefaction have been described in the long bones of the extremities, and in the spine, pelvis, ribs and clavicles. Pain may occur in the bones affected, especially the head, pelvis and thigh. Spontaneous fracture is not uncommon. When the pelvis is involved there may be deformity, including shortening of one lower limb. In some cases the skull escapes entirely, diabetes insipidus and exophthalmos being absent. Radiologically the deposits of cholesterol-ester are seen as irregular clean-cut translucent areas sometimes with a few coarse trabeculæ. In order to distinguish the condition from multifocal osteitis fibrosa it may be necessary to excise a portion of bone for histological section. The lesions tend to yield temporarily to treatment by X-irradiation.

DONALD HUNTER.

SECTION XIX

DISEASES OF THE SKIN

I. ANATOMY AND PHYSIOLOGY

In order that the diseases which affect the skin may be understood it is necessary to give a brief account of the anatomy, physiology and general pathology of the skin.

Anatomy.—The skin is a fibrous structure varying considerably in thickness in different parts of the body and covered externally by several layers of epithelial cells. On section its main bulk is seen to be made up of white fibrous tissue bundles running chiefly parallel to the surface and bound together by thin fibres of elastic tissue. The surface of this fibrous mass, which is called the *dermis*, is not level but is surmounted by a number of finger-like projections, called papillæ, which fit into corresponding depressions or pits on the under surface of the epithelial covering which is called the *epidermis*.

In the fibrous stroma of the dermis blood vessels, lymphatics and nerves ramify. The *arteries* form a plexus of large vessels at the junction of the dermis with the subcutaneous fatty layer and from this deep plexus arteries pass upwards, frequently near hair follicles or sweat ducts to which numerous twigs are sent, to another superficial or sub-papillary plexus situated just below the bases of the papillæ. From this smaller vessels pass upwards to end in the papillæ. The *veins* follow a similar course in the opposite direction.

Lymph circulates freely in the spaces between the cells of the epidermis and the fibres of the dermis, but definite lymphatic vessels are also found in the papillæ and in the dermis, accompanying the blood vessels.

The *nerves* of the skin are both medullated and non-medullated. They also follow the course of the blood vessels and are distributed to the hair-follicles, sweat and sebaceous glands, blood vessels, arrectores pili muscles and to the connective tissue bundles in their passage through the dermis. Losing their medullary sheath in the sub-papillary layer some fibres pass up and are distributed to the papillæ and to the basal and mucous layers of the epidermis, while other medullated fibres end in curious whorls in the papillæ, which are called the touch corpuscles of Meissner; a few end in small ovoid bodies, known as Pacinian bodies, in the subcutaneous tissue.

The *epidermis* consists of several layers of cells, varying considerably in thickness in various parts of the body. The layer nearest the dermis consists of regular cubical cells to which it is intimately attached, and it is from this layer that the rest of the epidermis is developed; it is spoken of as the *stratum germinativum* or *basal layer*. The layers above this consist

of cells in various phases of transformation into horn cells, which are seen in their final form in the outermost layers. Above the basal layer there are several layers of large polyhedral cells with large nuclei and a spongy cell substance; they are bound to one another by fine fibrils from which they have obtained the name "prickle" cells; this is the *mucous* or *Malpighian layer*. Above this are one or two layers of lozenge-shaped cells, lying parallel to the surface of the skin, whose protoplasm contains large deeply staining granules, giving to it the name *granular layer*. Then comes a thin transparent layer, the *stratum lucidum*, and above this the *horny layer*. Here the cells have lost their nuclei and protoplasm, and consist only of a cell capsule which has been converted into a highly resisting substance called keratin; the cells are intimately bound together and can only be separated with great difficulty. Thus a strong protective layer is produced which can only be destroyed by strong acids or alkalis or by violence.

In the cells of the basal layer are produced granules of *pigment* which act as a protection against light rays. The pigment is an iron-free substance named *melanin*, and its method of production is still a matter of controversy. In the dark races the deeper cells of the mucous layer also contain melanin granules, and these can also be found in wandering cells in the dermis but are not formed in these cells.

Dipping down from the epidermis into the dermis are certain epithelial structures, the hair follicles with their sebaceous glands, and the sweat glands.

The *hair follicles* are pockets of epithelium which contain in their walls all the layers of the epidermis in a modified form. They penetrate the whole thickness of the dermis and often pass into the subcutaneous tissue for some distance. The *hairs* grow from enlarged papillæ at the bottom of the pits and also consist of modified epidermis, so modified that the cellular structure is only visible on the outer layers formed of superimposed scale-like cells, the cuticle of the hair; the remainder of the hair structure consists of an outer fibrous part, the cortex, and a more succulent centre, the medulla. Hairs are present all over the skin except on the palms and soles, and vary very much in size. Their ordinary characteristics need no description. The hair follicle is inserted obliquely in the skin, and on the aspect where it forms an obtuse angle with the surface, a small band of unstriated muscle, the arrector pili, is found, attached below to the hair follicle near the papilla and above to the fibrous tissue underlying the surface epidermis. This muscle on contraction erects the hair.

From the same side of the hair-follicle, and lying between it and the muscle, so that it is compressed when the muscle contracts, is found a sacculated gland growing out of the follicle; this is the *sebaceous gland*. It secretes an oily substance which lubricates the hair and the skin surrounding the follicle. The secretion is produced by fatty degeneration of the cells of the gland itself, and is expressed by contraction of the arrector pili muscle. These glands vary much in size and in some cases far exceed that of the hair follicle; in this case they often open directly on the surface of the skin in common with the hair follicle. They are most developed on the face, back, chest and scrotum.

The other epithelial appendages are the *sweat glands*, which are found everywhere in the skin. They are tubular structures which pass down to the lowest part of the dermis or into the subcutaneous tissue and end in a coil,

the *sweat* or *coil gland*, the straight portion passing to the surface being the *sweat duct*. Both the duct and gland consist of a single layer of cubical cells which becomes continuous with the basal layer of the epidermis. The duct has no special epithelial lining through the epidermis. Involuntary muscular fibres, which expel the secretion of the gland and are under the control of special pilo-motor centres, are present among the coils of the glands. The secretion of the gland is a true secretion and is not produced by degeneration of its cells, as in the case of the sebaceous glands. Certain large sweat glands, called *apocrine glands*, occur in the axillæ, nipples and pubic region, which do, however, show breaking up of the cell protoplasm during activity.

The only other skin structures that require mention are the *nails*. These are simply modifications of the horny layer of the skin. The nail grows from that portion of the nail bed which is partly hidden by the nail fold and partly seen as the lunula of the nail, which forms a pale half-moon shaped area above that structure; this area is called the *matrix*.

PHYSIOLOGY AND PATHOLOGY.—The functions of the skin are four in number—(1) It forms a protective covering over the whole body; (2) it is an organ of secretion; (3) it is the seat of tactile sensation; and (4) it plays an important part in regulating the temperature of the body. The skin also allows of absorption, though this can scarcely be considered one of its primary functions. From the point of view of dermatology the two first functions are the most important.

The protective function is a double one: firstly the skin as a whole lying on a loose connective tissue pad, protects the deeper structures from damage by acting as a buffer; secondly, the resistant characters of the horny layer protect from irritants, not only the deeper structures, but also the layers of the skin lying beneath it, for the moist cells of the body unprotected by these dry keratinised cells would perish if exposed even to the ordinary atmosphere. Damage to the horny layer is responsible for a very large group of inflammations of the skin.

The horny layer, however, does not act quite alone: it is made more impermeable to simple external irritants by the presence of a thin layer of oil on its surface which is provided by the secretion of the sebaceous and sweat glands. As will be shown later, absence or deficiency of this oily secretion renders the skin much more susceptible to external irritants. On the other hand, excessive sweat secretion from the large amount of water it contains may make the horny layer sodden, and therefore more liable to damage. Similarly an excessive sebaceous secretion tends to make the horny layer thicker and is an excellent medium for the growth of organisms.

It must further be remembered that the horny layer does not form a complete sheet, but that innumerable invaginations which form the hair follicles and sweat ducts are present. These considerably weaken the protective power of the horny layer, and it will be found that at these spots inflammatory reactions, due to damage of this layer, are most likely to occur. It is also practically certain that absorption takes place at these follicular openings.

The secretions of the skin are the sweat and the sebum, the latter of which is the secretion of the sebaceous glands. The former is a watery fluid which contains traces of sodium chloride and other mineral salts, extractives, and a very small quantity of urea and fats. It varies very much in quantity, but

normally about equals the quantity of urine voided and, therefore, is responsible for the removal of nearly 50 per cent. of the total water excreted by the body. The main function of this excretion of water is to maintain the temperature balance of the body and, therefore, in hot weather the amount of sweat is increased in order to cope with more rapid evaporation and so keep the body surface cool, the quantity of urine being correspondingly diminished unless larger quantities of water are imbibed. In cold weather the reverse is the case.

A small amount of carbon-dioxide is also excreted by the skin, and the latter may therefore be said to be an accessory *organ of respiration.*

The sweat has special interest to the dermatologist not only from its lubricating effect on the horny layer, but also from the fact that certain drugs are sometimes excreted by it, and it is possible that some of the eruptions caused by the ingestion of these drugs may be produced by their irritating action during the process of excretion by the sweat.

The sebum is an oily secretion whose function appears to be entirely that of lubricating the hairs and surface of the skin : it not only helps to protect the skin from chemical irritants, but also from the actinic rays of the sun.

The other two functions of the skin, namely, the *tactile sense* and the *regulation of temperature*, will have been dealt with elsewhere, and as they affect the dermatologist but little, they will not be further considered here.

II. GENERAL DESCRIPTION OF SKIN DISEASES

The bulk of skin diseases fall into two great classes, inflammations and new-growths. There are in addition certain conditions which cannot be included under either of these headings, and will require special mention, namely, the disorders of secretion, of sensation, of the circulation, and of pigmentation ; atrophies of the skin and certain congenital abnormalities. It will also be necessary to describe the diseases of the hair separately. As so many of the inflammations depend upon disorders of secretion, sensation and circulation, it is proposed to deal with these first. Before proceeding, however, to deal with pathological conditions of the skin, it will be useful to define the terms used in describing clinical manifestations. It must be realised, however, that these terms are used very loosely, and are only a convenient form of nomenclature.

A *macule* is a spot which is not raised above the skin ; it may be vascular or pigmentary. The term is usually applied to small lesions up to the size of a pea, a larger lesion being called a " plaque " or " tâche." Large sheets of redness are generally called an " erythema."

A *papule* is a solid elevation usually not exceeding the size of a pea. If the surface is flat and smooth it is called a " plane " papule ; if pointed an " acuminate " papule.

A *tubercle* or *nodule* is an elevation usually between a pea and a hazel nut in size. The term nodule is also used for small solid swellings in the substance of the skin and subcutaneous tissue which do not necessarily project above the surface.

A *tumour* is a swelling exceeding a hazel nut in size. It need not

necessarily be solid, but this term is not usually applied to thin-walled superficial fluid swellings.

A *wheal* is a circumscribed elevation of the skin of a transitory character in which œdema is so marked as to force the blood out of the superficial capillaries and so produce a dead white elevation.

A *vesicle* is an elevation not larger than a pea containing clear fluid.

A *bulla* is a similar lesion of larger size; in other words, a *blister* or a *bleb*.

A *pustule* is a similar lesion to a vesicle, but contains pus instead of clear fluid.

A *scale* is a lamella of the horny layer of the skin.

A *crust* is a mass produced by the drying of exudates on the skin.

An *excoriation* is an abrasion of the superficial layers of the epidermis.

A *fissure* is a crack in the skin.

An *ulcer* is a circumscribed loss of tissue involving the whole thickness of the epidermis.

A. M. H. Gray.

III. CONDITIONS PREDISPOSING TO SKIN DISEASES

A.—DISORDERS OF SECRETION

Under this heading are included deficiency or absence of sweat and sebaceous secretion, and also excessive secretion.

ANIDROSIS OR DIMINUTION OF SWEAT SECRETION

This occurs in many diseases, but is seen in its most marked form in xeroderma and ichthyosis. It also is seen in hypo-thyroidism and in its more marked form myxœdema, in the degenerating skin of old people, and in poisoning by certain drugs, of which arsenic is one of the most frequent examples.

The milder cases of hypo-thyroidism show dryness of the skin, dryness, brittleness and thinning of the hair. They improve rapidly under the judicious administration of thyroid extract.

XERODERMA AND ICHTHYOSIS

These two names are applied to the mild and severe types of the same disease. The condition is one of abnormal dryness of the skin owing to the almost complete absence of sweat secretion accompanied by an overgrowth of the horny layer of the epidermis (hyperkeratosis).

Ætiology and Pathology.—The disease is inherited and often occurs in several members of the same family. It attacks both sexes equally. The disease is usually noticed about the second year of life, but some children are born with a condition closely resembling it (*ichthyosis congenita*): these children are frequently premature and generally stillborn. There is no very

definite evidence as to whether the changes in the epidermis follow the absence of secretions, or vice versa, or whether both are dependent on a common cause; possibly the overgrowth of the horny layer is an attempt on the part of Nature to compensate for the protection usually supplied by the only secretions. Histological examination shows very marked increase in the thickness of the horny layer, which is irregular and grows directly from the mucous layer, the granular layer being absent. The sweat glands are apparently normal histologically, although they do not function normally.

Symptoms.—In the milder cases (*xeroderma*) the skin is dry and rough, and there may be a certain amount of branny scaling on the surface. On the extensor aspect of the limbs the hair follicles are prominent and contain small horny spines. The palms and soles are more lined than normal, while the flexures of the body show little change. The hair is dry and lustreless, and occasionally stunted and brittle, while in a few cases only down grows on the scalp.

In the more marked cases (*ichthyosis*) the body is covered with large fish-like scales which are firmly adherent. They may be thin, transparent and colourless, or thick and dark in colour (the so-called alligator skin). In these cases the trunk and extensor aspect of the limbs are most involved, the face and scalp often showing little change, though the changes mentioned above may be present. This dry skin is particularly liable to become inflamed on account of alteration in its protective mechanism.

There is another form in which the disease develops in localised sheets, lines or bands (*ichthyosis hystrix*), but this condition is closely related to the linear nævi and will be dealt with under that heading.

Prognosis.—The disease persists throughout life, and although it can be relieved by appropriate treatment it never really gets well.

Diagnosis.—The dryness of the skin, the origin of the disease in early life, and its persistence, and the presence of fine or coarse scaling with the absence of inflammation render the diagnosis easy.

Treatment.—This consists in an attempt to replace the natural oil of the skin. Frequent warm baths, followed by the application of some oily preparation, are usually sufficient. One of the most useful preparations is glycerin. amyli, adip. lanæ hydros. āā ptes. æq., to which may be added 2 per cent. or 3 per cent. of salicylic acid if desired. Too vigorous use of soap is to be discouraged.

Some authorities recommend thyroid internally, on the grounds that the condition is due to deficient thyroid activity, but the results obtained have been scarcely sufficient to confirm this view.

HYPERIDROSIS

Definition.—This is a condition of over-activity of the sweat glands. It may be general or local.

Ætiology and Pathology.—Sweating in febrile illnesses is not included under this heading. The generalised forms are usually seen in adults, while the localised varieties are not infrequently seen in younger people. They are both probably due to disturbances of the nervous system, though it is difficult to say that they always occur in neurotic individuals. There is

no doubt, however, that hyperidrosis is very liable to produce a neurotic condition.

Symptoms.—*Generalised hyperidrosis.*—In this condition the patient sweats excessively, often on the least exertion or excitement. The sweating may be so severe that the patient has to change his clothes several times a day—even in cool weather.

Localised hyperidrosis.—There are certain regions of the body particularly liable to excessive sweating, namely, the palms and soles, the axillæ, and the genital region and perineum. The sweating is often very excessive, and may last for a very long time; there is, however, a tendency for the condition to diminish with age, it being most marked in the latter half of the second and the third decades of life.

The sweat allows certain saprophytic organisms to grow freely, with the result that decomposition takes place, and an extremely offensive odour develops. This is chiefly noticed in the feet, and is spoken of as *bromidrosis*. Occasionally the sweat is coloured (*chromidrosis*), due to bacterial activity.

The skin constantly soaked in sweat is subject to attacks by irritants, bacterial and otherwise, and various forms of dermatitis are frequent complications of hyperidrosis, especially the forms spoken of as *miliaria rubra* and *dysidrosis* (see p. 1414).

Prognosis.—Localised cases will generally respond to treatment; but the more severe generalised cases are apt to be very persistent.

Treatment.—For the *generalised cases* frequent warm baths are required. to keep the skin clean. Dabbing on a solution of tannic acid (1 per cent.) in 50 per cent. alcohol, or a dusting powder of talc containing 3 per cent. salicylic acid, is often useful. The general health should be looked to, and all dietetic errors and habits liable to cause sweating rectified. Some cases benefit by the internal administration of bromides and belladonna.

The *localised cases*, when extreme, are best dealt with by X-rays. Ten or twelve doses, each of 120 r ($\frac{1}{3}$ skin unit), given in groups of four doses at weekly intervals, with intervals of one or two months between the groups, usually give a satisfactory result. Bromidrosis of the feet is best dealt with by frequent washing and change of socks, by bathing in 1 in 4000 potassium permanganate solution, or by washing with lysoform, or other formalin soap. The feet should then be freely dusted with the powder mentioned above.

SEBORRHŒA

Definition.—By the term seborrhœa is meant an over-activity of the sebaceous glands, resulting in an abnormally greasy skin.

Ætiology.—This condition occurs from the time of puberty onwards, gradually diminishing as age increases. It tends to affect certain races and families, but is also influenced by the habits of individuals. Gastric disturbance, constipation, anæmia, uterine trouble and the like all tend to exaggerate the condition.

Pathology.—The condition appears to be due to some disturbance of metabolism not yet fully determined. Some authorities consider that infection by certain organisms play a part, but the evidence is inconclusive.

Symptoms.—The regions affected are the face—especially the nose, naso-labial folds—the scalp, chest and back. In the milder cases the skin is greasy; in the more severe cases it is thickened—giving rise to a muddy appearance—and the follicles are patulous. This condition Darier has labelled "la kerose." In other cases the sebaceous follicles are plugged with semi-solid sebaceous material.

Complications.—Seborrhœa is the underlying cause of many skin affections. Acne vulgaris is merely a more marked stage of the follicular plugging noted above. Infection by certain organisms producing seborrhœic dermatitis is very common, while the skin is especially liable to ordinary eczema and impetigo contagiosa. Acne rosacea is particularly liable to occur in seborrhœic individuals.

Treatment.—The general health must receive attention. Diet should be regulated to get rid of dyspepsia and constipation; especially should excess of sugars and starches be avoided. Iron and arsenic are indicated in anæmia, and uterine troubles should be appropriately treated.

Frequent washing with soap and water is necessary. Sulphur has a marked effect in diminishing the secretion and especially in preventing organisms from growing in it; it may be used as a powder—sulphur. precip. 5 parts, pulv. talc to 100 parts; or as a lotion, potass. sulphurat. min. 60; sp. vin. rect. fl. oz. 2, aquam ad fl. oz. 8.

B.—DISORDERS OF SENSATION

The disorders of sensation comprise hyperæsthesia, anæsthesia and paræsthesia.

Hyperæsthesia is generally symptomatic of some organic or functional disease of the nervous system, and has little or no importance in dermatology.

Anæsthesia also is usually symptomatic but one form occasionally comes under the notice of the dermatologist first, namely, that associated with syringomyelia. The individuals affected show anæsthesia with trophic changes in the skin of the fingers, often with whitlows and other signs of skin sepsis. Further investigation shows the lesions to be only part of a more general disease of the nervous system. This type is spoken of as Morvan's disease, and is dealt with elsewhere (p. 1731). Localised areas of anæsthesia, with redness, are frequently an early sign of leprosy (see p. 122).

Paræsthesia forms the most important group from the dermatological point of view, as it includes itching or pruritus.

PRURITUS

Under this heading are included those cases of itching of the skin in which there is no other obvious dermatosis. It may be general or local.

Generalised Pruritus

Ætiology and Pathology.—The causes of general pruritus, apart from that due to animal parasites, may roughly be classified as follows:

1. The presence of toxic substances circulating in the blood. For instance, in diabetes and jaundice from the presence of sugar and bile-salts in the blood. Similarly certain ingested drugs, such as opium, will cause it. It also occurs in gout and nephritis.
2. As a symptom of some blood diseases, such as leukæmia and lymph-adenoma.
3. In atrophy of the skin in old people, the so-called senile atrophy.
4. In a large group of cases in which no cause can be found, and which are considered of functional origin.

Symptoms.—In the majority of cases itching is the only or main symptom, but others, such as tingling and burning, may be present. It may vary very much in intensity, and may be intermittent. Some people suffer most in hot weather; but it is more frequent on exposure to cold. Hot baths sometimes being on attacks. In the more severe types the condition is most distressing, the patient rarely has any peace, but is constantly scratching, it keeps him awake at night, and as a consequence his general health suffers and he becomes a nervous wreck. In spite of this, it is extraordinary how little sign there is of scratching on the skin; some cases show a certain number of linear excoriations, but the scratch lesions are rarely as marked as they are in the localised forms and in parasitic affections. Sepsis of the skin is rarely seen.

Diagnosis.—It is essential to try and find the cause. Parasitic infection should be excluded in the first place, and then internal ailments, including the blood diseases. The presence of marked scratch lesions, especially with sepsis, suggests a parasitic origin; the special distribution of parasitic lesions will be considered under their appropriate headings (p. 1441 *et seq.*).

Treatment.—In the cases in which no definite cause can be assigned it is necessary to attend to the general hygiene of the patient. Diet requires careful regulation; alcohol, strong tea and coffee should be forbidden, as should all substances likely to produce urticaria, *e.g.* shell-fish, strawberries, etc.; hot and highly seasoned dishes and excess of nitrogenous food are better avoided. Any disturbance of digestion, especially constipation, should be treated. In bad cases sedative drugs may be required, of which bromides, belladonna, cannabis indica and valerian are the most useful. Injections of pilocarpine are recommended in dry skins. In cases of sleeplessness, hypnotics may be required. Opium should be avoided, as, apart from other reasons, it may increase the itching.

Local treatment depends on the conditions which excite the pruritus: for instance, in some cases baths are advantageous, while in others they increase the itching. If the skin is dry, as in senile pruritus or when associated with xeroderma, oily preparations are beneficial: glycerin of starch and lanolin in equal parts, or cocoa-nut oil with a little soft paraffin, are useful preparations, especially if 1 or 2 per cent. menthol or phenol is added. Liq. picis carbonis and liq. plumb. subacet. fort. aa min. 120, and milk to fl. oz. 8 is often satisfactory. Most cases, however, get most relief from alkaline

baths and lotions: for the latter lotio alkalina (sodium bicarbonate and borax, 1 per cent. of each in distilled water) answers well.

It is very important to see that the patient changes his undervest at night. Many patients do not do so, and this undoubtedly predisposes to pediculosis. Even, however, in cases where no pediculosis appears to be present, cases are often cured by attention to this detail.

Localised Pruritus

Certain parts of the body are liable to pruritus; these are the anus, vulva, and scrotum. Other local areas, however, may be attacked, such as the front of the ankle, lower part of the leg, thighs, back of neck and scalp.

Ætiology and Pathology.—Most of these localised cases probably start from some transitory cause, which gets better; but a vicious circle has been started, the scratching bringing on itching, and this causes scratching again. In the case of the anus, piles are a frequent cause. Some cases are, as Castellani has shown, due to fungus infection. Vaginal discharge frequently starts a vulval pruritus, as do sugar and other irritating substances in the urine. Sweating and friction of clothes, and possibly some parasitic condition, such as dhobie itch, may start a scrotal pruritus.

For the other cases it is generally difficult to find a cause, and it is usually necessary to treat symptoms.

Symptoms.—The localised itching is often followed by marked changes in the skin from rubbing and scratching. The usual change noted is that called *lichenification*, in which the skin becomes thick and rigid, the lines of the skin deeper, and the area assumes a dull purplish colour, and on clearing up often leaves deep brown pigmentation. This is well seen in the patches in the flexures and on the limbs, but is modified in the moist parts, where it usually takes on a white sodden and swollen appearance, surrounded by a bright red inflammatory zone. The surface is often covered by numerous excoriations or blood-stained crusts. Occasionally these excoriations may become septic, and ulceration may occur. The symptoms are often so severe as to affect the patient's health by sleeplessness and worry.

Treatment.—The treatment recommended for generalised pruritus is often indicated in the localised cases, such as that directed towards obtaining sleep.

The first thing to do is to remove any local cause; *e.g.* vaginal discharges may require treatment. The bowels should be made to act freely by paraffin, saline aperients or enemata; aloes is better avoided. Irritating food, especially coffee, alcohol, curries, etc., should be interdicted. Piles may require surgical treatment, and any rectal discharge, fistual or worms should be dealt with. All the parts should be carefully washed, mild alkaline lotions or weak antiseptics being useful, and afterwards dried thoroughly and a talc or zinc oxide powder applied. Further relief may be obtained by the application of 1 per cent. phenol and camphor cream, or 5 per cent. oleinatum cocainæ (B.P.C. 1923). If these milder measures fail, the parts may be painted with silver nitrate, grs. 10, ap. æther. nit. fl. oz. 1, twice or three times a week, and a bland cream or mild alkaline lotion applied. In cases due to fungus infection, Castellani's fuchsin paint (see p. 1438) usually proves efficacious.

The most radical results, however, are obtained by X-rays. Three or four doses of 120 r ($\frac{1}{2}$ skin unit) given at weekly intervals to the affected area will nearly always remove the itching completely, and the secondary changes in the skin will disappear. For localised body pruritus, excellent results are obtained by painting the affected parts with crude coal tar, which is allowed to dry, and a talc powder applied. This method should not be used if sepsis is present. Further, much relief is often given by exposures to the ultra-violet rays of the mercury-vapour lamp.

C.—DISORDERS OF CIRCULATION

Only certain circulatory disorders have any bearing on skin diseases, if we do not include those disturbances associated with inflammation. Those which are referred to below usually come to the dermatologist on account of secondary changes produced in the skin.

ACROCYANOSIS

Synonym.—Chilblain Circulation.

This is a condition most frequently met with in young women, though by no means confined to them, characterised by persistent blueness of the extremities, including the hands and feet, the nose and the ears. It includes the condition known as erythrocyanosis crurum puellarium frigida, which is fully described on p. 1079.

CHRONIC VASCULAR STASIS OF THE LOWER LIMBS

This condition occurs in almost all individuals approaching middle life, and progresses with age. In individuals suffering from varicose veins it commences earlier. As a rule no special symptoms are produced, but if the skin of the lower part of the leg is damaged—and it is particularly prone to injury—it does not heal well, and there is a great tendency for a dermatitis to be set up. In some cases, however, the venous congestion causes itching, and if the skin in this region is scratched a moist dermatitis is liable to arise, which becomes septic, and healing does not readily occur. In these ways we have the well-known "eczema of the leg" produced. These cases frequently go on to ulceration, and the familiar chronic *varicose ulcer* of the leg is the result.

ROSACEA (ACNE ROSACEA)

Definition.—This is a chronic vascular congestion of the nose and central part of the face, resulting from dyspepsia and other internal conditions, and followed by secondary inflammatory changes in the skin.

Ætiology and Pathology.—The disease is common in both sexes, but rather more so in women. It begins usually after 30, but is occasionally

seen before that age. It is generally associated with dyspepsia, usually of the flatulent type, though in many cases there is no very obvious gastric disorder. Cases have been recorded in which complete achylia gastrica was present, or in which there was considerable diminution in the hydrochloric acid in the gastric juice. Uterine disturbance and the menopause are responsible for some cases. Alcohol and strong tea drinking are potent causes.

The mechanism of this vascular dilatation is not quite clear. It is generally assumed that some toxic substance is absorbed, and acts on the vasomotor system; but it is more probably a neurosis. The follicular lesions are the result of the congestion and of the increased sebaceous secretion which the hyperæmia causes, as well as of increased activity of the skin cocci.

Symptoms.—The early symptoms are either those of transitory flushing of the face, or the nose gradually becomes red. Examination shows the presence of dilated vessels on the alæ of the nose. Later the congestion becomes more marked and not only affects the nose but the adjoining parts of the cheeks, the chin and the centre of the forehead. The redness may be persistent or remittent; it is worse after meals. There is usually an increase in sebaceous secretion so that the skin becomes abnormally greasy. Scattered red papules now appear at the follicular openings, and often a bead of pus is seen in them, but no sebaceous plug or comedo. This is the typical "acne" rosacea. If the skin is very dry, this papular rash may be absent; but the whole affected area may become dry and scaly, especially if exposed to the weather, showing that the congestion renders the skin more susceptible to mild external irritants. In other cases, these inflammatory conditions are absent; but the vessels become very dilated, and much disfigurement results. In the most severe cases there occurs an overgrowth of skin and subcutaneous tissue which converts the nose into a lobulated tumour—*rhinophyma*. A number of cases show a persistent type of conjunctivitis, sometimes associated with a keratitis and corneal ulceration. The severity of the eye symptoms does not, however, appear to correspond with that of the skin lesions.

The patients complain of few symptoms except dyspepsia and flushing of the face; but the unsightliness of the condition brings them for relief.

Diagnosis.—The "acne" variety must be distinguished from acne vulgaris, by the limitation of the lesions on the centre of the face, by the underlying congestion and vascular dilatation, and by the absence of the comedo. The age is also a help, as acne vulgaris is commonest between 15 to 30. It must be remembered that sometimes the two conditions occur together. In dry "eczemas" of the face, the possibility of an underlying rosacea should not be overlooked.

Treatment.—The cause must first be dealt with. A fractional test meal will give useful information as to digestive function. Easily digested food, with a minimum of carbohydrates and green vegetables, should be ordered, little or no fluid should be taken with meals, and alcohol and strong infusions forbidden. Sod. bicarb. grs. 15 to 20 with a bitter three times a day after food is of great help. Dilute hydrochloric acid, min. 20 thrice daily, may be given in achlorhydric cases. The non-dyspeptic cases often do

well on bromides and belladonna. Ichthammol grs. 3 to 5 (in capsules), or menthol, gr. 1, t.d.s., is often useful. The bowels should be regulated.

Local treatment should be sedative in the main. In the acneiform cases, calamine lotion with liquor calcis sulphuratæ (1 in 8) applied two or three times a day should suffice. In the dryer forms, ung. aquosum (B.P.) should be applied night and morning. When the veins are much dilated and unpleasantly prominent they may be destroyed by electrolysis or a fine pointed cautery. In the cases with much hypertrophy it may be advisable to remove some of the overgrown tissue with a knife. This can be done without leaving much scarring.

Of the other disorders of circulation which occasionally come under the notice of the dermatologist may be mentioned *Raynaud's disease* and *erythromelalgia*; but these are dealt with in other sections of this work (see pp. 1075, 1078).

A. M. H. GRAY.

IV. INFLAMMATIONS OF THE SKIN

Having dealt with some of those disorders which predispose to inflammatory changes, it is now possible to consider the Inflammatory Diseases of the Skin. These may be divided roughly into two great classes: (1) The superficial inflammatory dermatoses, due mainly to irritants applied externally; and (2) the deep inflammatory dermatoses, due mainly to toxic substances circulating in the blood. This division is not quite so definite as one might suppose, but it is a good basis on which to work. There are, however, a certain number of inflammatory dermatoses which cannot easily be placed in either group; these will have to be considered separately.

A.—THE SUPERFICIAL INFLAMMATORY DERMATOSES

These are produced as a rule by the application of external irritants to the skin, but there are a certain number of cases in which the external irritant cannot be traced, and in which the general symptoms suggest an internal toxin. External irritants may also cause deep-seated inflammatory dermatoses, but only when they are introduced through the epidermis; thus, the puncture of the hairs of the nettle may produce an urticaria, the infection of a crack an erysipelas, a syphilitic chancre or a patch of lupus vulgaris. Nevertheless, the general rule is that a superficially applied irritant produces a superficial dermatosis.

External irritants may be classified into the following groups: (*a*) chemical; (*b*) heat and cold; (*c*) actinic; (*d*) bacterial; and (*e*) mechanical. This order is chosen because the clinical types can best be explained in this way. The reaction of the skin to these different irritants is generally of the catarrhal type, which is known as "eczema." This term has, therefore, been

used freely to label lesions, but, as will be explained later, is used more rigidly in describing cases.

Ætiology and Pathology.—Chemical irritants applied to the skin may cause immediate, or primary, local necrosis, but only those reactions of the skin to irritants which do not cause local death of the tissues are dealt with in this section. Secondary local necrosis does, however, sometimes result from such reactions, as in the case of chronic leg ulcer following a varicose "eczema."

Chemical irritants applied to the skin produce different forms of reaction according to the intensity of the irritant. The reactions also vary considerably in degree according to the sensitiveness or susceptibility of the subject to varying irritants.

Recently a great deal of attention has been directed to the subject of "sensitiveness," or "allergy," of the skin. It is recognised that sensitivity may be congenital or acquired, and also that it may be specific for certain substances, or more or less general. For instance, certain individuals are congenitally sensitive to the "primula obconica," or Chinese primrose, and whenever they come in contact with this plant a dermatitis will result. On the other hand, persons who are not sensitive to this plant can be made so by rubbing the leaf into scarifications made in the skin, or by injecting into the skin, in appropriate doses, the active principle which has been isolated by Bloch. These are examples of congenital and acquired specific sensitiveness respectively.

General sensitiveness is less well defined, but again may be congenital or acquired. In this connection, congenital peculiarities of the skin, such as xeroderma, have to be considered.

If an intense irritant, such as a mustard plaster, is applied to the skin, the whole area to which it is applied becomes intensely red, owing to congestion of the papillary vessels; the epidermis becomes œdematous, and if the action is prolonged, small vesicles or even large bullæ develop under the horny layer. Lesions of this type are spoken of as *erythematous eczema.*

If a milder irritant is applied it may only attack the follicles, which are the most vulnerable part of the protective mechanism of the skin. In this case small follicular papules are produced, which in the more acute cases are surmounted by a small vesicle. These papules tend to group together on an erythematous base forming circumscribed patches. These are the *papular* and *vesiculo-papular eczemas.* With some irritants—croton oil, for example—follicular pustulation may also occur. The pus in this case is sterile, and the lesions dry up when the irritant is removed. This constitutes *pustular eczema.*

Lastly, there is a type in which the primary lesion appears to be produced by cracking of the horny layer. It is seen, for instance, on the face in children who dribble, and on the hands of those who use soap and water to excess. Under these conditions the horny layer becomes sodden with water, and this takes place more readily if alkalis, such as soap, are present. Then the skin dries quickly, especially when exposed to the wind, hot sun or a fire, and the horny cells tend to separate from one another, exposing the delicate mucous layer. In this type scaling first appears, followed rapidly by erythema. This is one form of *squamous* or *erythemato-squamous eczema.*

All these primary reactions are liable to undergo secondary changes.

Thus, fluid may exude from the surface from rupture of the vesicles and bullæ, producing a weeping eruption (*eczema rubrum*). Or, in the drier types, scaling may occur from irregular formation of the horny layer (this is the secondary type of *squamous eczema*). The moist cases may become infected with pus organisms, and the exudate may dry in the form of crusts (*eczema crustosum*). Thickening of the horny layer may occur, especially when the palms and soles are attacked, and this leads to cracking in the deeper folds of the skin (*eczema rimosum*). Occasionally in the lower extremities lymphatic obstruction and an overgrowth of the epidermis is produced (*eczema verrucosum*), or even elephantiasis may occur.

In order to classify these eczematous lesions a little more usefully it is advisable not to speak of a superficial inflammation produced by a known external irritant as an "eczema," but to call it a "dermatitis," qualified by the name of the irritant which causes it, as, for example, "formalin dermatitis." To use the word dermatitis without qualification is not so informing as to use the word "eczema."

For a large group of cases in which the external irritant cannot be traced, or in which it is one of those mild irritants to which every one is exposed, such as the air, or the friction of clothes, and also for certain cases in which the lesions are disseminated over the body, the term "eczema" is still used for want of further ætiological knowledge.

DERMATITIS FROM CHEMICAL IRRITANTS

These irritants are so numerous that it is impossible in a work such as this to attempt to give a complete description of them. They may, however, roughly be divided into the following classes: (1) Due to animal poisons; (2) due to plants; (3) due to chemical agents used in medicine; (4) due to chemical agents used in trades; and (5) due to decomposition of body secretions.

1. Superficial dermatitis due to ANIMAL POISONS is rare, most of the reactions being of the deep type, as they are injected by the stings and bites of insects. Some forms of caterpillar, *e.g.* the woolly-bear, however, occasionally produce an eczematous reaction.

2. PLANTS are probably responsible for more cases than are diagnosed. The *Rhus toxicodendron* or poison ivy produces the most marked symptoms, but this plant is rarely found in this country. The symptoms are an acute erythematous dermatitis, usually with much bullous formation, attacking chiefly the exposed parts, face and hands, but also affecting the moist parts of the body, the genitals, axillæ and flexures. Japanese lacquer, which is made from one of the *Rhus* family, may also give rise to a dermatitis in susceptible individuals. The commonest plant in this country to produce a dermatitis is the *Primula obconica*, but other species of the primula may attack susceptible individuals. The lesions are similar to those mentioned above, but much less severe. Among other plants which may produce a dermatitis are *Daphne mezereon*, oleander, rue, parsnip, daffodil, and chrysanthemum, while handling certain woods, such as teak, satin-wood and ebony, may produce similar effects. In all doubtful cases of "eczema" it is well to look for the presence of one of these irritating plants.

3. Of the CHEMICAL AGENTS USED IN MEDICINE some, such as cantharides, mustard, croton oil, chrysarobin and iodine, are used to produce varying degrees of dermatitis. Others may produce it unintentionally, among these being boric acid, iodoform, sulphur, carbolic acid and perchloride of mercury. Formalin, much used in pathological laboratories, produces a damaging effect on the horny layer, followed by a squamous and fissuring dermatitis. Sulphur, used in the treatment of scabies, is a common cause of an erythemato-squamous dermatitis on the flexor aspects of the limbs, on the abdomen and back, and is associated with intense irritation. Further, surgeons, students and nurses are apt to develop a dermatitis of the hands from the use of various antiseptics.

4. TRADE DERMATITIS.—This is very common, and the lesions produced are often specific. They are very numerous, for a description of the majority of which special works should be consulted. Among the more common are the soap and water dermatitis seen in washerwomen and in those engaged in household duties. This may take the form of a dry fissuring dermatitis on the back of the hands and forearms, or a papulo-vesicular dermatitis in the same situation. Its etiology has already been discussed. Grocers and bakers are subject to a vesicular dermatitis of the hands, from handling sugar and dough: the so-called grocer's and baker's itch. French polishers, photographers, leather workers, etc., are frequently subject to dermatitis from articles used in their trades. These affections are usually of the papulo-vesicular type.

An acute erythematous dermatitus affecting the exposed parts of the body has been seen in those engaged in making explosives, also a more acute form caused by "mustard gas." The lesions in this case closely resemble those produced by poison ivy, the same distribution being observed.

Tar and oil acne.—Tar and various oils commonly give rise to a folliculitis, with a central keratotic plug like a comedo, associated with perifollicular inflammatory papules and pustules, and found on those parts of the body which come into contact with the irritants.

Grouped comedones.—In infants who have been rubbed with camphorated oil an eruption often occurs about the chest, neck and chin. The lesions are small black follicular plugs, closely placed, and are often associated with troublesome inflammatory complications.

Hair dyes.—An acute dermatitis of the face, particularly affecting the eyelids, is seen in persons who use certain hair dyes, especially those containing *para*phenylenediamine.

Fur dyes.—Certain cheap furs, chiefly rabbit skin dyed with some of the phenylenediamine group of dyes, are responsible for a dermatitis involving the neck and chin. There is often a considerable latent period between the first wearing of the fur and the appearance of the eruption.

5. INTERTRIGO.—Decomposition of sweat and other body discharges may set up a dermatitis, usually of the erythematous type. This is best seen in fat women who are not too cleanly in their habits, the lesions being found under the breasts, in the folds of the abdomen and groins, and on the genitalia. A similar condition is often seen about the napkin region of infants. An erythema first appears, the horny layer of the skin, becomes sodden and is removed by friction of the parts, and a raw oozing surface results.

Jacquet's erythema infantum.—In some children an eruption consisting of pea-sized papules occurs about the prominences of the buttocks, thighs and abdomen under the napkin; the depths of the folds escape. Occasionally these lesions spread beyond the napkin area and frequently they are capped by a vesicle or crust. These cases appear to be due to ammoniacal urine and must be carefully distinguished from congenital syphilis. The condition is spoken of as "infantile erythema of Jacquet."

DERMATITIS FROM HEAT AND COLD

The erythema, followed often by blistering, as a result of a burn or scald, is well known. Similar but usually milder and more transient erythema may follow exposure to cold. The application of carbon-dioxide snow to the skin for purposes of treatment is a good example of the effects of extreme cold.

Erythema ab Igne.—Frequent exposure to the fire produces a curious recticular erythema, followed by pigmentation.

Erythema Pernio (Chilblains).—Chilblains are frequently seen after exposure to cold. They occur chiefly in children and old people, and particularly in those whose peripheral circulation is sluggish. The lesions are salmon-pink to purplish, varying in colour, which occur chiefly on the fingers, toes and the lower part of the legs, and which itch intensely. The lesions may ulcerate and produce extremely indolent sores. When the helices of the ears are attacked, as they sometimes are in old people, considerable loss of tissue may result. The treatment for this condition is the same as for "Acrocyanosis" (see p. 1079).

Trench Foot.—A somewhat analogous condition was met with in the trenches in France during the War of 1914–1918, in men who had to stand for long periods in the wet and cold. The feet became swollen and painful, the skin was reddened and blistering, and even necrosis occurred. The condition took a long time to subside.

DERMATITIS FROM ACTINIC RAYS

Erythema Solare.—Light, whether from the direct rays of the sun or from artificial sources, produces marked inflammatory changes in the skin. The sun's rays produce first a transient erythema which subsides, leaving pigmentation; but in other cases a more persistent erythematous dermatitis occurs, associated with œdema and thickening of the skin and scaling or blistering: this is the so-called "erythema solare."

Tropical Skin.—Exposure to tropical sun for many years may lead to atrophy of the skin with pigmentation and warty formation.

Prurigo Œstivale.—A rather rare condition occurs in some children in which it appears that the sun's rays are an exciting cause. It consists of the appearance on the face and hands of small very itchy papules which appear during the summer and disappear in the winter. They are not always limited to exposed areas, but these regions are always the most severely attacked. The condition is a very peristent one, and any treatment, except protection from the sun's rays, has little or no effect.

HYDROA ŒSTIVALE.—This is a much rarer condition than the preceding one and occurs in persons suffering from hæmatoporphyria congenita, though not in these cases only. The lesions are blisters, which appear on the parts exposed to the sun's rays, and scars are left when the blisters disappear.

X-RAY AND RADIUM DERMATITIS.—X-rays produce much more persistent forms of dermatitis than the sun's rays. If a slight overdose of X-rays is given, an erythema develops in the course of 1 to 3 weeks, which then gradually subsides. If a larger dose is given, the erythema may come on earlier and blistering may occur, which takes weeks to get well. Finally, in the still more intense burns, necrosis of the skin, with the formation of an extremely indolent ulcer, develops. In other cases, atrophy of the skin, with telangiectases and pigmentation, occurs, which may, after many years, break down into an indolent and painful ulcer, and this may in turn become epitheliomatous.

Radium may produce a similar series of changes.

ECZEMA

A description of the more specialised superficial dermatosis produced by mechanical and bacterial irritants will be left until those eruptions for which we reserve the term "eczema" have been discussed. The diagnosis and treatment of the dermatoses dealt with in the preceding paragraphs, together with that of eczema, will be considered at the end of this section. The reason for this is because it is probable that the lesions of eczema are produced, in part at least, by chemical, thermal and actinic irritants, and that pathogenic bacteria do not play an active part. Mechanical irritants do play a secondary rôle, and irritating chemical substances produced by saprophytic organisms are also concerned, but the latter are really chemical and not bacterial irritants.

Under the term "eczema" are included—(1) Certain cases of dermatitis, probably due to chemical irritants, the identity or nature of which has not been discovered. (2) Cases in which individuals are so susceptible to irritants that they react to mild stimuli that would not ordinarily be classed as irritants, such as a slight exposure to the sun, a cold wind, the warmth of a fire, or even to the friction of the clothes. (3) Cases which, having commenced with a simple dermatitis caused by an irritant, fail to get well on its removal and the patient becomes hypersensitive, to that fresh patches are produced, either in the neighbourhood of the original lesion or in other parts of the body. In fact, another factor is present which is spoken of as "sensitiveness."

Ætiology.—Many views are held as to the causes of this "sensitiveness." First there is the possibility of an inherited susceptibility or diathesis. This may be nothing more than some congenital peculiarity of the skin of which a recognisable form is xeroderma, already discussed. Abnormalities of secretion and of circulation alter the resisting power of the skin. So, probably, do certain toxic states, such as gout and rheumatism; deficient elimination, as occurring in nephritis; chronic infections, as in pyorrhœa and tonsillar sepsis; digestive disturbances and alcoholism. Disturbances of the nervous system, such as teething in infants, uterine troubles and the neuroses, may play a part.

More important, however, is the possible absorption of toxins from a local focus of dermatitis producing a hypersensitiveness or "allergic" condition, so that a violent local reaction occurs in the skin if the secretions from the original focus are brought in contact with other areas.

Pathology.—In eczema and superficial dermatitis the anatomical changes are most marked in the epidermis and papillary layers. There is congestion of the papillary vessels, with overgrowth (acanthosis) and œdema (spongiosis) of the mucous layer, and wandering cells may be present throughout the epidermis. Ballooning of the cell of the mucous layer occurs and minute vesicles appear. The horny layer is improperly formed, the cells retaining their protoplasm and nuclei, with the result that they shrink up on reaching the surface, from evaporation of water in the protoplasm, and so scaling is produced. This pathological condition is called *parakeratosis*.

Symptoms.—The general type of lesion found in eczema has already been described (p. 1397). It now remains to describe some of the common types of case met with, and this is conveniently done by referring to the regions of the body affected.

Face and Scalp.—Eczema of the face of a very definite type is frequently met with in infants. It usually occurs in the first year of life, and is more frequently met with in the winter months. It begins with a red irritable spot on one or both cheeks, and spreads fairly rapidly, so as to involve the whole face and often the scalp. In the more severe cases lesions are found on other parts of the body. The initial lesion is a red swollen patch or a group of follicular papules which later develop into an eczema of a scaly or weeping type. Itching is always intense but paroxysmal, the child rubbing the parts violently with the hands or against the pillow. In the moist variety septic infection may occur and thick yellow-green crusts form on the surface. Infantile eczema is often very resistant to treatment and may last from six months to a year, even under careful treatment; it usually dies out, however, during the second year of life.

This type of eczema occurs about three times as frequently in males as in females, and is often followed later in childhood by a condition frequently known as "flexural eczema," which is dealt with below.

Another type, also seen in infants, commences on the scalp, usually as a scaly or crusted patch, which becomes eczematised, usually as a result of scratching, and tends to spread down to the forehead and face.

In slightly older children a generalised eczematous condition of similar distribution, but of a septic type, is seen in association with nasal and aural discharge. Small follicular pustules are often present, and blepharitis is common. This is really an eczematised impetigo—that is, a direct bacterial infection, and not of the same nature as the first named, which is non-bacterial in origin.

Another common form of eczema met with on the face in children consists of sharply circumscribed scaly patches, always dry and with a surface like crêpe. These patches occur in the region of the mouth and nose, and can generally be traced to dribbling, running at the nose, the habit of licking the lip or smearing the face with a wet finger, or to the use of strong soaps. Some cases, however, are of streptococcal origin (p. 1423). The condition is produced by rapid drying of a sodden horny layer as described above, and goes by the name of "pityriasis simplex."

In adult life, especially in oldish people, an acute erythematous eczema of the face is apt to develop. It usually appears quite suddenly. The whole face becomes acutely red and swollen; the œdema of the eyelids often being so great as completely to close the eyes. In severe cases blistering may occur; but usually the acute œdema subsides and scaling ensues. This stage may either clear up completely or a chronic eczema characterised by redness, thickening of the skin, and scaling may follow. These acute cases are often associated with a similar condition of the hands and forearms, in fact the parts exposed to the air are most likely to be affected, and this condition is particularly prone to occur in cold weather. In some cases also a history can be obtained of a coexisting septic dermatitis elsewhere, frequently on the leg, and in these cases it is possible that some absorption from this has rendered the patient susceptible. Once a patient has had an attack he is always liable to recurrences, and great care must be taken to avoid exposure to extremes of temperature. Cases of this type may be limited to the eyelids, and a troublesome and chronic condition develops.

Occasionally the papulo-vesicular type of eczema is met with on the face; it is not infrequent on the forehead, generally in men under the hat-band, and often occurs in those who perspire freely.

Eczema of the scalp is usually of bacterial origin. This also applies to the ears (see Seborrhœic Dermatitis p. 1427).

"Flexural Eczema."—This is a well-recognised condition, which occurs usually in children, but may continue into adult life, and occasionally commences after puberty. It is a very specialised condition, and has been variously named "Besnier's prurigo," or "flexural prurigo." It frequently follows facial eczema in infants, and is also frequently associated with asthma. These three conditions form a syndrome and are manifestations of an underlying congenital condition named by Czerny the "exudative diathesis." The lesions are those produced by friction, and vary from moist eczematous patches to patches of chronic lichenification. The areas affected are chiefly the flexures of the elbows and knees, less frequently the backs and fronts of the wrists, the back of the hands, the sides of the neck and the face. Other parts of the body may be affected, and an extensive eruption is sometimes present. The condition is essentially a curious form of pruritus, the cause of which is not yet established. Experiments made with a view to demonstrating protein sensitiveness are still inconclusive. In the majority of cases the condition tends to die out before puberty.

Upper Limbs.—The hands and forearms, also being exposed to the weather, are subject to eczema. The erythematous type frequently complicates that of the face, and runs a similar course.

Papulo-vesicular eczema of the backs of the hands and the forearms is very frequent. It is generally produced by external irritants, whose nature can often not be determined. The lesions usually consist of rather sharply circumscribed red patches covered with numerous vesicles which rupture and leave oozing, pitted raw areas of the size of a pin's head. Sometimes the whole patch is considerably swollen with œdema. There is a great tendency in this type for fresh patches to appear in the neighbourhood, and even on distant parts.

A chronic form is sometimes met with in the palm, chiefly along the deeper folds. It begins as an ill-defined red patch, and subsequently marked

thickening of the horny layer takes place. Owing to its inelastic nature skin cracks and deep fissures are produced, which are very painful and very chronic. This type is spoken of as *eczema rimosum*.

An acute vesicular form is also seen on the hands, chiefly on the palms and sides of the fingers, especially in people whose hands perspire freely. Owing to the thickness of the horny layer on the palm, these vesicles are very deep-seated, and appear like sago-grains in the skin. At first they do not rupture, but run together and form large blebs which can often be seen to be purulent. The attacks usually come on quite suddenly, and the feet are often attacked simultaneously; they occur chiefly in the hot weather when sweating is profuse. This condition is called *dysidrosis* or *cheiropompholyx*, and was originally thought to be due to obstruction of the sweat ducts, with the formation of retention cysts. This is now known not to be the case, and that the vesicles are produced by an inflammatory exudate. It is probable that the skin is made sodden by excessive sweating, and this renders it susceptible to the attack of some external irritant. A similar condition has been observed from handling aurantia, a substance used in explosives, which shows that the condition may be produced by an external irritant. A number of these cases are due to fungus infection, the so-called "eczematoid ringworms" of the hands and feet (see p. 1437).

TRUNK.—Eczema on the trunk is nearly always secondary to patches starting elsewhere, if seborrhœic dermatitis and dermatitis due to irritants such as sulphur are excluded. There is, however, one type to which reference should be made. In people who sweat much, and especially in infants, an eruption of small vesicles, each surrounded by an inflammatory zone, sometimes appears on the trunk. The lesions appear to be formed around the sweat duct openings. This condition is called *miliaria rubra*, or *prickly heat*, and is probably of the same nature as the vesicular eczema of the hands, the mouths of the sweat follicles being softened by the sweat and some irritant, possibly a bacterial irritant, causing an inflammation.

The nipples are sometimes the seat of an eczema; but this is nearly always of external origin, either from careless treatment during suckling, or from injury from stays.

GENITALS AND ANUS.—The moist areas of the genital and anal regions are liable to be attacked. These are not infrequently secondary to a pruritus, a traumatic dermatitis being produced. On the anus and vulva, thickening of the skin, called *lichenification*, is most common, and has been already mentioned. The scrotum is occasionally the seat of an erythematous dermatitis very distressing to the patient, and very intractable. A considerable number of cases of eczema in the genito-crural region are due to infection with fungi, or yeast-like organisms, and in order to exclude these a careful microscopic examination of the scales should be made (see p. 1436).

LOWER LIMBS.—A special form of eczema is very common on the lower part of the legs. It is associated with chronic vascular stasis. It is generally met with in middle-aged or old people, but is frequently seen in younger persons who suffer from varicose veins, hence its designation *varicose eczema*. It begins either from an infected abrasion which does not heal, or from scratching an itchy leg. Once started the inflammation spreads, as the condition of the skin does not favour resolution. The extension is often due to ill-devised dressings which further lower the resisting power of the skin and

favour the retention of discharges. An extensive weeping or crusted dermatitis, therefore, follows, and this is rarely confined to the leg on which it starts, the other soon becoming infected, probably from contact in bed. Owing to the poorly nourished condition of the skin, ulceration is very prone to occur, and thus the chronic varicose ulcer, so familiar to the out-patient department of any hospital, develops. These cases are particularly prone to spread to other parts of the body by the mechanism referred to above.

The feet are subject to the same type of acute vesicular eczema as the hands.

The Nails.—The matrix of the nails may be involved in an eczematous process affecting the hands and feet, and may either show a marked irregularity of growth, with roughening of the surface of the nail, or the nail-plate may be pushed up from the nail-bed by parakeratosis beneath.

Diagnosis.—Keeping in view the types of eczema already described, the diagnosis of the lesions should present little difficulty; to determine the cause, however, is not so easy. Efforts must, however, first be directed to try and discover an irritant, and if it cannot be found, or if it appears to be one of those mild irritants which do not normally produce a skin reaction, the cause of the patient's susceptibility must be investigated. These causes have already been discussed and require no repetition. As to the nature of the irritant, some help is obtained by the type of reaction and by its distribution; for instance, in an acute eczema affecting the face and hands, exposure to the wind or sun or to some irritant, as the primula, is suggested. With trades certain parts of the body tend to be especially exposed. Lesions affecting the exposed parts and the moist parts of the body suggest some strong volatile irritant, such as rhus poisoning.

Acute erythematous eczema has occasionally been mistaken for erysipelas; but the absence of a sharp line of demarcation, a slowly spreading edge and high fever, should render the diagnosis simple. Acute giant urticaria of the face is unassociated with redness or vesication. The lesions of erythema multiforme are smaller, more sharply defined, and deeper-seated.

The squamous forms have to be distinguished from seborrhœic dermatitis; this is often difficult, but the characteristic features of this latter disease will be considered later.

Ringworm of the glabrous skin tends to occur in circumscribed circular patches or rings, and the fungus can easily be found under the microscope. A special form occurring in the groins is characterised by its bilateral symmetry, its sharp spreading edge, and the presence of fungus in the scales.

Pityriasis rosea in extreme forms may lead to confusion, but the acute generalised onset, and the presence of some of the typical oval lesions, with a collarette of scales attached about a millimetre from the free edge, will usually settle the diagnosis.

Psoriasis is rarely confused, owing to its characteristic distribution on the extensor aspects of the limbs, its usual sharply defined patches, and the dry silvery scaling, seen even in the smallest papules. A few cases, however, of isolated patches made up of small aggregated psoriasis papules may be very difficult to distinguish from localised patches of squamous eczema.

The moist forms have to be distinguished from impetigo contagiosa. In

this disease, however, the vesicles are larger but rarely seen, while the presence of isolated crusted lesions of varying size, with little or no inflammatory zone surrounding them, is characteristic.

The vesicular eczemas of the hands and feet may be caused by a ringworm fungus. This should always be suspected in the chronic spreading cases, and must also be looked for in the acute cases. The diagnosis is made by finding the mycelium of the fungus in the walls of the vesicles—a task not always easy. A curious type of fissuring eczema between the toes is almost invariably caused by a ringworm fungus.

The eczemas found in the course of animal parasitic affections, such as pediculosis and scabies, will be dealt with later.

Prognosis.—This is always uncertain. Most cases of dermatitis due to an external irritant applied on a single occasion get well readily when the irritant is removed. Those caused by the repeated application of the same irritant, as in trade dermatitis, are apt to be more persistent, while recurrent attacks may be extremely troublesome. Once the skin has been damaged subsequent attacks are more common and more resistant to treatment.

Those cases in which some underlying susceptibility exists are always apt to be resistant to treatment.

Treatment.—PROPHYLACTIC.—This depends on the search for the irritant, and its removal. The latter is not always possible in case of trades; but much can be done to insist on scrupulous cleanliness. It must not, however, be forgotten that the use of strong soaps, soda and turpentine to remove traces of a man's occupation are often the cause of the dermatitis. In cases where these substances have to be used, by washerwomen, etc., the use of a cold cream or some glycerine preparation to replace the grease of the skin will prevent a good deal of trouble.

Eczematous subjects should protect themselves from the sun, cold wind, and heat of the fire.

LOCAL TREATMENT.—This applies equally to the cases of dermatitis due to known irritants, and to those we have labelled "eczema." The main treatment in the early stages, after removing the cause, is to protect the skin and to provide soothing application to allay the inflammation. The use of soap and water will generally have to be forbidden.

In the early and acute stages lotions are most suitable, grease in any form being badly tolerated. Calamine lotion can be applied frequently and allowed to dry on the skin, the powder it contains forming a protective dressing over the surface; it is best used in the acute erythematous and papulo-vesicular form in which there is not much oozing. In the weeping cases, lead lotion applied on linen and kept moist is more suitable; it forms an insoluble albuminate of lead which acts as a protective layer. If, however, much sepsis is present, it is well first to use a mild antiseptic, baths of 1 in 4000 potassium permanganate, or lotions of 1 in 4000 perchloride of mercury, or 1 in 1000 acriflavine being very suitable. If these lotions dry the skin too much 3 per cent. glycerin may be added.

As soon as the acute stage has subsided oily preparations are better. It is well to begin with one containing a considerable percentage of water, the lin. calaminæ (B.P.C.) or linimentum calcis being the type. Ichthammol, 2 per cent., may with advantage be added in most cases, and if the itching is severe 1 per cent. to 2 per cent. phenol. Later the water can be given

up and either pure oily preparations as lin. calaminæ co. (B.P.C.), or ointments used. These latter are not satisfactory if there is much discharge; but this can be checked by painting the surface once every second or third day with 2 per cent. to 3 per cent. silver nitrate in sp. æther. nit.

Once the chronic stage has been reached pastes are the best means of applying medicaments. Zinc paste consists of zinc oxide, 25; pulv. amyl., 25; paraff. moll., 50 parts, and makes a firm dressing when spread on linen or lint. It not only affords good protection, but allows a certain amount of absorption to take place.

If the chronic cases do not respond to treatment stimulating preparations are required, and can be incorporated in the zinc paste. Ac. pyrogallic., 1 per cent. to 2 per cent.; coal tar, 1 per cent. to 5 per cent.; or oil of cade, 5 per cent. to 10 per cent., are useful, and where there is thickening of the horny layer 1 per cent. to 3 per cent. ac. salicylic. should be added. Chronic dry cases, and even moist ones, if not septic, often do well if painted with crude coal tar which is allowed to dry on. X-rays, 120 r ($\frac{1}{3}$ of a skin unit), repeated 3 or 4 times at weekly intervals, are extremely valuable in resistant cases, and cause rapid disappearance of the lesions.

In septic cases the crusts should be removed by warm oil or starch-poultices, and a weak mercurial or flavine lotion first applied, and afterwards a zinc paste containing 3 per cent. ammoniated or yellow oxide of mercury.

The gelatine paste of Unna is very useful in the chronic eczemas of the leg, after any sepsis has been removed by antiseptic dressings. Certain chronic eczemas of the legs do well when strapped with varicosan or elastoplast bandages recommended by Dickson Wright, and this method is particularly valuable when ulcers are present.

For facial eczema of infants, 3 per cent. crude coal tar in zinc paste, spread on a mask and continuously applied, is of great value; or the special tar paste devised by White of Boston, U.S.A., may be employed. The same paste is the most satisfactory application in cases of flexural eczema of the non-infective type.

General Treatment.—The patient must be examined for any conditions liable to lower his general resistance. Septic foci, such as pyorrhœa, or tonsillar sepsis, should be removed. In the more acute cases it is advisable to put the patient on milk diet, and to keep him in bed. In the less severe cases a light diet, the avoidance of alcohol, strong coffee and tea, hot and highly seasoned dishes, shell-fish, salted meats and cheese, should be prescribed. Constipation should be dealt with, while intestinal fermentation may be met by the exhibition of salol or bismuth salicylate, grs. 10 to 15; ichthammol, min. 2 to 5; or menthol, gr. 1 in capsules three times a day. In gouty subjects alkaline waters and colchicum are indicated.

In the infantile facial cases, the children are usually overfed and some reduction in diet is often required.

In debilitated cases cod-liver oil is of value, while arsenic and iron are helpful when anæmia is present. In acute cases vin. antimoniale, min. 5, t.d.s., has been much recommended.

Sleep is often disturbed, and will require sedative drugs to allay itching, and in the worst cases hypnotics: bromides are useful for the former, while for the latter sulphonal, methylsulphonal and chloral hydrate are among

the best. Morphine should be avoided, owing to the prolonged nature of the cases and to its tendency to increase itching.

Desensitisation.—As has been noted above, of recent years it has been realised more and more that many cases of eczema are dependent on the sensitiveness to specific irritant. The offending substance can sometimes be determined by the reaction produced when it is applied to the skin, or in doubtful cases a series of substances can be applied under pieces of strapping and can be introduced by puncture or scarification, all tests being carefully controlled. In the so-called "patch test," when the offending substance is applied under strapping, a local eczematous reaction appears; when puncture or scarification is employed, a wheal is produced.

If the cause of sensitiveness is thus discovered it is possible, in some cases, to desensitise the patient by injecting intradermically an extract of the offending substance in minute and gradually increasing doses. Further, in cases where no specific substance can be determined, it has been found possible to desensitise patients by the injection of non-specific protein substances.

A method much in vogue at the present time is to withdraw 5 to 20 c.c. of blood from a vein of the patient and to inject either the whole blood or the serum from it into the gluteal muscles. Another method is to inject 5 to 10 c.c. of sterile milk on several occasions, at 2 to 3 days' interval, intramuscularly. Peptone is also used by some, and may be given either intravenously or intramuscularly.

DERMATITIS FROM MECHANICAL IRRITANTS

Acute dermatitis due to mechanical irritation is best seen in the redness and blisters found on the hands after rowing or on the seat after riding, in those unused to these exercises. The chronic form shows itself as a thickening of the horny layer as seen in the callosities on the hands and feet. The form of dermatitis of mechanical origin, however, which requires special attention here is that produced by the fingers and finger-nails.

1. SCRATCH ERUPTION

Constant friction applied to a localised area produces changes in the skin of a characteristic type. The skin becomes thickened and loses its elasticity; the folds and lines are much exaggerated, and the angular areas of skin intervening become prominent and shiny, resembling the papules of lichen planus; the colour may be the same as the normal skin, or red, but generally purplish, and sometimes the surface is finely scaly or warty. In old-standing cases much brown pigmentation may be present. This condition is spoken of as "*lichenification*," and is seen at its best in localised pruritus, already described on p. 1403.

When general irritation is present the scratch lesions are more diffuse. The finger passing over the skin causes contraction of the arrectores pili muscles and the follicles are erected; the next sweep of the finger-nail scrapes the top off the erected follicle and a spot of blood appears, which dries as a blood-stained crust. In bad cases, linear excoriations are produced,

consisting of a line of blood-stained crusts. If sepsis supervenes, typical impetigo contagiosa lesions are produced, and these are particularly common in children; in other cases "eczematisation" occurs—that is, the inflamed papules group together to form a patch or patches, which may be dry and scaly or may weep. Patches of lichenification may also be found mixed with other scratch lesions, while in the most severe cases, ecthymatous lesions, boils and linear ulcers may occur.

2. CALLOSITIES AND CORNS

These are localised overgrowths of the horny layer, the result of local mechanical irritation. A corn differs from a callosity in that the central portion shows a much greater degree of overgrowth than the periphery, and forms an inverted horny cone which presses on the sensitive dermis, producing much pain. A corn may develop from a callosity, but frequently arises independently.

Symptoms.—*Callosities* are seen as a painless thickening of the horny layer over the ball of the foot and on the palms of the hands, in the latter situation especially in manual workers. They may also occur in other situations.

Corns may be of two kinds—(1) the hard and (2) the soft. The former are painful, horny elevations, chiefly seen on the feet, and especially in people who wear badly fitting boots. The common sites are on the dorsal surface of the little toes and on the plantar surface of the great toe and over the head of the first metatarsal bone. If the surface layers are removed with a razor a central "core," often stained black or dark brown from hæmorrhage, will be seen.

Soft corns are found on the lateral aspects of the toes in the interdigital spaces. They are usually lentil-sized raised swellings, covered with sodden epidermis, and intensely painful. Soft corns are invariably found associated with interdigital ringworm.

Treatment.—Callosities require no treatment. The principal point in the treatment of corns is to remove injurious pressure; this can be done firstly by fitting suitable boots, and secondly by taking pressure off the corn by wearing a ring of spongiopiline around it. The surface horny layer should be pared down with a sharp knife or razor and 10 per cent. salicylic acid plaster applied or salicylic acid collodion painted on, the softened horny layer being removed daily. Soft corns are treated as for interdigital ringworm (see p. 1438).

DERMATITIS ARTEFACTA

This is the name given to self-inflicted lesions of the skin. These are usually found in hysterical individuals, who produce them in order to induce sympathy, or in persons who are endeavouring to exact compensation or to avoid some unpleasant duty.

Symptoms.—The lesions are produced by various means, such as friction, the application of strong acids, or alkalis, or of blistering fluid, by heat or by the aid of some sharp instrument. All stages from simple erythema to actual destruction of the skin may occur. They may be single or multiple,

but are found on parts of the body easily accessible to the hands, and especially to the right hand (in left-handed people to the left hand). The lesions are very characteristic, especially those in which a liquid agent has been used. They have very sharp edges and the outline is angular, unlike that seen in any ordinary skin eruption; and not infrequently irregular patches near the main lesions have the appearance of having been produced by a spilt liquid. In addition, it may be noted that in the case of the malingerer the artefact may simply consist of keeping open an already existing lesion.

In hysterical cases anæsthesia of the palate has been frequently noted.

Treatment.—For effective cure the patient must be kept under observation, and caught in the act of producing the lesions. This may put a stop to further activities. Otherwise, occlusive dressing and mental treatment are required.

DERMATITIS FROM BACTERIAL IRRITANTS

Many different organisms are capable of producing dermatitis of external origin, and the eruptions produced are usually characteristic of the organism causing them. These will be described under the organisms concerned.

1. PYOGENIC INFECTIONS

It is not always possible on clinical examination to determine whether a given lesion is produced by the streptococcus or the staphylococcus. It used to be held that the superficial infective vesicular lesions were due to the streptococcus, while the follicular pustular lesions were of staphylococcal origin. While this appears to be true for the latter, it is now recognised that certain vesicular lesions may be of staphylococcal origin.

(*a*) Impetigo Contagiosa

Symptoms.—This is an affection chiefly seen in children. It affects mainly the exposed parts, such as the face and hands. The initial lesion is a small pea-sized clear vesicle, which, owing to its superficial position between the horny and mucous layers, has an extremely thin wall and ruptures very easily. Before rupture, however, the fluid often becomes turbid, and if cultured in this condition contains both streptococci and staphylococci. If cultured, however, in the very early stages, pure growths of streptococci may usually be obtained. Once ruptured, fluid exudes freely from the base of the blister and dries as a crust. The crusts vary in thickness and character according to the amount of secondary infection, being thin and amber-coloured if little secondary infection is present, but thick and greenish if it is considerable. Usually the lesions are numerous; they are asymmetrical and obviously spread by local inoculation.

When the lesions occur in folds, such as at the angles of the mouth or nose and behind the ears, a troublesome fissure is likely to form, and generally crusting is absent, the fissure being surrounded by a moist, sodden, red area.

The disease is very contagious and children inoculate one another freely, any slight abrasion being sufficient to allow the entrance of the infecting

organism. One particularly common cause is pediculosis capitis, and in this case the scalp is usually first affected. In all cases of impetigo of the scalp or back of the neck, search should be made for pediculi.

Occasionally the blisters do not rupture early, but spread centrifugally, flattening down in the centre as they progress, and leaving a ring-like bullous margin (*impetigo circinata*). In other cases a large number of bullous lesions appear very rapidly, with little or no crust formation (*impetigo bullosa*). *Staphylococcus aureus* can usually be grown in pure culture from cases of these types.

Any of these varieties may occur in adults, but the crusted form has generally smaller crusts than in children. One of the most frequent areas to be affected in adults is the beard region, and impetigo contagiosa is one of the forms of so-called "barber's rash."

Diagnosis.—This is usually easy. The presence of scattered crusts, with little or no surrounding erythema, and the occasional small, very thin-walled blister, and an asymmetrical distribution chiefly on the exposed parts, is unlike any other condition.

Treatment.—In most cases the treatment is easy. The crusts should be removed by bathing in warm water, by fomentations or by warm olive-oil compresses, or in bad cases by starch poultices, and the raw surface covered with 2·5 per cent. ammoniated mercury ointment. In most cases it is advisable to incorporate the ammoniated mercury in Lassar's paste and spread this on lint and tie it on. The acutely spreading bullous form is treated in the first instance by pricking the blisters and dressing with 1 in 1000 acriflavine lotion. In very resistant cases, injections of mixed strepto- and staphylococcal vaccine have proved useful, but are rarely required.

(*b*) Pemphigus Neonatorum

Synonym.—Impetigo Neonatorum.

This is a form of bullous impetigo seen in newly-born infants and is characterised by the presence of varying-sized blisters on the skin.

Ætiology and Pathology.—Pemphigus neonatorum has precisely the same cause as impetigo contagiosa, but produces its characteristic features on account of the ease with which the horny layer separates from the underlying mucous layer in small infants. Infection is usually conveyed on the fingers of the mother or nurse. Pure cultures of *Staphylococcus aureus* can usually be obtained from the bullæ in their early stages.

Symptoms.—The eruption usually appears in the first few days of life. A clear blister appears, which rapidly increases in size, and others soon occur in the neighbourhood. There is little or no tendency to crust formation, though the blisters frequently rupture, the raw surface being protected by the loose blister wall which lies over it. Blisters vary in size from a pea up to a florin or larger, and in severe cases may be very numerous, covering practically the whole surface of the body. The lesions may commence on any part of the body, but are frequent about the napkin area. In the most severe forms the horny layer is so rapidly separated over large areas of the body that blister formation is not an obvious feature. This variety is known as *dermatitis exfoliativa infantum* or "Ritter's disease," and ends fatally in a large proportion of cases.

Diagnosis.—The pemphigoid syphilide must be distinguished from pemphigus neonatorum. In the former condition the eruption is symmetrical, is chiefly found on the prominences of the buttocks, on the palms and soles; other symptoms of syphilis are present, such as wasting, snuffles, fissures at the angles of the mouth, and other syphilitic skin eruptions. A Wassermann reaction will in doubtful cases settle the diagnosis.

Prognosis.—Mild cases respond rapidly to treatment, but in the more rapidly spreading cases the prognosis is always grave.

Treatment.—The bullæ should be opened and their contents absorbed with cotton-wool. Strips of lint soaked in 1 in 1000 acriflavine lotion should be applied, and changed three times a day or more often if necessary. It is important that the blister edge should be removed by forceps, so that the lotion may act on the spreading edge of the lesions. The child should be well wrapped up to prevent loss of heat.

(*c*) Ecthyma

In this condition local gangrene of the skin occurs and an ulcer, surrounded by a deep inflammatory zone and covered by a crust, is produced. The lesions are not always of pyogenic origin, but may be brought about in various ways; but as they have some resemblance to impetigo contagiosa, it will be well to describe them here.

Ætiology and Pathology.—The type seen in children is often of streptococcal origin and begins as an impetigo. Scratching or a debilitated condition of the patient allows of a more violent reaction, and necrosis occurs. The frequency with which ecthyma is associated with urticaria papulosa, scabies and pediculosis points to trauma as an ætiological factor. The large round adult type, referred to below, is nearly always preceded by a boil, which is a staphylococcal infection, while the linear type can be shown to be produced by violent scratching, to which is added secondary pus infection.

Symptoms.—All varieties are most often seen on the legs and buttocks. The lesions are usually discrete and few in number, but there are exceptions. They have the appearance of impetigo contagiosa lesions, but there is a wide congested area around the crusts, and these latter are not "stuck on" but firmly fixed. On removal an ulcer the size of the crust is found. This type is usually found in children. Another variety is seen in adults especially, in association with pediculosis vestimentorum, and was seen very frequently during the War of 1914–1918. Two types are seen: the large circular type, which has the characters of those mentioned above, but the individual lesions are larger, and the linear or gutter-shaped type, in which long ulcers, often 2 or 3 inches in length and covered with a thick crust, are present.

Diagnosis.—This has to be made from the ecthymatous syphilide, usually a late tertiary manifestation. In this condition there is a tendency to grouping of the lesions, and they are of a more chronic type. Other syphilitic manifestations, a positive Wassermann reaction, and rapid response to anti-syphilitic remedies will settle the diagnosis.

Treatment.—Local treatment is similar to that of impetigo contagiosa. The crusts should be removed by baths or starch poultices, and Lassar's paste with 3 per cent. ammoniated mercury tied on. In the adult cases, after

the sepsis has been removed by 1 in 4000 perchloride of mercury or 1 in 1000 acriflavine dressings, Unna's paste should be applied and changed every 2 or 3 days until healing takes place. Where debility and malnutrition are present, suitable internal treatment must be resorted to, cod-liver oil and malt, and the preparations of iron, arsenic and the phosphates being most useful.

(*d*) Pityriasiform Dermatitis

Certain forms of circumscribed, dry, superficial dermatitis, with fine branny scales, are sometimes seen in association with impetigo contagiosa and appear to have the same origin. In fact, all stages between the two conditions can be traced. The name *impetigo pityroides* is sometimes applied to this type of case. In other cases dry scaly patches are found without any impetigo contagiosa lesions, and streptococci have been isolated from them. These cases are sometimes indistinguishable from the scaly patches which occur on the faces of children, and which are described in the section on Eczema (p. 1412), where it is suggested that moisture and soap play the chief part in their production. It would thus appear that the streptococcus may produce lesions clinically identical with those produced by these physical and chemical causes. It has been thought also that some forms of circumscribed scaly dermatitis found about the neck and trunk, and also in the flexures of the limbs, and which have in the past been loosely grouped as seborrhœic dermatitis, are probably of streptococcal origin, but further investigation is necessary in order to group them clearly.

These lesions are often resistant to treatment. They are frequently associated with a good deal of itching, and are often followed by secondary changes due to friction, namely, "lichenification" and "eczematisation."

Treatment.—The early cases sometimes respond well to applications of dilute ammoniated mercury ointment; others, however, do best on ac. salicyl., grs. 15; liq. picis carbonis, min. 15; past. zinci ad 1 ounce. Once a condition of lichenification is established, the treatment should be on the lines laid down for local pruritus (p. 1403).

(*e*) Follicular Impetigo of Bockhart

This is the name given to a superficial pustular eruption of staphylococcal origin seen in connection with the hair follicles.

Symptoms.—The lesions consist of small beads of pus situated quite superficially at the mouths of the hair follicles, each being surrounded by a narrow red zone. Generally the hair can be seen penetrating the centre of the pustule. There is no tendency for the lesions to run into one another, each remaining quite distinct. Usually groups of them occur in localised areas, but sometimes their distribution is very extensive, cases occurring in which almost every stout hair is surrounded by a pustule. The most frequent sites are the fronts of the thighs, the legs, the genitals and the backs of the forearms. A very troublesome variety is seen on the scalp of children between the ages of 2 to 5, the infection being usually derived from a discharging ear or nose. The whole scalp is affected, and the condition is combined with a superficial septic dermatitis which affects also the face, and often spreads to other parts of the body. Ciliary blepharitis is a frequent complication.

This is the condition which was formerly described as *pustular eczema*. The majority of localised cases occur in conjunction with other forms of pyodermia; they are seen in scabies and pediculosis, and also in people suffering from boils.

Treatment.—The general health of the patient must be attended to, and all local foci of sepsis dealt with on surgical lines. A search for parasitic infestation must be made and appropriate measures adopted. In the localised cases, the pustules should be punctured, and 1 in 1000 acriflavine lotion applied; if this proves too irritating, lead or calamine lotion should be used, the accumulation of powder from the latter being bathed away daily with a weak alkaline lotion. Mercury lotions are better avoided, as they tend themselves to produce follicular pustulation.

The more extensive cases are very resistant to treatment. Shaving the affected areas, followed by the application of mild antiseptic lotions or sedative lotions and alkaline baths, is sometimes effective. Staphylococcal vaccines should be tried in addition, and in some cases stannoxyl (an oxide of tin) and injections of collosol manganese have given good results. In the pustular eczema of the scalp, the crusts should be removed with warm oil or starch poultices, and the lotions indicated above or acriflavine 1 in 1000 in liniment. calcis applied. At the same time nasal and ear discharges must be appropriately treated. These cases take a considerable time to cure, but the results repay the attention necessary.

(*f*) Furuncle

Boils or furuncles are deep-seated infections of the hair follicles with the *Staphylococcus aureus*.

Ætiology and Pathology.—The exciting cause of a boil appears to be the presence of virulent staphylococci in the hair follicles which occasion an intense reaction sufficient to cause local necrosis. This is the more liable to occur where the skin is thick, owing to the pressure exerted on the dense fibrous-tissue bundles and the consequent obstruction to the circulation. Scratching, which conveys the causative organism to the follicles and damages their orifices, predisposes to boils, as is seen by their frequent occurrence in parasitic affections. Lowering of tissue resistance, such as occurs in diabetes and in other conditions of lowered vitality, is also a predisposing cause. In other cases it is probable that a condition of allergy and hypersensitiveness to the staphylococcus is present, and this probably accounts for the constant recurrences which occur.

Symptoms.—Boils may attack any part of the body where hair follicles are present, but are most commonly seen on the neck, back and buttocks, regions where the skin is thick and exposed to pressure and friction. The lesions are usually single or few in number, but they tend to recur with great persistence, and recurrences may continue for a long period. The patients attacked are often in a low state of health. Boils are particularly liable to occur in diabetics, and the urine of patients should always be examined for sugar. A boil commences as a deep, tender infiltration, which rapidly increases in size so as to form a painful red swelling, up to an inch in diameter, which projects above the surface of the skin. Later, a small pustule appears in the centre of the swelling and this eventually bursts, exuding a small quantity of pus, which relieves the pain. Later still, a small

slough separates from the centre of the swelling, and when this has come away the boil heals, leaving a pitted scar. Some boils, however, subside without bursting. Sometimes the earliest lesion is a superficial pustule, which is followed by the rapid formation of an inflammatory zone. Later, infiltration of the deeper tissues follows, and a slough forms and is discharged, as in the first-mentioned type.

Treatment.—The general condition of the patient must first be dealt with on general lines. Certain internal remedies, such as Vitamin A, yeast and calcium sulphide, have occasionally proved of value. Vaccines and toxoid of *Staphylococcus aureus* produce results in some cases, but cannot be looked on as a specific. Injection of collosol manganese, or injection of manganese butyrate, suggested by McDonagh, beginning with 0·5 c.c. and repeated twice a week, in slightly increasing doses, for 3 to 4 injections, produces dramatic results in certain cases; others, however, are completely resistant. Stannoxyl, given by the mouth 2 to 3 tablets t.d.s., has also been claimed to produce excellent results.

Local measures are of great importance. Before the boils have ruptured, applications of kaolin poultice (antiphlogistine) are helpful in relieving pain and causing absorption of the exudate. Short-wave diathermy and small doses of X-rays may also produce a similar result. After rupture, dressings of 1 in 4000 perchloride of mercury, or pasta magnesii sulphatis (B.P.C.) are indicated. Boric acid fomentations should be avoided, as they spread the infection. Early or deep incision into boils is better avoided as it tends to spread the infection.

(*g*) Carbuncle

A carbuncle is a boil or group of boils in which the subcutaneous tissue has become involved in the infective and necrotic process.

Symptoms.—Usually only a single lesion is present. It may at the commencement appear like an ordinary boil, but the spread is rapid, and soon a large, red, indurated, painful area is produced. The lesion may attain a diameter of many inches. After a few days numerous points of pus appear on the surface of the swelling, and these burst and exude pus. The bridges of tissue between these openings may subsequently break down and reveal a large slough, which may take several weeks to separate if not removed by surgical means. Fever and other constitutional symptoms are generally present.

Treatment.—The general treatment is the same as for boils. Local surgical treatment may be required, and consists either of complete excision of the carbuncle, with the surrounding inflammatory tissue, or of making a crucial incision and removing the slough, the open wound being packed with bismuth-iodoform-paraffin paste or an appropriate antiseptic dressing.

(*h*) Sycosis Barbæ

This is a staphylococcal infection of the hair follicles of the beard region, and is one of the three forms of "barber's rash," the other two being impetigo contagiosa of the beard region and ringworm of the beard.

Ætiology and Pathology.—The disease is produced by inoculation of staphylococci into the hair follicles in the beard area, either primarily or as a secondary infection to an impetigo contagiosa. Many cases doubtless start from infection conveyed in the barber's shop, but a considerable number also occur in patients who shave themselves. Scratches from the razor subsequently inoculated by the patient's finger are probably as common as direct infection from a barber's brush or razor.

Symptoms.—The disease usually begins at one spot in the beard or moustache area by the formation of pustules around the hairs. These pustules tend to occur in groups, and become surrounded by an inflammatory zone. As the deeper parts of the follicles become infected, nodules form and the whole affected area becomes swollen and œdematous. Pus discharging from the ruptured pustules dries and forms crusts. Subsequently some of the hairs loosen and can be pulled out without pain. Each hair on removal is seen to be surrounded by a swollen and transparent root-sheath, and often a bead of pus escapes from the follicle. The disease is progressive, and eventually the whole beard and moustache area, and not infrequently the eyebrows and eyelashes, may be attacked. It tends to become chronic, and in old-standing cases a large number of the hairs are lost, leaving a smooth, red, atrophied patch, not unlike lupus vulgaris, to which the name *lupoid sycosis* has been given. The presence of some follicular pustules and the absence of lupus nodules are, however, sufficient to separate the two conditions.

Diagnosis. — In addition to the diagnosis from lupus vulgaris just mentioned, sycosis has to be differentiated from impetigo contagiosa, and from ringworm. From the former the diagnosis is made by the involvement of the deeper structures of the skin and the presence of pus in the hair follicles; from ringworm by the absence of fungus in the scales and hairs (see Tinea barbæ, p. 1436).

Treatment.—The acute cases should be treated much in the same way as other acute inflammations of the skin, without any attempt being made directly to attack the organism responsible for the disease. Frequent bathing in warm water or oil should be used to remove crusts, or boric-starch poultices may be used. Lead lotion, or 1 in 1000 acriflavine lotion, should be applied on lint and changed frequently. When the acute stage has subsided the parts should be kept clipped short with scissors. Hairs from infected follicles should be epilated and the skin dabbed with 5 per cent. ichthammol in calamine lotion or 1 in 4000 perchloride of mercury. As an adjunct staphylococcus vaccines or toxoid may be given. The local application of a vaccine has sometimes proved useful. In some cases excellent results have been obtained by the use of "quinolor" ointment (Squibb). Epilation by X-rays has been recommended, but the results are not very satisfactory, recurrence being frequent. Small doses of X-rays are, however, helpful.

2. ANTHRAX INFECTIONS

These lesions, which resemble in some respects those produced by the staphylococcus, are dealt with elsewhere (p. 57).

3. DIPHTHERIA INFECTIONS

The lesions produced by the diphtheria bacillus are rare, but are seen sufficiently often to require notice. Diphtheritic infection of wounds is a well-known condition, but does not need to be considered here. In children suffering from diphtheria, gangrenous patches occasionally develop, chiefly on the trunk, from which cultures of the organism may be obtained, but the organism may also attack the skin of otherwise healthy persons.

Symptoms.—A single lesion usually occurs, but there may be more than one. It begins as a clear blister, like an impetigo vesicle, and ruptures very easily; on about the second day a considerable red zone is present around the original lesion, and a central slough has formed, comparable to a small burn. This condition persists for some time, if not treated, and eventually the slough separates and the spot heals. Constitutional symptoms may be present. The writer has recently seen a case of paronychia from which a pure culture of the Klebs-Loeffler bacillus was obtained.

Treatment.—Prompt injection of diphtheria antitoxin, with the application of a local antiseptic dressing, is all that is required.

4. INFECTIONS BY THE SEBORRHŒIC ORGANISMS

Three organisms are commonly found in cases of seborrhœic dermatitis, but the part each plays is not yet conclusively proved, so that it will be convenient to group the seborrhœic conditions under one heading. The organisms found are the *acne bacillus*, the *bottle bacillus* (pityrosporon of Malassez), and the *Staphylococcus epidermidis albus*. The first named is a small bacillus which is found chiefly after puberty and is present in very large numbers in the comedo of acne vulgaris. The bottle bacillus is a yeast-like organism which buds and often shows itself as a flask-shaped body, and is found most plentifully in seborrhœic dermatitis of the scalp. The white skin staphylococcus is found pretty universally over the skin.

(*a*) Seborrhœic Dermatitis

Under this term we include a chronic scaly condition of the scalp, formerly called seborrhœa sicca, and also certain "eczematous" lesions of the face, chest and back, and occasionally on other parts of the body, which are characterised by the presence of more or less circumscribed reddish patches covered by greasy scales.

Ætiology and Pathology.—The histological changes in the skin are those of a chronic superficial dermatitis. The three organisms mentioned above are met with in the scales in all adult cases, but the origin and spread of both seborrhœic dermatitis of the scalp and the figurate type on the body suggest that the views of Sabouraud and Whitfield, that the bottle bacillus is the chief ætiological factor, are correct. Further, the ease with which most lesions clear up under treatment by sulphur supports these views. There is no doubt that an underlying seborrhœa is the main factor in causing the activity of these organisms.

Symptoms—Seborrhœic dermatitis of the *scalp* is the well-known

"scurfy head," and is an extremely common affection, most individuals having it to a greater or less degree. It probably begins in early infancy, and is sometimes seen as a ringed lesion on the scalp of young infants. These lesions have been shown by Whitfield to contain the bottle bacillus in large numbers. These rings may disappear spontaneously, but the infection, which has presumably been conveyed from the mother or nurse, persists and lights up again later in life in certain individuals, especially in those prone to seborrhœa (see p. 1400). In the adult the affection consists of a diffuse branny scaling on the scalp, usually unassociated with any obvious inflammation of the skin. On close examination the scales are seen to be formed around the hairs, indicating that the inflammation is perifollicular. Varying degrees of scaliness are met with; in some cases it is scarcely perceptible, in others it consists of thick, greasy masses. Symptoms are generally absent, but occasionally a good deal of irritation is present, which leads to scratching, and small crusted lesions are then found among the scales. Sometimes a more acute inflammation supervenes, and the scalp becomes red and hot, and an exudate of fluid may occur, producing crusting. In these cases the inflammation usually extends for a centimetre or so beyond the hairy margin. The persistence of scaly seborrhœic dermatitis is considered by some to be an ætiological factor in producing that form of baldness known as alopecia prematura, which is characterised by the recession of the hair from the forehead and baldness on the crown of the head. It is probable, however, that other factors, such as heredity, also play a part in this condition.

The *face* may also be affected, especially the eyebrows, forehead, naso-labial folds, beard and mastoid regions. Here the lesions are dry, reddish or pale patches, surmounted by greasy scales or crusts. On close examination it can usually be seen that the lesions are follicular in origin and that the patches are formed by the aggregation of these follicular papules. The ears may be affected, especially the retroauricular sulcus and the concha, and some forms of blepharitis appear to have a seborrhœic origin. The lesions on the face are very liable to become infected with pus organisms and become thickly crusted. An intractable scaly inflammation of the lips, *cheilitis exfoliativa*, is also considered to be of seborrhœic origin.

On the *chest and back* ringed or figurate lesions are frequently seen, but here follicular papules may occur. The centre of the sternum and the interscapular area are the common sites. Occasionally patches occur among the pubic hairs.

Some authorities include under this heading cases in which circumscribed pinkish or red circular or oval patches, covered by fine branny scales, occur on the trunk and limbs. They are resistant to treatment, especially to the remedies useful in seborrhœic dermatitis, and there is some evidence that they are forms of streptococcal dermatitis. This type is prone to attack the flexures of the limbs, chiefly the axillæ and groins, as are other streptococcal infections.

Diagnosis.—All cases of scurfy head in children should be considered to be ringworm until careful examination has excluded this cause. The presence of stumps and the demonstration of the fungus will settle the diagnosis. In body ringworm the distribution is irregular, the lesions are sharply circular, and the scaling is not greasy. Fungus can be found in the scales.

Impetigo contagiosa of the small crusted type has a close resemblance to seborrhœic dermatitis, especially on the face. The presence of some definite impetigo vesicles and crusts, and the history of its unilateral spread, may help to clear up the diagnosis.

Pityriasis versicolor occurs in the same regions as the body form of seborrhœic dermatitis, but it has a fawn colour and no inflammatory reaction, and the fungus can be found in the scales. Pityriasis rosea can be distinguished by the presence of oval lesions with a collarette of scales within the edge of the lesion, by its acute onset and by its symmetrical distribution.

Prognosis.—The figurate variety on the trunk can always be kept under by appropriate treatment, but frequently recurs. The face is more resistant to treatment, and when much septic infection has taken place may take a long time to cure. On the scalp constant treatment is necessary, and a permanent cure can scarcely be hoped for, as the organisms invade the follicles. With proper hygiene and appropriate treatment, however, the condition can be kept quiescent.

Treatment.—*Scalp.*—Frequent washing is necessary to remove the scales and accumulated dirt. Unless there is any acute inflammation present, men should wash the scalp two or three times a week or even daily with sp. sapon. kalin. (B.P.C.), or ext. quillaiæ liq. (B.P.C.); sulphur or tar soap may be used. In women the washing should be done once a week. After drying, in severe non-inflammatory cases, an ointment containing 3 per cent. each of ac. salicylic. and precipitated sulphur in a basis of gr. 120 soft paraffin and gr. 360 cocoa-nut oil should be rubbed into the scalp. Resorcinol, thymol, anthrasol, thiol or ammoniated mercury 3 per cent. may be used as alternatives or in various combinations. In the milder cases lotions are preferable. Resorcinol or chloral hydrate min. 60, sp. vin. rect. fl. oz. 1, aquam ad fl. oz. 8, is a useful lotion. Resorcinol should not be used in fair or white-haired patients owing to its staining properties. In the acutely inflamed cases, washing with soap should be avoided, though crusts may be bathed away with warm water. After removal of the crusts, ichthammol gr. 30 in 1 fl. oz. of lin. calcis should be applied, the hair being cut short if necessary.

On the *face*, sulphur and salicylic acid ointment may be used in the chronic cases; if, however, sepsis is present the crusts must be removed and calamine or ichthammol liniment applied.

On the *body*, sulphur and salicylic acid ointment is usually all that is required.

(*b*) Acne Vulgaris

This condition is characterised by the presence of greasy plugs, known as comedones, in the pilo-sebaceous follicles—particularly those on the face, shoulders, chest and back—often associated with perifollicular inflammation. It is an extremely common affection in its milder forms and by no means rare in its severest types.

Ætiology and Pathology.—The disease occurs chiefly in individuals between 15 and 25 years of age, and is seen in both sexes. There can be no doubt that it is dependent on the development of the sebaceous glands which occurs at puberty, and that there is, in addition, an individual pre-

disposition, probably inborn, to develop the affection. The affected individuals suffer from seborrhœa.

If a comedo is examined it is found to consist of epithelial cells, sebaceous material, and the three organisms which are associated with seborrhœic inflammations and, in addition, a small acarus, the demodex folliculorum, is sometimes found. In the greater mass of the comedo, the acne bacillus occurs almost pure, the other organisms being found chiefly near the mouth of the follicle. Accumulated evidence seems to show that the acne bacillus is the chief exciting cause of the comedo, but that secondary suppuration may be due to the activity of staphylococci, though this has been denied by Sabouraud. The bottle bacillus and the demodex appear to play no active part in the production of the disease. The excessive oily secretion of the skin, with the patulousness of the follicles which accompanies this condition (the so-called "kerose" of Darier), offers a field for the activities of the acne bacillus, which flourishes in the sebaceous secretion. The actual comedo is formed by exfoliated epithelial cells—produced by an inflammatory hyperkeratosis of the follicle—mixed with sebum.

Symptoms.—The earliest lesions are the comedones or "blackheads." These are small, black spots which are seen filling the dilated orifices of the pilo-sebaceous follicles, most frequently on the face, but also in the other sites mentioned above. If pressure is exerted on a follicle, a cocoon-like plug can be squeezed out, which is of a cream colour, except for the portion which fills the mouth of the follicle, where it is black. Isolated comedones are extremely common, but when large numbers of them occur the term *acne punctata* is applied to the condition. Frequently, however, the presence of these follicular plugs predisposes to an acute perifollicular inflammation, and the comedo becomes surrounded by a red zone; later, a small pustule may occur in the centre. This lesion is generally painful. When these inflammatory lesions predominate, we speak of the case as one of *acne papulosa*, or *pustulosa*; but it must be noted that all varieties tend to be present together. In some cases the inflammation does not start superficially around the follicular orifice, but deeper, in the region of the sebaceous gland. Here we find first a deep-seated lentil- or pea-sized nodule, often painful, which gradually increases in size, reddening the skin as it pushes upwards, and then sometimes bursts at once and discharges a small quantity of turbid yellow fluid with the remains of the comedo; or it may attain the size of a filbert, and present signs very similar to those of a sebaceous cyst. Sometimes the nodules disappear without rupturing. This type is usually spoken of as *acne nodularis*, and is particularly liable to appear on the back. It is the most persistent type, and often leads to much keloidal scarring.

Diagnosis.—Rosacea, especially the acneiform type, when it occurs in young people, may sometimes be mistaken for acne vulgaris, and indeed the two conditions may occur together. In rosacea, vascular congestion is the prominent symptom; the lesions are generally localised to the centre of the forehead, the nose and central portion of the cheeks and the chin—they are painless and the comedo is absent.

Acneiform lesions produced by the internal administration of bromides and iodides may simply be an exaggeration of a pre-existing acne vulgaris; but if not, the lesions tend to be more grouped and to produce tumour-like swellings. Other eruptions characteristic of these drugs may also be present.

The acne produced by the irritation of tar and paraffin is usually localised to the forearms and lower limbs.

Prognosis.—The condition tends to die out between the ages of 20 to 30; but the nodular type may often continue till a considerably greater age. Though improvement is sometimes slow, treatment materially hastens a cure. Bad scarring is sometimes left in severe cases.

Treatment.—As the causative organism is situated deeply in the follicle, it cannot be reached by the ordinary anti-parasitic remedies. Treatment must, therefore, be directed to emptying the follicles. In the mildest cases this is best done by frequent washing with soap and hot water. This is followed by gentle squeezing massage over the affected areas in order to empty the grease from the follicles. Comedones should also be squeezed out, preferably with a comedo extractor. After this a mild sulphur preparation, such as calamine lotion containing 2 per cent. or 3 per cent. of potass. sulphurata or sublimed sulphur should be dabbed on, or if this dries the skin too much 3 per cent. precipitated sulphur in ung. aquosum may be used. Ointments, however, should be avoided as far as possible, as they tend to block up the follicles. This treatment must be persisted in for a considerable period. More drastic treatment consists in exfoliating the skin with a resorcinol paste or with the mercury-vapour lamp.

Vaccines have not given very satisfactory results, though staphylococcal or mixed acne and staphylococcal vaccines have been of some value in the pustular cases.

Very satisfactory results have been effected by means of X-rays. It must be remembered, however, that atrophy and telangiectases sometimes occur many years after treatment. It should therefore be reserved for the more resistant cases and especially those which are tending to develop scars, and should only be given by those who have special experience.

In addition to local treatment the patient's general health must be attended to, constipation rectified, and such conditions as dyspepsia, anæmia and menstrual disturbances treated. A low carbohydrate diet should be advised.

(*c*) Acne Varioliformis

Synonym.—Acne Necrotica.

An inflammatory condition of the hair follicles, accompanied by local necrosis, and leaving pitted scars resembling those seen in variola.

Ætiology and Pathology.—The disease is seen chiefly in middle-aged persons of both sexes. It is believed to be of bacterial origin, and is attributed by Sabouraud to the acne bacillus. It occurs in seborrhœic individuals.

Symptoms.—The affection occurs chiefly on the scalp and forehead, but is occasionally seen on the face, neck, chest and back. The lesions usually come out a few at a time, and the attacks may persist for long periods; but there are generally intervals of complete freedom. Often change of residence has the effect of stopping or determining an attack.

The lesions at the commencement are pinhead-sized vesicles situated at the mouth of the hair follicles. These increase in size to that of a lentil or pea. The vesicles rapidly dry up without bursting, and scabs are formed. These are seen to be depressed below the surrounding skin. When the

scabs fall off after a week or so a small punched-out scar remains. The onset is usually accompanied by a good deal of itching or burning.

Diagnosis.—The condition has to be distinguished from the scattered crusts which occur in seborrhœic dermatitis of the scalp as a result of scratching. The diagnosis can be made by the pre-existing vesicular lesions in the case of acne varioliformis, and by the scarring left.

Treatment.—These cases are often resistant to treatment. The general health should be attended to, and often change of air is very beneficial. Local anti-seborrhœic remedies should be applied, such as salicylic acid and sulphur ointment (3 per cent.), ammoniated mercury ointment (10 per cent.), or lotions of potass. sulphurat. and zinc sulphate.

(*d*) Acne Keloid

A hypertrophic inflammatory condition occurring on the back of the neck just below the hair margin.

Ætiology and Pathology.—The disease occurs in young adult males. Very little is known of the cause. It occurs at a point where the collar rubs the back of the neck, and friction appears to play a part in its production. The condition has been studied closely by Adamson, who can find no evidence of previous comedo formation. Though he considers that it is produced by a combination of trauma and bacterial infection, he does not consider that the acne bacillus or the *Staphylococcus pyogenes* plays any part in its formation.

Symptoms.—The condition commences with small firm nodules, which gradually increase in size and eventually merge into one continuous mass, closely simulating a keloid.

Treatment.—Adamson recommends X-rays as the only satisfactory method of treatment.

DERMATITIS DUE TO FUNGI

1. RINGWORM

Ætiology and Pathology.—Tinea or ringworm is the name given to certain inflammatory affections of the skin produced by the growth in it of certain of the hyphomycetes or moulds. These fungi grow for the most part in the horny layer of the epidermis or its appendages, the hairs or nails, and by their growth produce an inflammatory reaction. The fungi which are commonly seen in this country belong to three genera—the *microsporon*, the *trichophyton* and the *epidermophyton*, the latter of which is characterised clinically by not attacking the hairs. To these must be added a fourth, which, though of the same family, is not usually included under the term "ringworm," namely *favus*, the fungus of which belongs to the genus *Achorion*. The fungus of ringworm is transmitted to man either from another human being or from certain animals, some fungi being only found in man. The types which are common in one country are not necessarily so in another, and in tropical zones a very large variety occur which are not considered here, but are dealt with fully in works on tropical medicine. The microsporon,

or small spored ringworm, attacks almost entirely children under the age of about 16, while the epidermophyton is not frequently seen in young children. The trichophyton, however, attacks children and adults indiscriminately. The genera can usually be distinguished without difficulty from one another both clinically and by examining the hair or scales under the microscope in liq. potassæ. The different species can, however, only be distinguished by their cultural characteristics. The same ringworm fungus grows differently on different media, and in order to compare cultures the fungus is by tacit agreement grown on what is known as Sabouraud's "proof medium," for the reason that this observer has collected and illustrated in his book, *Les Teignes*, a very large number of the known ringworm fungi. The common nomenclature of the fungi is that adopted in this work.

Ringworm is found on the scalp, where it almost universally travels along the hairs into the hair follicles, on the beard region, where the hairs are often but not always affected, or on the glabrous skin, where it usually remains confined to the surface horny layer. The nails are also sometimes attacked.

(*a*) Ringworm of the Scalp

Ætiology and Pathology.—Ringworm of the scalp, *tinea tonsurans*, is essentially a disease of childhood, the adult scalp being so rarely attacked as to be considered a curiosity. In this country about 90 per cent. of cases of scalp ringworm are produced by the microsporon fungus, the large majority of these being produced by a human species, *Microsporon audouini*, the rest (not more than about 5 per cent.) by the microspora of the cat, dog and sometimes other animals. Another 10 per cent. or so of cases are due to trichophyton fungi of which there are several species. The microsporon fungus first attacks the horny layer on the surface of the scalp; it reaches the hair shaft at the mouth of the follicle and grows down on and beneath the cuticle of the hair, destroying the cuticle and fibrillating the hair, and finally terminates in a fringe of mycelial processes just above the expansion of the bulb of the hair. The mycelial processes on the surface of the hair give off small round spores, which are packed so closely together that, when examined in liq. potassæ under a $\frac{1}{8}$-inch objective, they are seen to form a thick mosaic sheath round the hair. As a result of the damage produced, the hairs first lose their elasticity and then fracture. This fracture usually takes place about $\frac{1}{8}$-inch above the mouth of the follicle.

Symptoms.—*Microsporon ringworm.*—In the bulk of cases the disease begins with a small circular scaly patch on the scalp. Very soon the hair on the patch is noticed to be thinning. Several patches may appear simultaneously. On close examination with a lens, these circular patches are found to be covered with fine, branny scales of a greyish colour, the follicles are prominent, giving the patches a nutmeg-grater-like appearance, and numerous broken hairs are seen. At the edge some hairs may be found unbroken but bent at sharp angles, as though a sort of greenstick fracture had occurred. These hairs and the stumps are often covered with a whitish powder, which is the spore sheath referred to above.

On pulling one of the stumps with forceps the former will come away, but usually breaks off above the hair bulb, leaving the latter behind; a great deal of perseverance is necessary to remove the stump intact. The hair

thus removed and examined in liq. potass. has the appearances mentioned above, and in addition the fibrillation of the hair will be noted, especially the irregular fracture of the distal end. In old-standing cases the regular circular outline of the patches may be lost, the whole scalp having a moth-eaten appearance, and stumps being scattered irregularly over large areas. The microsporon ringworms contracted from animals have similar appearances.

Endothrix ringworm.—The fungus of this type is not contracted from animals. The clinical appearances may be similar to microsporon ringworm, but two other types are seen. In some cases no patches are present, but a general thick scurfiness of the scalp occurs. On very careful search with a lens isolated stumps may be found scattered all over the scalp. In other cases sharply defined bald patches occur, which on inspection show no stumps, but every follicular opening is filled with a small black spot. By the careful use of pointed epilation forceps, such as those devised by Whitfield, one or more of these spots may be removed, and on examination the fungus can be demonstrated. This type is called *black-dot ringworm*, and has to be distinguished from alopecia areata.

When the stumps from an endothrix ringworm are examined in liq. potass. under the microscope the spore sheath is found to be absent, the fungus being entirely inside the hair and the cuticle intact. The fungus itself consists of longitudinally running mycelial filaments, which are divided up into small square, round or oval segments, the whole having a ladder- or chain-like appearance.

Ectothrix ringworm.—The fungus which produces this type is of animal origin, and generally produces a much more inflammatory type of lesion than the other varieties. In the majority of cases suppuration occurs, the fungus itself being responsible for pus formation. These suppurating ringworms are spoken of as *kerion celsi*. The affected area is much swollen and red, and often raised considerably from the surrounding skin. The swelling is boggy to the touch, and often gives the sensation of fluctuation, which to the uninitiated suggests abscess formation. On the surface pus is seen to exude from numerous follicular openings, but broken hairs are also seen. These if examined in liq. potass. show fungus, both within and without the hair; the cuticle is destroyed and the mycelium has similar characters to the endothrix fungus, the spores being arranged in chains and not packed together, as in the microsporon type.

Diagnosis.—This is usually simple, the presence of the stumps containing fungus being diagnostic. In cases where stumps are few in number, great help can be obtained by examining the child's scalp under a mercury-vapour lamp, screened by what is known as "Wood's glass." In microsporon ringworm the affected stumps fluoresce brilliantly and can be readily seen. This method is particularly valuable in determining whether a case is cured after treatment. Fluorescence does not occur in endothrix ringworm. From favus the diagnosis is made by the presence of yellow favus cups. From seborrhœic dermatitis the diagnosis should not be difficult if it is always remembered that a scurfy head in a child must always be considered to be ringworm until this has been excluded. Great care has, however, to be taken to make a thorough search for stumps in the endothrix cases. In alopecia areata a smooth, shiny centre with, perhaps, a row of scattered stumps at the periphery of the patch is found. These stumps, however, are club-shaped, are very thin

as they enter the scalp, and when pulled out always come away with a shrunken bulb attached. No fungus can be seen on microscopic examination.

Treatment.—The cardinal fact to remember in the treatment of scalp ringworm is that up to the present no means has been discovered of killing the fungus in the hair follicles. It is, therefore, necessary to epilate the hairs in order to obtain a cure. This can be done by three methods: by X-rays; by producing sufficient inflammation in the affected areas to make the hairs fall out; or by the administration of thallium acetate internally. This second method is the way Nature cures some cases. In kerion the suppuration is sufficient to loosen the hairs, and all that is necessary is to assist this process by hot fomentations and epilation with forceps. In the ordinary microsporon type, however, the production of the necessary inflammatory reaction is not so easy. Various irritants have been used—the most satisfactory of which is croton oil. The application of this, however, requires great care, and is not suitable for ordinary out-patient practice. Probably the best application available at present is an ointment of equal parts of common salt and soft paraffin. The scalp is shaved and washed daily with soap and water, the healthy portion then smeared with a weak mercurial ointment, such as 2·5 per cent. white precipitate ointment, and the salt ointment rubbed vigorously into the ringworm patches. After a time the patches inflame, and the hairs loosen and fall out. Cure by this method in fairly localised cases takes 2 or 3 months if the treatment is vigorously and conscientiously carried out; otherwise it may take 12 or 18 months to effect a cure. X-ray treatment is generally preferable. The method used is that devised by Adamson and Kienbock, and consists in treating the scalp from five different points with an epilation dose, the points being so arranged that the whole scalp is uniformly irradiated. A modified four-area method introduced by Schreuss is gradually becoming more popular. This should cause all the hair to fall out in 3 weeks, and a complete cure should take place.

It has recently been shown, chiefly owing to the work of Buschke and his associates, that, if thallium acetate in a single dose of 8 mgrms. per kilo body weight be administered orally, the scalp hair will fall out after about 18 days, leaving the eyebrows and eyelashes unaffected. This method has now been used in a large number of cases of ringworm, and gives satisfactory results. It does, however, often produce well-marked toxic symptoms, chiefly severe joint pains and gastro-intestinal disturbance, and some fatal cases have been reported as a result of accidental overdosage. Its final beneficial results are probably not equal to those of X-rays. It should only be given to children who are perfectly healthy.

(*b*) Ringworm of the Beard

Symptoms.—Ringworm of the beard, *tinea barbæ*, occurs in two types: (1) the superficial, scaly type, and (2) the suppurative type. The former begins as a small scurfy patch, which spreads slowly in ring fashion and resembles the scaly type on the scalp. The hairs are usually attacked, and if removed fungus can be demonstrated in them and also in the scales The fungus is usually of the endothrix type, and as such is transmitted from man to man. It is not infrequently caught in the barber's shop, and is one of the three forms of "barber's rash."

The suppurative type produces an irregular lumpy swelling of the affected part. The "lumps" are soft and boggy to the feel, and pus may be seen exuding from various follicular openings; the case bears a close resemblance to kerion celsi, but has not the same sharp circular edge, being more irregularly distributed. The hairs are attacked by the fungus, which in this case is generally of the ectothrix type, and is usually transmitted from animals, being frequent among grooms and cattlemen.

Diagnosis.—The scaly variety must be distinguished from seborrhœic dermatitis and the pityriasform type of streptococcal infection. This is easily done by the presence of fungus in the hairs and scales of ringworm.

The suppurative type may be confused with the staphylococcal sycosis; but the latter never forms the tumour-like masses which are seen in ringworm, while again the presence of fungus will settle the diagnosis.

Treatment.—The same principles apply as in scalp ringworm. For the scaly type X-rays form the most certain form of treatment. Alternatively 3 per cent. salicylic and 5 per cent. benzoic acid ointment should be rubbed in daily and the hairs epilated, a few at a time, with forceps. The hair should be kept cut short.

With the suppurative variety hot fomentations and epilation with forceps should be used.

(*c*) Ringworm of the Glabrous Skin

This can be divided into four types. (1) *Tinea circinata*, the small ring- and disk-like patches seen about the face, neck, body and limbs; (2) *tinea cruris, eczema marginatum* or *dhobie itch*, seen chiefly as sheet-like patches in the inner side of the thighs, and on the perineum and scrotum; (3) the *eczematoid ringworms* of the hands and feet; and (4) the *pustular body ringworms*.

Symptoms.—1. *Tinea circinata.*—This condition may occur by itself or in combination with scalp ringworm. In the latter condition it usually occurs on the neck or face. In the microsporon cases of human origin the lesions take the form of small disks, usually not larger than a threepenny bit, which show little tendency to grow, and no tendency to clear in the centre or to form rings. The patches are of a pale pink colour, and are covered with branny scales, in which mycelial filaments can be demonstrated by examining them under a $\frac{1}{6}$-inch objective in liq. potassæ. The other varieties of microsporon and the endothrix trichophytons show a much greater tendency to form rings and to attain a larger size. In these cases the earliest spots are similar to those described above, but as they spread the centre loses its scaliness, becomes a paler colour, and eventually the skin resumes its normal character. The spreading edge presents the same branny scaling, and often small pinhead-sized vesicles and pustules. As before, mycelial filaments can be demonstrated in the scales. Itching is often present to a greater or less degree. In rare cases these rings are very numerous, and concentric rings may form. This is well seen in some tropical varieties, such as *tinea imbricata*, where the whole body is covered with concentric ring-formations.

2. *Tinea cruris.*—This condition, also known as *dhobie itch*, is produced by the genus *Epidermophyton*. It is so named because of the commonly held view that clothes are infected by the washerman or *dhobie*. Originally a tropical type, it is now extremely common in this country, being much more

often seen in private than in hospital practice, and almost entirely in males. It is usually seen as a superficial, flat, brownish-red patch situated bilaterally on the inner surface of the thighs in their upper third. The patches usually meet on the perineum, and often involve the whole scrotum, and sometimes spread forward into the groins. The patches, which were formerly known as *eczema marginatum*, have a very sharply defined margin, which is very slightly scaly, but no vesicles are present. Scrapings from the scales show a chain-like mycelium. The patches, though usually confined to this region, are occasionally seen on the umbilicus and in the axillæ, and are frequently associated with one type of eczematoid ringworm seen between the toes. There is generally intense itching felt in the patches.

3. *Eczematoid ringworms.*—There are several varieties of this type seen. The commonest is that which occurs between the toes. It occurs first between the little and fourth toe, and is generally bilateral. The skin in the web of the toe becomes thickened, whitish and sodden, and fissuring is prone to occur. It may spread to adjoining interdigital spaces, and on the dorsum and sole of the foot. In severe cases this area becomes covered with vesicles or large blebs, which may become purulent. It is not always easy to demonstrate the fungus in the thickened skin between the toes; considerable time must be given to soaking in liq. potassæ the skin removed, and many slides may have to be made before the search is rewarded.

The most common type seen on the hands consists of rather sharply circumscribed patches of a vesicular dermatitis. They may occur on any part of the hand or fingers, and are generally single and unilateral. They spread slowly, and are itchy. The lesions are usually produced by the trichophyton fungus. The demonstration of the fungus is necessary to distinguish them from other forms of localised dermatitis. When the lesions occur on the palm much thickening of the horny layer is produced, and cracking in the deeper folds may take place.

In another form an acute dermatitis which may involve both hands and feet, is set up, as has been shown by Whitfield. The cases are clinically indistinguishable from the type of acute dermatitis known as dysidrosis or cheiropompholyx, and in all such cases a careful examination must be made for a ringworm fungus.

4. *Pustular body ringworms.*—These occur in sharply defined patches, chiefly on the limbs and neck. The patches are of dull red colour, and sharply raised from the surrounding skin; they have a soft boggy feel, and pus can be seen exuding from the follicles. The fungus in this case is usually of the ectothrix variety.

Diagnosis.—This is only difficult in the acute eczematoid varieties, when it must be distinguished from cheiropompholyx and the localised forms of dermatitis and eczema. This can only be done with certainty by demonstrating the fungus. The circinate patches have to be distinguished from seborrhœic dermatitis and the scaly streptococcal lesions, and on the face from pityriasis simplex. The presence of fungus, and the ease with which patches respond to Whitfield's ointment, as well as the tendency to ring-formation, and asymmetrical distribution, will enable a diagnosis of ringworm to be made.

Treatment.—This is simple in the flat body patches and in tinea cruris. The number of antiparasitic remedies is large but the most satisfactory is

fuchsin paint (Castellani). This is painted on the patches once or twice daily, and can be used in the most inflamed cases. Other preparations include ung. ac. benzoici co (B.P.C.) (Whitfield's Ointment) and liq. iodi mitis (B.P.). Most patches will clear up in a week or two with these remedies, but it is well to continue them for some days after the lesions have disappeared in order to prevent recurrence.

Eczematoid ringworm of the toes can be treated with Whitfield's ointment, the sodden epidermis being removed daily after washing with soap and water; it is well to use this intermittently for 2 weeks at a time, powdering the toes well with a bland powder during the alternate 2 weeks, in order that the keratolytic action of the salicylic acid may subside and give a better indication of the results of treatment. In resistant cases 10 per cent. chrysarobin in spirit may be used in addition. These cases are always resistant to treatment, which requires to be carried on for long periods.

The acute eczematoid ringworms of the hands are often made worse by strong parasiticides, and it is generally better to start treatment with a wet dressing of 1 in 4000 potassium permanganate, subsequently trying small areas tentatively with the preparations mentioned above. The suppurative type can also be treated with 1 in 1000 acriflavine, or 1 in 4000 perchloride of mercury dressing, and subsequently with Whitfield's ointment, if not cured by the former methods. Resistant cases respond well to X-ray treatment.

(*d*) Ringworm of the Nails

This is fortunately not a very common affection, but occurs with sufficient frequency to be on the look out for it. It may be caused by the endothrix or ectothrix fungus.

Symptoms.—Usually several but not all the nails are affected. The disease usually commences under the free end of the nail, and travels slowly upwards. The nail bed becomes much thickened, and the epithelium sodden, and can be scraped away. As the disease spreads the nail becomes a greenish-grey colour and separated from its bed; the growing edge can be seen as a yellowish line above the discoloured and separated nail. In other cases the nail becomes soft or brittle and breaks up, exposing the underlying sodden nail bed. Very rarely the sides and base of the nail may be primarily affected. The toe nails are frequently affected in interdigital ringworm of the feet.

Diagnosis.—The diagnosis has to be made from eczema, psoriasis and syphilis. This can only be done with certainty by finding the fungus. Portions of nail near the growing edge should be taken and soaked for some hours in liq. potassæ. The under surface is then scraped and mounted, and a search made; and this may require several preparations before the mycelium is found. Cultures can often be made direct from pieces of nail; but contamination is very frequent.

Treatment.—The nail must be removed, either surgically or by softening in strong potash and scraping it away. Afterwards one of the stronger anti-trichophytic remedies can be applied. Norman Walker recommends covering the affected nails with lint soaked in Fehling's solution and applying a rubber finger-stall for 24 hours or longer, so as to remove the nail completely. The solution must not be applied to the surrounding skin.

2. FAVUS

Favus is a disease due to the growth of a fungus allied to ringworm, belonging to the genus *Achorion*. It differs from the former in forming thick, yellow, circular cups which cause local scarring and atrophy of the hair follicles. It is a much rarer disease in this country than formerly; but cases are still occasionally seen.

Symptoms.—Favus attacks the *scalp*, the glabrous skin and the nails, and has been recorded on the mucous membranes. On the scalp it appears as a collection of pea-sized or slightly larger circular yellowish crusts standing up from the skin and having a central depression, through the centre of which the hair projects. This is the favus cup or scutulum. Very large areas of the scalp may be involved in the process, the whole having a honeycombed appearance. Where the disease has been cured, scars and permanent alopecia are left. In section the yellow cup is seen to be made up of masses of mycelium radiating from the centre. Favus on the *glabrous skin* shows a somewhat similar appearance, a collection of bright yellow cups forming a massive crust, the whole being surrounded by an inflammatory zone. When seen in this country the lesions are generally very few in number and on the exposed parts, but in some countries where the disease is common the whole body may be covered with great masses of favus scutula. Favus of the glabrous skin in this country is often of mouse origin, and a different species to the scalp favus. Favus of the *nails* has somewhat similar characteristics to that of ringworm of the nails.

Treatment.—The only satisfactory treatment for favus of the *scalp* is X-rays. The risks of alopecia mentioned in the treatment of ringworm need not be considered here, as alopecia will result in any case from the disease. As a preliminary to X-Ray treatment the crusts should be removed and the scalp cleaned up with appropriate antiseptic applications.

In *body* favus the scutula must be removed, and the patches treated with either Whitfield's salicylic and benzoic ointment or a 4 per cent. chrysarobin ointment.

Favus of the *nails* is treated in the same way as ringworm of those parts.

3. MONILIA INFECTION

A good deal of attention has recently been paid to lesions closely resembling those produced by the ringworm fungi, but attributable to the growth of yeast-like organisms resembling those found in thrush. The lesions are chiefly found in moist situations, such as the groins, under the breasts and between the toes. The same fungus has been found to be responsible for a sodden condition between the fingers, to which the name *erosio blastomycetica interdigitalis* had formerly been applied. It has also been found in the nail folds, producing a curious bolster-like swelling of these structures, and has also attacked the nails themselves.

The *treatment* of these conditions is similar to that employed in ringworm.

4. TRICHOPHYTIDES

Of recent years a variety of generalised eruptions have been described in association with cases of fungus affection. These have been shown to

be produced in a way analogous to that in which the tuberculides are produced in cases of tuberculosis (see p. 1463). In certain fungus affections the skin becomes sensitive to the toxin of the fungus, as can be demonstrated by intradermal injection of extracts of the fungus concerned. It is presumed that either the fungus itself or its toxins enter the circulation and that eruptions at distant sites are thus produced.

The eruptions vary considerably in type; the lichenoid variety, consisting of numbers of pinhead-sized papules scattered over the trunk and analogous to the lichenoid tuberculide, is the commonest, but eczematous, scarlatiniform, morbilliform and urticarial eruptions have been described, and also lesions resembling erythema multiforme and erythema nodosum. Many of the vesicular eruptions of the palms and soles, associated with interdigital ringworm of the feet, are believed to be trichophytides.

The eruptions are described as microsporides, trichophytides, epidermophytides, favides and levurides, according to the nature of the primary affection, the last named being associated with monilia infections.

The diagnosis rests on the presence of an existing or recently pre-existing fungus infection, together with a proved cuti-sensitiveness to the toxin of the appropriate fungus.

No special treatment is required beyond that required for the primary affection, together with palliative treatment of the lesions.

5. TINEA VERSICOLOR

This is a superficial infection of the horny layer with the *Microsporon furfur*, and is frequently seen among hospital out-patients.

Symptoms.—It usually forms very thin, greenish-yellow patches or a continuous sheet over the chest and abdomen; but may cover larger areas of the body. It is said to occur chiefly in people who wear thick woollen underclothing and perspire freely. If the patches are scraped scales can be removed, and these examined in liq. potassæ show thin mycelial threads with large round spores among them.

Treatment.—The treatment is the same as for other body ringworms, salicylic and benzoic acid ointment or a sulphurous acid lotion causing rapid cure. The underclothing should, however, be sterilised, or reinfection will occur. Precautions against over-clothing should also be taken.

6. ERYTHRASMA

This is an uncommon disease in this country, and is due to the infection of the horny layer with an extremely small fungus, the *Microsporon minutissimum*.

Symptoms.—The affection occurs as superficial, reddish-yellow patches and plaques, more or less symmetrically arranged, chiefly in the groins and axillæ.

Diagnosis.—The malady is to be distinguished chiefly from tinea cruris, and this can readily be done by noting the size of the mycelial elements under the microscope. In erythrasma they are so small as to require a $\frac{1}{12}$-inch objective, and under it appear as small bead-like chains, with masses

of spores intermingled, while in tinea cruris chain-like mycelium can easily be seen under a ⅛-inch objective.

Treatment.—The treatment is the same as for pityriasis versicolor.

7. LEPOTHRIX

This is a not very uncommon affection of the axillary hairs in which they become surrounded with dark reddish concretions.

According to Castellani, this affection is caused by a bacillary-like fungus, *nocardia tenuis*, acting in symbiosis with a red pigment-forming coccus, *micrococcus castellanii*.

The treatment consists in dabbing the affected hairs twice daily with alcoholic formalin (2 per cent.), and rubbing in at night a 2 to 5 per cent. sulphur ointment. Calamine lotion may be used to allay any irritation caused by the treatment (Castellani).

DERMATITIS DUE TO ANIMAL PARASITES

The affections of the skin due to animal parasites are of a mixed variety, but for general purposes may be classed under the superficial dermatoses. Animal parasites produce their effects on the skin either by puncturing and injecting an irritating substance or by burrowing in the skin; but what have chiefly to be taken into consideration are the secondary effects produced by the irritation these creatures produce. In tropical countries the number of animal parasites which produce skin lesions is very large; it is proposed here, however, to consider only those seen commonly in this country.

1. BITES AND STINGS

The common flea, the bed-bug, gnats and the pediculus family are the common biting insects seen in this country, while of the stinging insect bees, wasps, hornets and ants may be mentioned. Excluding pediculi, which require more detailed description, the lesions produced by all these insects are wheals of varying size, depending on the particular insect, and also on the susceptibility of the person attacked. The lesions are familiar to all, and require no detailed description.

Treatment.—As most of these stings are due to an acid irritant, the application of weak solution of ammonia and other alkalis gives most relief. In the case of the bee the sting should be removed if still in the skin.

2. PEDICULOSIS

Three forms of pediculi attack man: the *Pediculus capitis*, the *P. vestimentorum* or *corporis*, and the *Pediculus* or *Phthirius pubis*.

The first two are merely varieties of the same species—the *Pediculus humanus linnæus*.

Pediculosis Capitis.—**Ætiology.**—This condition is caused by a small insect, 2·5 to 3 mm. long, with an oval body consisting of a narrow thorax and wide abdomen, to the former of which are attached six legs, each being provided with a hook-like extremity, with which it hangs on to the hairs. The head is small, oval, and provided with two antennæ, a powerful mandible

and a proboscis with which it punctures the skin in order to suck the host's blood. This variety is found among the scalp hairs, chiefly in female children of the lower classes. Pediculi breed with great rapidity, laying their eggs on the hairs. The eggs are contained in a chitinous, ovoid cell, with a movable lid or operculum, and are known as nits; they are laid from the scalp outwards, and each is stuck on to the hair by a drop of cement extruded by the female as she moves along the hair. Nits can only be removed by unthreading them from the hairs.

Symptoms.—Itching is the only symptom produced by the *P. capitis*, and this is due to an irritating substance injected by the insect when it bites. A large number of infested individuals feel no itching; they are, however, a source of danger, as they infect others. If the itching is severe, scratching follows, and this frequently causes impetigo contagiosa, which is most marked at the back of the scalp, but may spread to the vertex, eventually involving the whole scalp and matting the hair down among thick crusts. Similarly it may spread to the back of the neck and shoulders, and involve large areas of the body. Even when impetigo is absent, the presence of scratch marks on the back of the neck and shoulders is almost diagnostic of *P. capitis*.

Diagnosis.—All cases of impetigo of the scalp, especially in children, should be examined for pediculi. The diagnosis is easily made by finding the pinhead-sized, white, shiny oval bodies attached to the base of the hairs, and in bad cases the transparent little insects themselves can be seen scuttling about among the hairs.

Treatment.—The insects are easy to kill, but the nits are more resistant. The favourite method is to saturate the scalp with paraffin and tie it up for 12 hours; this has the disadvantage of being messy, and is not free from danger if the head is brought too near a naked light. Whitfield's method of saturating the hair with 1 in 40 phenol and then tying the hair up in it for half an hour is very efficacious, especially when much impetigo is present. After this, the crusts can be removed and the nits combed out, and a weak ammoniated mercury ointment applied.

PEDICULOSIS VESTIMENTORUM.—**Ætiology.**—The causative parasite has exactly the same anatomical character as the preceding, but is usually slightly larger, up to 3 to 4 mm. in length. It is not very common in civil life, being only seen in the habitués of the casual ward and the common lodging-house. In war-time, however, it becomes one of the chief causes of sick wastage of armies, being almost universal in its incidence and causing an enormous amount of skin disease.

The insect lives chiefly in the clothes, coming on to the body in order to feed; it is chiefly found, therefore, in those parts of the clothing which come into most intimate contact with the body. In civil life the *Pediculus vestimentorum* is rarely seen, but its nits may be found in the seams of the underclothing of infected persons. Occasionally in heavily infested people nits may be found on the axillary, pubic and perineal hairs.

Symptoms.—The skin lesions in this condition are mainly those produced by scratching. Closely placed, small, red macules may occasionally be seen, the results of the insect bites, but this is unusual. The scratch eruption has a characteristic distribution and type. In civilians, it is most marked about the back of the shoulders and around the waist and upper part

of the buttocks. In soldiers, it is even better marked on the legs and about the knees, owing to wearing the puttee. The lesions in earlier cases are papules, surmounted by hæmorrhagic crusts and linear excoriations. In cases of longer standing, areas of eczematisation and lichenification occur, and the skin becomes irregularly pigmented. Septic complications are not very common in civil life, but in the field are the rule. Boils and linear, gutter-shaped ulcers, described under ecthyma on p. 1432, are extremely common under these latter conditions, chiefly on the legs.

Diagnosis.—This has chiefly to be made from scabies, but the presence of the burrows and the distribution of the rash—described in detail in the article on that disease (p. 1444)—should enable a diagnosis to be made. From senile pruritus the diagnosis can only be made by finding lice or their nits.

Treatment.—Disinfection of the clothing and bedding of the infected person is all that is required, except in those who harbour nits on their hairs, in which case the latter should be cut short or shaved. Most local sanitary authorities will carry out the necessary disinfestation if duly notified; the methods employed scarcely come within the scope of this work. Local lesions can afterwards be treated with sedative lotions and creams, and impetiginous lesions as already described (p. 1421).

Pediculosis Pubis.—**Ætiology.**—The *Pediculus* or *Phthirius pubis* has a different appearance from that of the above-mentioned varieties; the body is shorter, wider and almost triangular in shape. It is usually about 1·5 mm. long and about the same width, and is provided with six legs, which are more curved than in *Pediculus humanus* and are also provided with hook-like extremities. This louse can move with considerable rapidity along the hairs, but has very limited powers of movement on a flat surface. When found among the hairs it is seen clinging with its legs to two adjacent hairs. Its eggs are laid in the same manner as with other varieties.

The pubic louse is found almost exclusively in the pubic and perineal hair, but in severe cases the hair in front of the abdomen, chest and thighs may be infested, as may also the axillary hairs, the beard, the eyebrows and eyelashes. It is extremely rare on the scalp. It is usually transmitted during coitus.

Symptoms.—There are two main symptoms, itching and the presence of small bluish stains on the skin. The itching is often intense and may lead to loss of sleep, but is localised to the area attacked. Scratch lesions are not very common, doubtless owing to the protection afforded by the stout pubic hairs; they do, however, occur. The bluish stains found on the skin in regions infested by the crab-louse are now known to be produced by the bites of the insect. They are 4 to 10 mm. in diameter, not raised above the skin, and do not disappear on pressure. They are known as *maculæ cæruleæ*.

Diagnosis.—This is made by finding the louse and its nits attached to the base of the hairs.

Treatment.—The best results are obtained by clipping the hair short and rubbing in 5 per cent. betanaphthol ointment. Ung. hydrarg., phenol lotion (1 in 40), and petrol are also used, but the former of these may set up a severe dermatitis if not carefully used. On the eyelashes, the insects and their nits should be removed by forceps.

3. SCABIES

Ætiology.—Scabies is a disease caused by a spider-like, acarine parasite, the *Sarcoptes scabiei*. The acari form a large group of animal parasites which attack man and the lower animals. The parasite generally found in man (var. *hominis*) is a special variety and is not contracted from animals. Various other acari, however, which attack animals may also attack man, but they do not produce identical symptoms.

The *Sarcoptes scabiei*, commonly spoken of as the acarus, is a minute round body, just visible to the naked eye, and of white shining appearance. The body bears eight legs, which differ in the two sexes. In both sexes the two anterior pairs bear suckers; in the male the third pair bear long bristles and the fourth pair bear suckers, while in the female both hind pairs bear bristles. The female is larger than the male, and burrows in the horny layer of the skin to lay her eggs. If undisturbed the female may live for 2 to 3 weeks and lay up to about 30 eggs. The eggs are laid in the burrow and the young hatch out there, the complete cycle from egg to mature acarus being completed in about 10 days. The larvæ, however, hatch out in 3 to 3½ days.

The female acarus has certain favourite sites for burrowing, namely, the genitals, the fronts of the wrists, the web and sides of the fingers, the ulnar border of the hand, the backs of the elbows, the anterior axillary folds, the nipples in women, the umbilicus, the sides of the gluteal cleft and lower part of buttocks, the front of the knees, the ankles and the dorsum of the feet. In infants the palms and soles are also frequently affected.

Symptoms.—The eruption of scabies is of two kinds—the acarine burrows and the follicular papular eruption. The burrows occupy the sites named above. They are seen most clearly on the hands, where they usually form thin, sinuous lines, from a millimetre up to a centimetre in length and occasionally even longer. The burrow is generally easily seen, as dirt accumulates in it, but quite often it can only be recognised by a lens. The oldest part of the burrow has a splay mouth, while at the other end the small white body of the acarus, with a black spot in its fore part, can be easily seen with a lens and often with the naked eye. Frequently a clear vesicle or vesicles are seen beneath the burrow, but as a rule on the hands no redness is present unless secondary infection has occurred. When blisters are present, secondary infection is frequent, and pustular, weeping and crusted areas are produced. In other sites vesicles are not common, but a large pea-sized papule usually underlies the burrow, and the burrow itself and its acarus are not so easily seen; these lesions are frequently seen on the penis, scrotum and anterior axillary folds, and are usually diagnostic.

The follicular papular eruption is arranged in smaller or larger circles round the areas where the burrows occur. The main distribution is on the anterior aspect of the body, from the nipples to the knees, and in a semi-circle around the anterior axillary fold. The back is free, except in severe cases, down to the top of the gluteal cleft, but scratch lesions occur on the lower part of the buttocks, where ecthyma is often a complication, and on the back and inner parts of the thighs. On the limbs the eruption occupies both front and back of the forearms, up to about the centre of the arm, and

also occurs around the ankles. The lesions are first pinkish or whitish elevations of scattered hair follicles, but soon they become covered with bloodstained crusts from scratching. Linear scratch marks are rare in scabies. It is not clear what produces the scratch eruption in scabies, but the work of J. W. Munro suggests very strongly that the follicular lesions are produced by the acarine larvæ, and the distribution of the lesions adds confirmation to this view.

In old-standing cases almost the whole body may be affected, though the face and scalp are practically never attacked in adults; but in small children even these areas may suffer.

Diagnosis.—In well-marked cases no difficulty arises, as the burrows can be seen, but in treated cases the diagnosis may be very difficult and a diagnosis from pediculosis may have to be made. Also the two conditions may occur together. The distribution and character of the rash will usually settle the point, but a careful search with a lens for burrows and acari should always be made.

Treatment.—This depends more on the carrying out of detail than on the actual parasiticides used. Three things are necessary, namely, the opening of the burrows by scrubbing, the subsequent application of a parasiticide to the body, and the disinfectation of clothes and bedding. The body should be soaked in a hot bath, then rubbed with soft soap, and finally scrubbed with a brush, particular attention being paid to areas where burrows occur. After this sulphur ointment is rubbed in all over the body (face and scalp excepted), and the patient again dresses, his clothes having been disinfected in the meanwhile. On the two following days the ointment is again rubbed in, but no bath given (as it tends to increase the liability to sulphur dermatitis), on the fourth day nothing is done, and on the fifth day the patient has a bath—to wash off the ointment—and puts on clean things, all dirty linen being sent to the wash. If any dermatitis from the sulphur arises, lin. calaminæ, to which 2 per cent. liq. pic. carb. is added, may be smeared on, and if there is much sepsis appropriate treatment can then be applied. Another satisfactory method is to paint the body, after the bath and before drying, with a lotion composed of benzyl benzoate, soft soap and industrial spirit, in equal parts. This is allowed to dry, and the painting repeated at once. Twenty-four hours later a cleansing bath is given. Other preparations which have been used with success are ung. potassii polysulphidi (B.P.C.) (Marcussen's or Danish ointment), 5 per cent. betanaphthol, and 12 per cent. balsam of Peru ointment.

B.—THE DEEP INFLAMMATORY DERMATOSES

Under this heading are included those inflammatory conditions which start in the dermis or hypoderm, and only involve the epidermis secondarily. It is often easy to decide clinically whether an inflammation starts in the dermis or in the hypoderm, and strictly these conditions should be described separately; but as the same exciting cause may often produce either condition, it is simpler to describe them together.

The causative irritant may reach the point attacked in three ways—namely, (1) through a crack or puncture in the epidermis, (2) by the lymphatics, or (3) by the blood stream. In the first group are included those cases in which certain chemical poisons are introduced into the skin by the bites and stings of insects (already dealt with on p. 1441), and cases in which micro-organisms are introduced into abrasions, as in the case of erysipelas from the streptococcus (p. 19), syphilitic chancre from the *Spirochæta pallida* (p. 193), soft sore from Ducrey's bacillus, lupus vulgaris and lupus verrucosus from the tubercle bacillus (pp. 1460, 1462), and actinomycosis, sporotrichosis, etc., from certain fungi. The second group includes certain lesions produced by bacterial irritants, such as are seen in the lymphangitis abscess in tuberculosis and the sporotrichial gummata. The third group includes the drug eruptions and other dermatoses, which are labelled toxic eruptions and which are presumably due to chemical poisons circulating in the blood, and also eruptions due to the circulation of micro-organisms, such as are seen in the syphilides and tuberculides. For convenience of description it is proposed to deal with the majority of deep inflammatory dermatoses under two headings—(1) the toxic eruptions, and (2) eruptions produced by living organisms. It must be understood, however, that in the present state of knowledge the ætiology of many of those included in the former group is still very obscure. There is also a third group of dermatoses whose characters make it difficult to place them in either group, and these have, therefore, been described as (3) *dermatoses of unknown origin*.

TOXIC ERUPTIONS

It is practically impossible to produce experimentally in animals any of the toxic eruptions, owing to the fact that no animal has a skin comparable to that of man. Consequently, all our experimental knowledge of toxic eruptions has to be derived from the observed effects of drugs and foodstuffs on the human skin. It is, therefore, proposed to consider first the eruptions produced by these substances.

1. DRUG ERUPTIONS

These fall into two great classes—those produced by non-protein-containing and those produced by protein-containing drugs. Extracts of organs given by the mouth rarely, if ever, produce eruptions and are, therefore, not specially considered.

(*a*) Non-Protein-Containing Drugs

These include all the ordinary galenicals.

Two classes of eruption are produced by non-protein-containing drugs. (1) Non-specific eruptions, which may be produced indiscriminately by many different drugs, and (2) specific eruptions, which are peculiar to certain drugs.

(1) Non-Specific Eruptions

Symptoms.—These are generally erythematous, urticarial or purpuric. The erythematous rashes may be scarlatiniform, morbilliform, or, more

rarely, of the erythema multiforme type; sometimes the lesions are vesicular. Urticarial lesions are usually of the simple urticaria type, but occasionally the giant forms are seen. Purpuric lesions are often erythematous at the start and develop hæmorrhages later. It is difficult to classify drugs into any special groups by the reactions they produce, but it may be noted that the under-mentioned types of eruption may be produced by the drugs named:

Erythematous.—Acetanilide, alcohol, arsenic, aspirin, barbituric acid and its derivatives, belladonna, benzoic acid, cantharides, capsicum, chloral, chloralamide, chlorbutol (chloretone), chloroform, copaiba, cubebs, digitalis, ipecacuanha, mercury, opium, phenazone (antipyrine), pilocarpine, phenacetin, quinine, rhubarb, salicylic acid and the salicylates, stramonium, strychnine, sulphonal and turpentine.

Urticarial.—Antimony, arsenic, barbituric acid and its derivatives, benzoic acid, chloral, copaiba, digitalis, opium, phenacetin, pilocarpine, quinine, salicylic acid and the salicylates, santonin, turpentine and valerian.

Purpuric.—Arsenic, chloral, chloroform, copaiba, ergot, hyoscyamus, iodoform, mercury, phosphorus, quinine, salicylic acid and the salicylates, stramonium and sulphonal.

(2) Specific Eruptions

Symptoms.—Certain drugs give rise to eruptions which are characteristic of the drugs. Arsenic, bromides, iodides, phenazone (antipyrine), phenolphthalein, mercury, silver and gold are the most important.

Arsenic.—In addition to simple erythematous and urticarial lesions, an acute generalised exfoliative dermatitis may develop. This is especially seen after injections of arsphenamine (salvarsan). Herpes zoster also occurs. Pigmentation, especially about the trunk, though it may be more or less generalised, is seen in chronic arsenical intoxication. It usually presents a fine reticular pattern. Hyperkeratosis occurs chiefly on the palms and soles; it may be diffuse or occur in localised, corn-like projections. Occasionally these localised hyperkeratoses develop into epitheliomata. Excessive sweating of the palms and soles (hyperidrosis) may occur, and the nails may become striated and brittle.

Bromides.—Two main types of specific eruption are seen. Bromide acne is a follicular hyperkeratosis, often closely resembling acne vulgaris and seen in the same situations, but often more extensive, involving the legs and arms, as well as the face, chest and back. It is seen chiefly in epileptics who have taken bromide for some time. The other form is the so-called "anthracoid" form, which is most commonly seen in infants and children; in the former the drug is often conveyed in the mother's milk. Nodules and tumours varying in size from a pea up to an inch or two in diameter are found, chiefly on the face and legs. The tumours are of a deep red colour and studded with minute pustules; in the larger lesions the surface is often crusted, and in some cases ulceration occurs. The lesions may develop and persist for a considerable time after the drug has been discontinued.

Iodides.—The most typical lesions produced by iodides are papules which look like vesicles and bullæ, but when pricked only blood escapes. They are sometimes spoken of as "pseudo-bullæ." They are common on the face and extremities, and often appear after taking quite small doses of iodides,

and within a very short time, even as quickly as 24 hours. They are most common in patients suffering from nephritis. These lesions may increase rapidly in size and produce large tumour-like masses, studded with pustules or with a crusted or ulcerated surface, and when occurring in patients who are seriously ill may hasten a fatal termination from septic absorption. In the early stages the cases have been mistaken for small-pox. An acne similar to that produced by bromides is also seen.

Phenazone (*Antipyrine*).—In addition to producing the more generalised types of eruption phenazone may produce large erythematous reddish or purplish patches, situated discretely over the body, of sharply circular outline and giving rise to a sensation of burning. When they subside they leave a very marked pigmentation, which disappears very slowly.

Phenol-phthalein.—This drug, now largely used as an aperient and contained in many proprietary remedies, occasionally produces an eruption similar to the last named. The patches are of dull purplish colour and come out on face and limbs, but often also affect the mucous membrane of the mouth. The lesions belong to the group known as "fixed eruptions," as they tend to recur at the same site if the drug is repeated.

Mercury.—This drug occasionally gives rise to a severe erythema in the groins and axillæ, and also on the palms and soles. There may be also purpuric spots and vesicles. Other symptoms of mercurialism, such as nephritis and ulcerative stomatitis, may also be present.

Silver.—Long-continued ingestion of this drug produces a peculiar slaty-grey pigmentation of the skin, generally universal, but most marked on the exposed parts. It scarcely comes under the heading of inflammations, but is included for the sake of convenience.

Gold.—Injections of gold may give rise to a general exfoliative dermatitis, similar to that of arsphenamine.

(*b*) Protein-Containing Drugs

These include serums and vaccines. Vaccines rarely cause marked cutaneous eruptions, but when they occur they are of similar nature to those produced by sera. Serum eruptions form a very interesting group, as it is reasonable to suppose that their method of production is closely analogous to that of those toxic eruptions whose ætiology is obscure. For it has been assumed that these are due either to absorption of poisonous proteins produced by the body or to the toxins of pathogenic bacteria which are present in the body.

Serum eruptions are supposed to be an anaphylactic phenomenon and, though this seems to be a reasonable explanation in those cases where the rashes follow a second injection of a foreign protein given at least 14 days after the first, it does not fit in so well for cases in which the eruption follows the first injection of serum. In these cases a specific allergy must be assumed to exist.

Symptoms.—Any of the above-mentioned non-specific eruptions may develop, but there is a greater tendency for the lesions to be of the *erythema multiforme* type. Often the rash is very extensive, the trunk, face, and limbs being covered with disk-like, sharply circumscribed, infiltrated red lesions; these often become bullous, and hæmorrhages may occur in the

centre of the lesions. In other cases ringed lesions occur, which spread peripherally and clear in the centre—*erythema gyratum*. Not infrequently these lesions are associated with fever, and pain and swelling in the joints, and gastro-intestinal disturbances, such as diarrhœa and vomiting and albuminuria. In other cases the lesions are more of an urticarial nature, with transitory, very itchy wheals and swelling of the skin of the face. These eruptions usually come out about a week or 10 days after the injection of the serum and clear up in about the same time.

Similar eruptions sometimes develop in persons vaccinated against small-pox, though in addition a true vaccinial eruption, in which the lesions have the characters of the vaccine vesicles, may develop.

Urticarial lesions develop in certain individuals who are sensitive to certain food-stuffs, after ingestion of these substances. They will be considered more fully under Urticaria (p. 1451).

(*c*) The Treatment of Drug Eruptions

The first thing is to stop the drug causing the eruption. In the erythematous and urticarial types local soothing lotions are indicated, of which the most useful are lotio evaporans (B.P.C.), or phenol min. 120, lot. calaminæ (B.P.C.) ad fl. oz. 12. Alkaline and bran baths are often very useful.

In the serum eruptions, calcium chloride or lactate is recommended and may be given in 10-grain doses three times a day. Quinine, grs. 1 or 2 three or four times a day, is sometimes of value. In the more severe cases the patient must be kept in bed.

2. THE ERYTHEMATA

The term erythema may be used to signify any transient redness of the skin, such redness being frequently produced by external irritants; and these have already been dealt with under the superficial inflammatory dermatoses. When, however, the term is used to describe a composite clinical picture, two main types have to be considered, namely, the non-infiltrative and the infiltrative.

(*a*) The Non-infiltrative Erythemata

These include two classes, the congestive and the inflammatory. The congestive type has little or no dermatological importance. It is seen in blushing, which is a pure vasomotor phenomenon, and also in such transitory rashes as that seen during ether administration. The inflammatory type includes the rashes seen in scarlet fever, measles and rötheln, drug eruptions just referred to, and certain other toxic conditions.

Ætiology.—One of the commonest varieties of erythematous rashes is that occurring as the result of septic absorption from a wound, and many of the cases of so-called surgical and puerperal scarlet fever belong to this group. They also occur in ptomaine poisoning and in other infections of the gastro-intestinal tract, but there always remain a number of cases in which no cause can be found.

Symptoms.—Erythematous rashes are usually of either the scarlatiniform, morbilliform or figurate type. The scarlatiniform cases differ from

true scarlet fever in the absence of other typical signs, such as high temperature combined with rapid pulse, the date of appearance of the rash, the presence of sore throat and the characteristic appearance of the tongue. The morbilliform erythemata differ from measles in the absence of coryza, conjunctivitis and respiratory catarrh. The temperature is atypical and Koplik spots are not found. The figurate variety consists of patches or groups of disk-like lesions which tend to spread peripherally and clear in the centre so as to leave circinate and gyrate patterns. It is seen most commonly in drug eruptions, and can hardly be confused with anything else. In all these varieties as the eruption subsides there is a tendency to scaling, usually of the fine branny type, and this may often be extensive; the glove-like scaling of the palms and soles, seen in scarlet fever, may also occur in the simple types of erythema.

Hæmorrhage may sometimes take place into the erythematous patches, especially when these occur on the lower limbs. Most cases of simple purpura really belong to the erythema group. The mucous membranes may be affected similarly to the skin, and other general symptoms, such as diarrhœa, vomiting, fever and albuminuria, may be present.

Treatment.—Attempts must be made to find and remove the cause. All possible septic foci, such as pyorrhœa, tonsillar sepsis and chronic appendix trouble, should be dealt with. The bowels should be made to act freely and a light diet ordered. Cases should generally be put to bed, and always when there is fever or any marked constitutional symptoms. In cases of streptococcal infection, sulphapyridine may be given.

(*b*) The Infiltrative Erythemata. Erythema Multiforme

Ætiology.—Erythema multiforme may occur as a drug eruption, and especially as a serum eruption, as already noted, but it generally appears without any special cause being determinable. It occurs especially in young adults and may often recur, some cases doing so year after year at regular intervals. Individual attacks may clear up rapidly, but in many cases fresh crops appear, and the disease may go on for weeks or months. The joint swellings which sometimes accompany the skin lesions led to the supposition that the condition was of rheumatic origin, but it is probable that these are only a manifestation of a similar affection of the synovia of the joints.

Pathology.—Microscopic examination shows a dilatation of the vessels of the dermis with a leucocytic exudation. There is much local œdema. The epidermis is œdematous, and fluid may accumulate beneath the horny layer or less frequently beneath the epidermis.

Symptoms.—The lesions of erythema multiforme differ from those mentioned in the last section in forming raised infiltrated lesions, which vary in size from a pea to a five-shilling piece or larger, and which have a well-defined distribution. They are usually found on the backs of the hands, wrists, and forearms and on the face, but are not infrequently found on the palms, and may also involve the trunk and lower limbs. In the milder cases they consist of red papules and patches with a sharply-defined border and are usually completely circular in outline. In the more severe forms hæmorrhages occur in the centre, or they become surmounted by bullæ. There is some tendency to slow peripheral extension, with clearing up of the centre,

so that ringed lesions may be formed. In these a play of colours may be noted, the outer red ring surrounding a purple hæmorrhagic ring, which in its turn surrounds a brownish pigmented centre; these lesions are sometimes called *erythema iris*. In rare cases the bullæ so predominate as closely to resemble a pemphigus. The subjective symptoms are often slight, but sometimes itching and burning occur. Lesions may appear on the mucous membranes. Pain and swelling in the joints are not infrequent, and gastro-intestinal disturbance may occur, as may also fever and albuminuria.

Treatment.—Care must first be taken to remove any possible cause. Of the drugs which are of value are calcium lactate, the salicylates and quinine. The former is best given in 240 minim doses on alternate nights. Local treatment is not really necessary, but calamine lotion or liniment may be applied to relieve itching or burning.

Erythema nodosum is closely related to erythema multiforme, and is dealt with on p. 296.

3. GRANULOMA ANNULARE

This is a very chronic, raised, ringed eruption, of dead white colour, seen chiefly on the dorsum of the hands.

Ætiology and Pathology.—The cause of this condition is unknown, but various intermediate types between it and erythema multiforme have been noticed, and this suggests a relationship with the latter condition. Histologically a dense cellular infiltration, associated with degeneration of the collagen bundles, is found in the deeper layers of the dermis, especially in the neighbourhood of the sweat coils.

Symptoms.—The earliest lesions are small white nodules, seen most commonly on the back of the finger joints. Such lesions often occur in groups. They spread slowly, the centre of the group becoming flattened, and surrounded by a raised, white festooned margin, which can be seen to be made up of nodules of the same character as those of the original lesions. The disease is very slowly progressive, and may last for months or years if not treated. The lesions are generally localised to the hands and wrists, but are occasionally seen in other parts of the body, such as the nape of the neck, the buttocks, elbows and knees. In some cases subcutaneous fibrous nodules have been described in the neighbourhood of the elbow joints and elsewhere. Subjective symptoms are generally absent.

Treatment.—Internally, quinine and the salicylates may be given. X-rays will often cause the lesions to disappear, but no other local treatment has much effect.

4. THE PURPURAS

The purpuras form a group which are closely related to the erythemata and are very often erythematous at the start. In them, however, the blood vessel walls are damaged and hæmorrhage occurs into the dermis. They may be of toxic or of bacterial origin. They are considered in detail on p. 810 *et seq.*

5. THE URTICARIAS

The urticarial eruptions are characterised by the presence of wheals, or localised areas of œdema. These are usually transitory in character and

are accompanied by severe itching. Several different forms are recognised—(1) Simple urticaria, (2) factitious urticaria, (3) giant urticaria, (4) papular urticaria, and (5) urticaria pigmentosa.

Ætiology.—As is pointed out above, urticaria can be produced by the ingestion of certain drugs and by injections of foreign sera. It can also be produced by the ingestion of certain food-stuffs in susceptible persons; for example, porridge, strawberries, shell-fish, eggs and milk. It also occurs after the consumption of decomposing food. As far as is known it is not due to the direct attack of any micro-organism, though syphilitic urticaria has been described. It is clear that it may be produced not only by protein poisons, but by non-protein poisons circulating in the blood. The actual mechanism by which the lesions are produced is not altogether clear. At one time it was thought to be a pure vasomotor neurosis, and that the poisons mentioned acted on the vasomotor centres; but in recent years it has been demonstrated that the lesions are true inflammations, and, therefore, it is probable that the action of the poison concerned is a local one. At the same time external stimuli, such as friction, seem, in many cases, to play a part in determining the points where the poison acts. Lewis believes that the lesions are produced by the liberation of a histamine-like substance from the tissue cells. It must also be noted that urticarial lesions may be directly produced by the injection of poisons into the skin. This is well seen in the bites and stings of insects, and the stings of plants, such as the nettle. In a large number of cases of urticaria, however, it is difficult to find any cause, and these are usually considered to be auto-toxic. The auto-toxin may be generated in the intestinal tract, or in infected foci, such as septic tonsils and teeth and inflammatory trouble in the pelvis. In the giant urticaria cases there is usually a considerable functional element present, and these cases are considered to be vasomotor neuroses. Nothing is known of the ætiology of urticaria pigmentosa.

Symptoms.—*Simple urticaria.*—This is the form most frequently met with in adults. It may occur in an acute or in a chronic form. In the former the eruption appears suddenly, is often accompanied by general symptoms, such as fever, diarrhœa and vomiting, and subsides more or less rapidly. In the chronic type the eruption appears in crops; the individual lesions run a more or less rapid course, but fresh crops continue to come out at intervals and the condition may persist for many weeks, months or even years.

The lesions of simple urticaria are in their earliest stages pale pink papules or patches, varying in size from a pea to an inch or two in diameter. In a short time—sometimes a few minutes, at others an hour or so—the central part of the patch becomes a dead white colour, is firm to the touch and raised a millimetre or two from the surrounding skin. The lesions are intensely itchy. They may be few in number or very numerous; sometimes the whole body may be covered with patches of all shapes and sizes, and figurate patches are common. The eruption is most common on the trunk, but any part of the body, including the mucous membranes, may be affected.

Factitious urticaria.—This is a condition of the skin in which the slightest trauma, such as a slight scratch, will bring out a wheal. This condition is often present in simple urticaria, but frequently exists apart from any spontaneous eruption. The condition is sometimes referred to as *dermatographism*, as it is possible to produce letters in urticarial wheals on the patient.

Giant urticaria.—In this condition the lesions are not so much wheals as circumscribed patches of œdema. They are particularly liable to occur about the face—the eyelids, cheeks and lips often swelling up quite suddenly—burning or itching being an accompanying phenomenon. The mucous membranes are not infrequently attacked, and in a few cases sudden œdema of the larynx may produce dangerous asphyxial symptoms. The lesions are very prone to recur, and these recurrences may persist for years. This condition is sometimes spoken of as *angio-neurotic œdema* (see p. 1073).

Papular urticaria.—This type may be a distinct disease or only a variant of simple urticaria, but is that commonly seen in infants and young children. It is not very commonly seen in breast-fed infants, though it does occur, but otherwise is chiefly seen in the first two years of life; it may in some cases, however, persist, with intermission, up to about 7 years of age. The lesions appear, just like those of the adult form, as pink oval patches, usually about ¼ inch in diameter, but instead of the bulk of the whole patch being converted into a wheal only a central pinhead-sized wheal is produced. Itching is intense and often paroxysmal. When the lesion is scratched the central papule becomes inflamed and a bloodstained crust is formed on its summit, and it persists after the surrounding pink zone has disappeared. The cases usually present discrete pinhead-sized papules, covered with bloodstained crusts, suggesting a parasitic origin. Not infrequently vesicles surmount the wheals and occasionally quite large bullæ are found.

The eruption comes out in crops, especially at night, and chiefly on the extensor aspect of the lower limbs, the buttocks and the extensor aspect of the forearms, but may occur almost anywhere on the body. The children seem to suffer little in general health, though sleep at night is often lost, its effects being often more obvious in the parents.

Urticaria pigmentosa.—This is a rare condition and it is still a question whether it should be grouped with the other urticarias. It is chiefly a disease of infancy and childhood, but a certain number of adult cases are on record. The condition may appear within the first few days of life, and in a few cases lesions are said to have been present at birth.

The lesions usually appear as wheals, ¼ to ½ inch in diameter; and as these disappear a yellowish-brown colour is left, and the lesion may remain raised above the surrounding skin or may flatten down to a pigmentary macule. These pigmented lesions generally persist for years. Itching may or may not be present. Sometimes marked factitious urticaria can be elicited. It would appear that occasionally simple urticarial lesions may leave behind pigmentation, but the condition described above is something quite distinct. In true urticaria pigmentosa there is generally a great increase in the mast-cells of the dermis which is absent in ordinary urticaria leaving pigmentation.

Diagnosis.—Simple urticaria may be confused with dermatitis herpetiformis and with the premycosic stage of mycosis fungoides. In the former, small deep-seated vesicles usually occur; but as they are not always present the diagnosis may be difficult. From the latter a diagnosis cannot be made with certainty, though when occurring in old people and persistent, mycosis fungoides must be considered.

The giant forms must be distinguished from erysipelas and acute erythematous eczema. In the former, high temperature is present, the lesion has

a sharply defined, slowly spreading margin, and is often blistered. In the latter, the eruption is extensive and symmetrical, the skin is red, and vesicles are frequently present. Chronic erysipelas of the lip is a persistent, slowly increasing condition and usually arises from a persistent crack in the lip, while urticaria has a sudden onset and disappears again.

Papular urticaria in children is most frequently confused with scabies. The diagnosis can be settled by the presence of burrows and the finding of acari in the latter condition. In the vesicular form cases may be confused with varicella, but the course of the eruption is quite different.

Urticaria pigmentosa is not likely to be confused with any other condition.

Treatment.—If a cause can be found it must be removed: articles of diet known to cause the eruption must be avoided and all possible septic foci dealt with. If the cause is not clear, various types of food must be stopped one by one in order to exclude a possible source of trouble. Recently a cuti-reaction to various foodstuffs has been devised to detect the causative agent, and it is possible to desensitise patients from the particular poison to which they are susceptible. Apart from this, mild purgation and the administration of intestinal antiseptics, such as salol, ichthammol, creosote and calomel, can be recommended. Some patients improve on tonic drugs, such as iron, arsenic and quinine. Calcium chloride or lactate given over prolonged periods is efficacious in some cases. In others complete freedom from work and even rest in bed are necessary. In cases of unknown ætiology, non-specific protein therapy, such as injection of whole-blood, milk or peptone, is of great value (see p. 1418).

In the papular form in children excessive intake of sugar plays a part in a proportion of cases, and by a rigid cutting down of jams, sweets, etc., relief is often obtained.

In the giant form nerve sedatives, such as valerian and the bromides, are of value.

Locally, anti-pruritic lotions are most useful. Solution of coal tar and subacetate of lead, min. 120 of each to fl. oz. 8 of water; or liq. potass. hydroxid. min. 60, glycerin min. 60, to fl. oz. 8 of water, may be used and can be applied frequently; alkaline and bran baths also give considerable relief. In children a teaspoonful of liq. picis carbon. added to a warm bath before going to bed is a valuable remedy, and in some cases sulphur ointment grs. 15 to 1 ounce has proved useful; but lotions are usually better tolerated.

There is no known treatment which affects urticaria pigmentosa.

6. PRURIGO

Prurigo of Hebra is a condition which is rare in this country, but is not uncommon in Eastern Europe. It is apparently closely connected with papular urticaria, but most authors consider it a distinct affection. It begins usually in the first or second year of life, by the appearance of intensely itchy, pinhead to lentil-sized papules on the extensor aspects of the limbs, chiefly on the legs and forearms; these soon become covered with bloodstained crusts, and eventually the whole of the skin of the affected area becomes thickened (lichenified), pigmented and excoriated. The lesions may eventually involve the whole of the limbs, but the flexures usually escape. The trunk, neck and face may become eczematised and lichenified. The glands

in the groins and axilæ become much enlarged. The milder cases (prurigo mitis) may eventually respond to treatment and get well about the time of puberty, but the more severe cases (prurigo ferox) persist throughout life, the patient eventually succumbing to the disease.

Treatment.—There is no specific treatment. Baths and sedative lotions and ointments, together with sedative drugs, to relieve itching and to ensure sleep, should be employed.

7. DERMATITIS HERPETIFORMIS

Dermatitis herpetiformis or Duhring's disease is a condition characterised by the appearance on the body of crops of erythematous or urticarial papules or patches, usually surmounted by herpetic vesicles or bullæ, and giving rise to intense itching.

The evidence for placing this disease among the toxic eruptions is not conclusive, but is sufficiently suggestive to make it justifiable. In this connexion may be mentioned its occurrence as one of the rarer toxæmias of pregnancy (hydroa gestationis), and its close clinical resemblance, in some cases, to the urticarias and the erythemata.

Ætiology and Pathology.—The disease may occur at any time of life; it is rare in infancy and childhood, although cases have been reported; it is fairly common in young adult life, but most cases occur in middle life. Both sexes are pretty equally attacked. A special form occurs in association with pregnancy, and is apt to recur with each pregnancy. The malady does not appear to be associated with the presence of any particular micro-organism in the body, and cultures from vesicles and bullæ are sterile in their early stages. Blood cultures are also negative.

It has been considered by some to be due to some nervous derangement, and it is true that it is sometimes associated with neuroses; it is probable, however, that these are a product rather than a cause of the disease. It is probable that the condition is produced by an unknown toxin.

Microscopically lesions show a dense, cellular infiltration of the superficial part of the dermis, chiefly around the vessels. There is always considerable superficial œdema, which in the vesicular and bullous cases collects under the epidermis, lifting it from the underlying dermis; the fluid of the vesicles contains a large number of eosinophil corpuscles.

Symptoms.—The eruption is essentially polymorphous, that is to say, all the types of lesions mentioned above may be present in the same case at the same time. Most commonly the lesions look like irregularly figurate urticarial wheals which are surmounted by numerous shotty vesicles. In other cases the lesions are more frankly erythematous, while in others larger vesicles or bullæ form, either with or without an underlying erythematous or urticarial patch. In all cases, except when the bullæ are large, there is intense itching in the lesions, with the result that they are scratched, and small bloodstained crusts or excoriations are seen mixed up with the other manifestations of the disease. The limbs and the trunk are most frequently affected, but any part of the cutaneous surface may be involved, though rarely the palms and soles, and the mucosæ are attacked in a considerable percentage of cases. There is a great tendency for the lesions to recur, fresh crops coming out at frequent intervals, and the disease may

persist for years; the writer has under his care a case of over 40 years' duration.

The general health usually suffers very little, in spite of the fact that sleep is often disturbed. Gastro-intestinal symptoms, such as diarrhœa and vomiting, may occasionally occur, and in fatal cases lesions have been found in the gastro-intestinal tract, which possibly account for the above-mentioned symptoms. An increase in the eosinophil corpuscles in the blood occurs in the majority of cases.

Diagnosis.—From erythema multiforme it can be distinguished by the irregular distribution, the shape and the polymorphic character of the lesions in conjunction with the intense itching which occurs; from urticaria by the presence of vesicles and bullæ, which are almost unknown in simple urticaria, though not infrequent in the papular variety, and by the persistence and recurrence of the lesions; and from pemphigus by the itching, the polymorphous character of the lesions, and the comparatively slight effect on the general health.

Treatment.—This calls for much patience on the part both of the patient and the physician. In the first place a careful examination, both clinical and bacteriological, must be made to find any focus of disease. Of the internal remedies most reliance has been placed on arsenic, and in some cases the eruption ceases when a certain dose is reached; but this is by no means always the case. Arsenic may be given by the mouth as Fowler's solution or Asiatic pill, or by injection, the cacodylate of soda, enesol and arsphenamine (salvarsan) being the favourite preparations. The dose should be small to start with, and increased to the limit of tolerance; and the drug should be discontinued if no definite result is obtained. Aperients and saline lavage of the bowel are satisfactory in severe cases; in others quinine, salicin and sodium bicarbonate have proved successful. In any case attempts should be made to check the itching. Alcohol and coffee should be stopped, and also all excess of sugar in the diet. Phenacetin and phenazone are useful, and sedatives may be given occasionally at night. The injection of certain non-specific protein substances, such as the patient's own blood, horse serum, sterilised milk or peptone, has occasionally produced a cure.

Local remedies consist mainly of anti-pruritic applications. The most useful is a lotion containing 2 to 3 per cent. phenol, 1 per cent. liq. potass. hydroxid., or 2 to 5 per cent. liq. picis carbonis. Alkaline and bran baths are valuable, especially in the bullous cases—in which cases also weak (5 per cent.) sulphur ointment sometimes acts well.

8. PEMPHIGUS

An inflammatory condition of the skin, characterised by the eruption of blisters usually occurring in crops, and associated with constitutional symptoms.

Four different varieties are recognised: (1) acute pemphigus, (2) chronic (pemphigus vulgaris), (3) pemphigus foliaceus, and (4) pemphigus vegetans. Acute pemphigus is now known to be a definite bacterial infection, and should not strictly be included in this group; but it is placed here for convenience of description. In the other three varieties the cause is unknown, but it is believed that they are of toxic origin.

(*a*) Acute Pemphigus

Ætiology.—This is a rare condition which occurs almost entirely in butchers, and appears to be due to inoculation of some abrasion with a pathogenic micro-organism, the diplococcus of Pernet and Bulloch. The lesions are not produced by local spread, as in impetigo contagiosa, but are distributed through the blood stream, and symptoms of acute toxæmia occur simultaneously with (or even before) the appearance of the eruption. The diplococcus can be obtained from the bullæ, as well as from the blood.

Symptoms.—The disease commences acutely with fever, malaise, nausea and vomiting. Bullæ then appear suddenly on the apparently normal skin; they are usually very numerous, and as big as a pigeon's or hen's egg. They may burst, leaving a red oozing surface. The lesions usually involve the mucous membranes of the mouth and throat, and even of the intestinal tract, causing pain and difficulty in swallowing, diarrhœa and vomiting, and secondary bronchitic and broncho-pneumonic complications. In a large proportion of cases a general septicæmic condition supervenes and the patient dies, but in a few milder cases the lesions dry up and the patient recovers. Rarely cases may become chronic.

Treatment.—The cases are so infrequently seen that little can be said on this point. The main principles are to keep the patient in bed, puncture the vesicles, and apply mild antiseptic dressing, *e.g.* 1 in 4000 potassium permanganate, with a thin layer of paraffin gauze between it and the skin, or 1 in 1000 acriflavine emulsion. Quinine is recommended as the best internal remedy. No observations have been made, as far as the writer knows, with regard to specific therapy.

(*b*) Chronic Pemphigus

Symptoms.—The affection, which is also rare, is characterised by the appearance of crops of bullæ in various parts of the skin and mucous membranes, each bullæ appearing on the skin without any pre-existing erythematous or urticarial lesion. The eruption is not associated with itching, but the general health suffers, thus differing from dermatitis herpetiformis. Further, the bullæ are usually sterile in their early stages, though both the *Staphylococcus pyogenes albus* and the *Bacillus pyocyaneus* have been found; but these are almost certainly secondary infections.

The bullæ usually dry up in the course of a week, leaving an erythematous and scaly patch, which subsequently disappears; but fresh crops of blisters constantly come out, and this state of affairs may persist for months and years. The general tendency is for the disease to continue, while the general health steadily deteriorates, and finally death supervenes.

Diagnosis.—This has to be made from dermatitis herpetiformis and from the bullous form of erythema multiforme. The main points in the diagnosis of the former have been considered in a preceding paragraph. In erythema multiforme the lesions are especially distributed on the extremities, and some of them show the definite coin-shaped erythematous patches. The attack usually lasts only a week or two.

Treatment.—This is very unsatisfactory. Arsenic in full doses has

given good results, and quinine and salicin are also recommended. Suramin (antrypol, germanin Bayer 205) appears to give good results in some cases. Gastro-intestinal antiseptics and colon lavage are useful. Intramuscular injection of horse serum, or of the patient's own serum, may be tried. Local treatment is the same as for acute pemphigus.

(*c*) Pemphigus Foliaceus

This is probably only an extensive type of chronic pemphigus.

Symptoms.—Bullæ appear frequently and over large areas of the body, and as a result set up a condition resembling generalised exfoliative dermatitus. When this stage is reached fresh bullæ are not properly formed, owing to the permeability of the improperly formed horny layer, abortive flaccid lesions constantly appearing on the affected areas. Crusting, scaling and a tendency to warty formations, together with much pigmentation, are present. The trunk, neck, face, scalp and limbs may all be attacked, but usually the hands and feet are much less affected.

The general health is usually much affected; but this is not always so. The writer has had under his observation a case of 20 years' duration who, apart from the skin condition, was otherwise well. Usually, however, cases end fatally in a year or two.

Diagnosis.—The only condition likely to be confused with this is generalised exfoliative dermatitis; but in this latter condition bullous formation is absent.

Treatment.—This is the same as for chronic pemphigus.

(*d*) Pemphigus Vegetans

Symptoms.—The lesions in this type frequently first appear in the mucous membrane of the mouth, but may appear on other parts of the body. When fully developed they are chiefly localised to the flexures of the axillæ, elbows, groins, knees and around the anus and vulva. The initial lesion is a flaccid blister, which on rupture develops fungating granulations from its base, which discharge much fetid secretion. The patient's health suffers rapidly from septic absorption, and he usually succumbs in the course of a few months.

Diagnosis.—The condition when fully established is characteristic, but in the early stages the lesions might be mistaken for syphilitic mucous tubercles. The diagnosis can be settled by the presence of other syphilitic lesions, by finding the spirochæta pallida, and by the Wassermann reaction.

Treatment.—No treatment is known to influence the course of the disease. Local antiseptics are required for the lesions, weak perchloride of mercury and eusol being the most likely to be satisfactory. Otherwise treatment is on the same lines as for pemphigus chronicus.

9. DERMATITIS EXFOLIATIVA

Synonym.—Pityriasis Rubra.

This is a generalised inflammation of the skin, characterised by redness and profuse scaling. There are many types of this condition, and divers

causes. It is customary to divide dermatitis exfoliativa into primary and secondary varieties. The former occurs without any pre-existing dermatosis, while the latter really represents the generalisation of some other skin inflammation, such as eczema, seborrhœic dermatitis or psoriasis. When such diseases generalise there is a tendency for them to take on the character of a primary exfoliative dermatitis, presently to be described.

The primary variety occurs in its most striking form in salvarsan poisoning, and may also occur in such diseases as leukæmia and mycosis fungoides —diseases closely related to one another. There still remain, however, a number of cases in which no cause can be found, and which we are probably justified in considering as toxic eruptions.

Symptoms.—The cases due to arsphenamine may be taken as typical of the group. In these the eruption usually commences as bright, scarlatiniform patches on the flexor aspect of the forearms and on the abdomen and chest. The rash spreads rapidly, so that in a day or two the whole body is covered. At first it is found to consist of distinct pinhead-sized macules, chiefly around the follicles, but soon it becomes one continuous red sheet. Almost immediately the eruption begins to scale; the scales may be of the fine branny type, or large like fish scales. The amount varies in different cases, but is often very considerable, the bed having to be swept out several times a day. The onset is not always as described; sometimes the initial eruption is an urticaria, or even like an acute erythematous eczema, involving the face and forearms, and in a case recently under the writer's care it was erythemato-vesicular at the commencement. Once the eruption is fully established it usually takes 2 to 3 months to disappear. In an uncomplicated case the rash gradually subsides, scaling ceases, and the skin assumes its normal colour, though some thickening may remain for a considerable time. The flexures of the limb and the neck usually are the last to clear. The hair is frequently completely shed, but grows again later, and the nails may also be lost temporarily, though this is less frequent. An irregular thickening of the nails is, however, more common. At the onset there may be fever, malaise and intestinal disturbance; later, in the course of 3 to 4 weeks, bronchitis and broncho-pneumonia may supervene, and sometimes cause a fatal issue. Nephritis may also occur, and may cause permanent renal changes. If careful nursing is not provided the skin may become infected, and septic absorption may occur. There is always much enlargement of the lymphatic glands, which are soft and spongy, and conjunctivitis is sometimes present.

Most of the idiopathic cases run a similar course; but several different varieties have been described, among which the condition known as pityriasis rubra of Hebra is apt to be associated with visceral complications and with skin atrophy, and runs a very fatal course.

Diagnosis.—The primary cases must be distinguished from those due to leukæmia and mycosis fungoides. In the former the blood picture will probably clear the diagnosis, and in the latter the severe itching, which usually accompanies it, and which is usually absent in the simple exfoliative dermatitis cases.

Prognosis.—This is always uncertain, and should be very guarded. Cases may clear up in 2 or 3 weeks, or may persist for years, with gradually increasing prostration ending in death.

Treatment.—In the arsphenamine cases sulphur appears to be the best remedy. It may be given as sodium thiosulphate by intravenous injection. The main internal remedies must be directed to maintaining the general health, and to countering complications as they arise. Complete rest in bed is indicated in all cases, however mild they may at first appear, and the warmth of the body must be maintained. Warm bran baths may be given if no fever is present, and dusting the skin with talc powder makes the patient comfortable. Local septic complications must be dealt with by mild antiseptic creams or pastes.

ERUPTIONS DUE TO BACTERIA AND FUNGI

Having dealt with the deep inflammatory dermatoses produced by toxins circulating in the blood, it is now necessary to consider those which are caused by living organisms reaching the skin by the same channels. Three of these form a very important group of dermatoses, namely, tuberculosis, syphilis and leprosy. The two latter have been dealt with on pp. 193 and 121 respectively. There are, however, certain others which require notice. It is probable that the eruptions of certain specific fevers may be due to the presence of the infecting organisms in the tissues; this is known to be the case in the rose spots of typhoid fever. The erythematous and purpuric eruptions sometimes seen in malignant endocarditis and other septicæmic and pyæmic conditions are also probably due to the direct action of the streptococcus, while it will be necessary later to describe the cutaneous manifestations produced by the gonococcus when it enters the blood stream.

1. TUBERCULOSIS CUTIS

The tubercle bacillus may attack the skin in several different ways. The commonest variety is a superficial granulomatous formation known as lupus vulgaris; this variety can apparently be produced both by local inoculation and through the blood stream. Lupus verrucosus, a variant of this type, is generally a local inoculation, and is accompanied by warty overgrowths. Miliary tuberculosis of the skin may accompany general miliary tuberculosis, and local tuberculous ulcers may also form, but are chiefly seen on the mucous membranes. In addition, an infection of the skin may occur when a tuberculous abscess, either from a suppurating lymphatic gland or bone, bursts through the skin, and this is spoken of as scrofulodermia. There are also groups of cutaneous and subcutaneous tuberculous lesions, produced by bacilli circulating in the blood, which are called tuberculides, and include several varieties, the lichenoid or lichen scrofulosorum, the acneiform or acne scrofulosorum, the papulo-necrotic, and the gummatous (erythema induratum or Bazin's disease).

(*a*) Lupus Vulgaris

Pathology.—The lupus nodule is composed of a group of ordinary miliary tubercles, such as are seen in the lungs and elsewhere. It consists of groups of epithelioid cells, surrounding giant cells, often with peripherally arranged

nuclei, the whole being surrounded by a dense mass of round cells. Tubercle bacilli have been demonstrated in the lesions, and inoculation into guinea-pigs will produce tuberculous lesions.

Symptoms.—Lupus vulgaris usually attacks the face ; but it is not uncommon to find patches on other parts of the body. In this latter site it may be symmetrical. Usually on the face it is asymmetrical. It is most frequent on the nose or cheek, and frequently begins in childhood. The earliest lesion is a small, dull-red pinhead-sized spot, to which other similar spots are soon added, the whole being surrounded by an erythematous zone. On pressure with a lens, however, these original spots can be distinctly seen as yellowish points or nodules compared in appearance to apple jelly. They are very soft, and if a pointed match is applied to one of them it sinks easily into the nodule. These patches may slowly spread so as to involve considerable areas, and may persist for a long period without ulceration. In other cases, however, ulceration may supervene, and considerable destruction of tissue take place, especially on the nose, which is often completely destroyed up to the edges of the nasal bones. The bone itself is not attacked ; but the cartilage may completely disappear. If healing occurs, a soft, superficial scar is produced ; but fresh nodules are liable to appear in it. Any part of the face may be attacked ; but the scalp usually escapes. The glands in the neck may enlarge and occasionally break down, but this is uncommon. Facial lupus vulgaris is frequently complicated by similar lesions in the mucosa of the nose and mouth, and these situations are sometimes the primary seat of the disease. On the mucous membranes the nodules are not visible, but sharply defined, raised, rather warty-looking patches occur. It is commonly seen on the inner aspects of the cheek, gums, palate and nasal mucosa ; but the pharynx and larynx may be involved.

On the body the patches may attain great dimensions ; they often spread at the margins and heal in the centre, forming irregular gyrate patterns. As a rule they are of the non-ulcerating type ; but in some cases ulceration occurs. In some cases, too, considerable contraction of the skin results, leading to deformity ; in others the lymphatic vessels become blocked, and a condition of elephantiasis may supervene.

The disease usually spreads very slowly, and lasts a great number of years. Some cases remain practically stationary almost indefinitely. A few, however, spread rapidly and defy treatment.

In old-standing cases there is a definite tendency to the development of carcinoma. This is of the squamous type, and does not as a rule give rise to secondary carcinomatous glands. It can, therefore, generally be removed locally.

Diagnosis.—Lupus vulgaris is most easily confused with lupus erythematosus (p. 1466). In the former definite nodules are present, and there is a tendency to ulceration ; the disease usually begins in childhood and persists for many years. In the latter the disease is non-ulcerative, has a great tendency to be symmetrical, rarely appears before adult life, and is especially liable to occur in the middle-aged. The scalp is often attacked, while this is rare in lupus vulgaris. In lupus erythematosus thick adherent scales, fixed down by epithelial plugs, form, and the scar is often covered with pits of varying size ; in lupus vulgaris the scale is of a very superficial type and easily removed, and there are no plugs.

From tertiary syphilis the diagnosis may occasionally be difficult, and the two conditions may be combined. The absence of nodules, the tendency to form sharply cut, rather deep ulcers, the presence of a positive Wassermann reaction, and the rapid response to anti-syphilitic remedies will generally settle the diagnosis.

Rodent ulcer is distinguished by its appearance fairly late in life, by its firm rolled edges of pearly white colour, and by its tendency to involve the bony structures of the face.

Treatment.—Of prime importance is the general health of the patient. Good ventilation, sunlight, warm clothing and plenty of good food are necessary if cases are to do well. In the absence of a good supply of natural sunlight excellent results are obtained by exposing the body to the rays of the carbon-arc or mercury-vapour lamps. As to drugs, cod-liver oil, malt, iron and arsenic are often of considerable value.

Local measures should also be taken to destroy the lesions. Small patches may be excised; but this method is only rarely applicable. If the patches are non-ulcerating, and not too extensive, excellent results are obtained by the Finsen light; but this method is rarely available, and is very slow. The nodules may be destroyed by the application of 20 per cent. ac. salicylic plaster with cresote, or 10 per cent. pyrogallic acid ointment rubbed in daily until a violent reaction is produced. Adamson has recommended rubbing acid nitrate of mercury into the patches, and this gives very satisfactory results. In the larger ulcerating patches a preliminary scraping, followed by the application of acid nitrate of mercury or zinc chloride stick, is usually satisfactory. The use of X-rays and CO_2 snow has nothing to recommend it, and the former is very dangerous if given over prolonged periods. On the other hand, some satisfactory results have been reported after treatment with "Grenz" rays.

(*b*) Lupus Verrucosus

This is due to the local inoculation of the tubercle bacillus, and is chiefly seen in those who handle infected meat, and in those who conduct autopsies. It is also known as *verruca necrogenica* or *post-mortem wart*.

Symptoms.—The lesions usually occur on the hands, chiefly the dorsum and on the knuckles. The earliest lesion is a small, red, firm papule, which spreads slowly. The centre soon becomes raised and warty; but there is always a well-marked inflammatory zone around this warty growth. Serum and pus may exude between the papillæ of the wart, and the whole may be crusted. The lesion is generally single, and may attain several inches in diameter. Rarely numerous lesions are present.

Treatment.—Small lesions are best excised. Destruction by the actual cautery, or by diathermy, may be practised in some cases. In this variety a pastille dose of X-rays may flatten down the warty growth, and this may be followed by the use of salicylic acid or mercurial plasters, or by painting with acid nitrate of mercury.

(*c*) Local Tuberculous Ulcers

These occur usually as complications of tuberculosis of other organs. They are frequently present on the mucous membranes, or around the orifices

of the body. Little can be done except palliative treatment if they are numerous; but isolated ones can be destroyed by one of the methods already described.

(*d*) Scrofulodermia

This term is applied to secondary infection of the skin from the bursting of deep-seated tuberculous abscesses. The lesions either take the form of a thick crust overlying an area of unhealthy-looking granulation tissue, or are purplish-red shiny areas surrounding a sinus.

The term is also applied to single or multiple subcutaneous abscesses, not infrequently seen in children, which contain pus, in which numerous tubercle bacilli can be found. They are sometimes called *tuberculous gummata.*

Treatment.—The treatment of the underlying condition is essentially surgical and where possible the affected skin should be excised, otherwise scraping, followed by painting with acid nitrate of mercury, is the best treatment.

(*e*) The Tuberculides

These lesions, which are due to the lodgment of tubercle bacilli in the peripheral capillaries, with the production of a local inflammatory reaction, differ from the foregoing tuberculous diseases of the skin in that there is no tendency for the individual lesions to spread. They are thus comparable to the secondary syphilides, and like them are of several different types.

The Lichenoid Tuberculide.—**Symptoms.**—This condition, also known as *lichen scrofulosorum,* is chiefly seen in young children with glandular tuberculosis. The lesions come out in crops, chiefly on the trunk, and are arranged in circular or oval groups, made up of pinhead-sized acuminate follicular papules. These lesions may be of the same colour as the normal skin, or of bright red colour. There is usually a small crust on the summit of each papule, or sometimes a small pustule. The disease lasts from a week or two to many months.

Diagnosis.—In lichen spinulosus there is less obvious inflammation, and a horny spine projects from the centre of the papule, which can be removed by forceps.

The small follicular syphilide occurs in adults, and is associated with other syphilitic phenomena.

Treatment.—No special treatment of the skin has any effect. The treatment is that for glandular tuberculosis.

The Acneiform Tuberculide.—**Symptoms.**—This condition, also known as *acne scrofulosorum,* occurs in children and adolescents who are suffering from some form of tuberculosis, and chiefly affects the buttocks and thighs, but may be more extensive. The lesions are lentil-sized, acuminate, follicular papules and pustules, and are generally distributed discretely. They are of bright red colour and pustular or crusted.

Diagnosis.—The affection is sometimes difficult to diagnose from staphylococcal folliculitis; but the individual lesions run a much slower course, and are usually more numerous and not painful.

Treatment.—This is the same as for the lichenoid tuberculide.

THE PAPULO-NECROTIC TUBERCULIDE.—**Symptoms.**—In this variety of tuberculide the lesions are small lentil- to pea-sized nodules starting deep in the dermis or in the hypoderm, eventually softening and bursting through the skin with the production of a small rather indolent ulcer. After healing, pitted scars are left. The lesions are usually numerous and come out in crops, which may continue to appear over a period of some years. The parts affected are chiefly the distal extremities of the limbs, *e.g.* the backs of the hands and feet, the sides of the fingers and the extensor aspects of the forearms and legs. Lesions in these regions have been named *folliclis*. Somewhat similar lesions have been described on the face and termed *acnitis*, but it is still not quite clear that they belong to the same group. The eruption nearly always occurs in patients who have some other manifestations of tuberculosis, and occurs chiefly in young adults.

Diagnosis.—These cases can be distinguished from erythema multiforme by their deeper site of origin, and by their tendency to ulcerate and produce scars.

Treatment.—As for other tuberculides. No local treatment has any effect on the lesions.

THE GUMMATOUS TUBERCULIDE.—**Symptoms.**—This condition, which also goes by the name of *erythema induratum* or *Bazin's disease*, is not uncommon, and is almost entirely confined to the legs, especially the calves, and is usually bilateral. It occurs chiefly in girls and young women between the ages of 15 and 25. The initial lesion is a deep-seated nodule, from a pea to a hazel-nut in size, starting in the subcutaneous fat. The nodule slowly increases in size, involves the skin, which becomes purplish in colour, and eventually softens and bursts. The ulcer thus produced has a ragged edge and an unhealthy purplish-red base, often covered by a dirty greenish slough. These ulcers are very sluggish, and take weeks or months to heal. Fresh lesions are constantly forming, and a dozen or more lesions may be found simultaneously on the two limbs. There is often considerable pain in the lesions.

Diagnosis.—From syphilitic gummata.—In this condition the lesions are less numerous—indeed often single—and are rarely so symmetrical. The lesions are usually painless. The edge of the ulcer is sharper and more cleanly cut, and the base is cleaner, or has a characteristic wash-leather slough. Other stigmata of syphilis may be present, and the Wassermann reaction is positive.

In older patients, mainly women, similar nodules occur, which do not break down and ulcerate. These are probably of the same nature but have been called *hypodermic sarcoids*, and must not be confused with *cutaneous sarcoids* described under *sarcoidosis*.

Treatment.—The ulcers heal readily if the patient is kept in bed, but are liable to recur when she gets up again. General tonic treatment should be given, and in many cases arsphenamine has proved to be a potent remedy. Locally antiseptic baths and dressings are required.

2. LUPUS ERYTHEMATOSUS

An inflammatory condition of the dermis, usually chronic but occasionally running an acute course, characterised by the presence of circumscribed

red patches, with or without adherent scales, and which on recovery leaves scars.

Ætiology.—This is still unknown. It has for many years been thought to be due to toxins of the tubercle bacillus and is frequently associated with tuberculosis, but cases occur in which this disease cannot be traced. Lately a good deal of attention has been called to focal sepsis as a cause, but the evidence is no more conclusive than for tuberculosis. It is thought that it may be produced by more than one variety of toxin, or that it may be due to a specific organism as yet undiscovered. There can be little doubt that exposure to sunlight tends to bring out the lesions. The disease is chiefly found in middle age, but may begin before the age of 20. It is more frequent in women.

Pathology.—The chief change in the skin is an infiltration in the neighbourhood of the vessels of the dermis with round cells, which may destroy the hair follicles and sweat ducts. In the epidermis there is a hyperkeratosis, which is especially marked at the follicular openings, so that horny plugs are formed.

Symptoms.—Two main types are seen—(1) The erythematous, and (2) the scaly or fixed type.

1. *The erythematous type.*—This is less frequent and has a greater tendency to be generalised. It may run an acute course or may develop into the scaly type. The lesions are chiefly seen on the cheeks and form circumscribed disk-like lesions, raised and slightly infiltrated and of a pale red to a purplish-red colour. These often show patulous follicular openings on the surface. They may also occur as diffuse flat non-infiltrated sheets of redness. This type is very apt to be associated with lesions in other parts of the body, particularly the backs of the hands and fingers, the arms and forearms, the chest, neck and ears. Occasionally an almost universal eruption appears. The patches may sometimes become bullous and hæmorrhage may occur into the bullæ. These disseminated cases may be associated with acute visceral diseases, such as pneumonia, pleurisy and nephritis, and even in the absence of these high fever may be present. Usually in this type of case, if the patient survives, the eruption clears up without much scarring.

2. *The scaly type.*—This is by far the commonest variety, and is generally very chronic and localised, but may occasionally be acute and generalised. The lesions are chiefly seen on the nose, cheeks, ears and scalp, but are not uncommon on the backs of the hands. They are very apt to be distributed symmetrically in the shape of a bat's wing on the nose and two cheeks. The lesions are usually irregularly shaped red patches, often sunk below the surface of the skin, and covered with greyish scales, which are extremely adherent. When removed horny plugs are seen to penetrate into the epidermis, and when the patches clear up a depressed scar is left, often with numerous pits on its surface. When the scalp is attacked the hair is lost permanently. The mucous membranes may be attacked, the most frequent sites being the vermilion border of the lips and the palate.

Pain sometimes occurs in the patches and sometimes they itch, but generally no local sensations are present. The patient's health is usually below par, and there is often considerable neurosis, but severe constitutional symptoms are usually absent.

The course is exceedingly chronic, the patches often persisting for years in spite of treatment.

Diagnosis.—The condition is differentiated from lupus vulgaris by the absence of nodules, the symmetry of the lesions, the absence of ulceration and the age of the patient; from erysipelas, by the slowness of the spread and the absence of high fever; and from erythema multiforme, by the chronicity of the lesions and the presence of destructive effect on the skin shown by scarring.

Treatment.—The acute erythematous cases should be kept in bed and complications treated. All possible sources of focal infection should be removed. The drug which appears most to influence cases is quinine, which should be given in full doses. Local treatment is not usually required in the acute erythematous cases. In all cases, especially the very acute types, sulphapyridine is worthy of trial.

In the chronic scaly cases, quinine and general tonic treatment are indicated. Good results have been obtained by the intravenous injection of gold compounds, such as myocrysin, krysolgan, triphal, solganal, or sanocrysin It is advisable to keep the doses of gold preparations small compared with those given for tuberculosis. Intramuscular injections of bismuth salts have also given good results. Rest in bed is always beneficial, and the patient should not be allowed to go out in a strong wind or in the hot sun, as these aggravate the condition.

Local treatment is chiefly directed to removal of the scales and the production of a mild inflammatory reaction in the patches. For the former ac. salicyl. ointment, 3 to 5 per cent., or plaster, 5 to 10 per cent., may be employed. For the latter 5 to 10 per cent. pyrogallic acid, painting with pure carbolic acid, or applications for a few seconds of CO_2 snow.

3. GONORRHŒAL KERATOSIS

The lesions in this condition are probably produced by gonococci curculating in the blood stream, although they have not been demonstrated.

They occur in patients suffering from gonorrhœal arthritis and other manifestations of general gonococcal infection, and usually appear on the palms and soles, though other parts of the hands and limbs may be affected.

The lesions are red patches covered with cone-shaped horny thickenings, and are generally numerous. In addition, a general hyperkeratosis of the palms and soles may occur.

Treatment.—General treatment for gonorrhœa is required, together with ung. ac. salicylic. locally.

4. SPOROTRICHOSIS

In addition to those bacterial conditions which attack the skin by way of the blood stream, a certain number do so by way of the lymphatics. Lymphangitis with abscess formation from pyogenic organisms is well known, and the same condition in tuberculosis has already been described under the title of "scrofulodermia." Actinomycosis is another such condition, and has already been dealt with (p. 185). Somewhat similar conditions to the

two last mentioned may be produced by certain fungi, of which the only one which requires special notice is sporotrichosis.

Symptoms.—Infection may take place through a crack in the skin, usually on the hand or foot. From this a lymphangitis starts, which spreads up the affected limb, and subcutaneous cold abscesses soon appear at points along the affected lymphatics. These eventually burst and leave indolent fungating ulcers, which show little or no tendency to heal spontaneously. A good deal of pus or yellowish fluid exudes.

Diagnosis.—Cases are usually diagnosed as tuberculosis, and a certain diagnosis can only be made by obtaining the fungus in culture. This should be done on Sabouraud's proof medium and incubated at room temperature.

Treatment.—The lesions usually disappear under large doses of potassium iodide administered internally.

ERUPTIONS DUE TO FILTRABLE VIRUSES

Certain affections of the skin are now known to be due to filtrable viruses. Among these are:

(1) Herpes zoster (see p. 1583).
(2) Herpes simplex.
(3) Herpes preputialis.
(4) Verruca vulgaris.
(5) Molluscum contagiosum.

It is more convenient to deal with warts and molluscum contagiosum when discussing tumours of the skin (pp. 1481 and 1482), while zoster is described elsewhere (p. 1583).

1. HERPES SIMPLEX

Herpes Simplex or Herpes Febrilis is a condition to which some people, and especially children, are prone whenever they develop a slight febrile attack or even a slight cold.

Ætiology.—The disease is produced by a filter-passing virus which, when injected into rabbits, produces a fatal form of encephalitis, and is closely related to the virus of encephalitis lethargica.

Symptoms.—The lesions consist of small groups of vesicles, on an inflamed base, which come out chiefly in the neighbourhood of the mouth. They are irregularly distributed, have no relations to any nerve trunks, and are generally bilateral. They disappear in the course of a week or so, after crusting over, and leave no scars. In one type, seen especially in children, recurrent attacks occur on the cheek, often at regular intervals and without any special cause. These attacks also clear up and leave no scars. A recurrent type is also found affecting the buttocks in adults.

Treatment.—A bland protective ointment, such as zinc cream or Lassar's paste, or a dusting powder, such as bismuth subgallate, is all that is required. In recurrent cases, small doses of X-rays given during the quiescent period appear to diminish the liability to fresh attacks. Treatment by vaccines prepared from the virus have been tried, but results are uncertain.

2. HERPES PREPUTIALIS

This is the name given to small crops of two or three to half a dozen or more small vesicles which sometimes appear on the under surface of the prepuce. The vesicles quickly rupture and leave behind pinhead-sized ulcers which are painful. There is no tendency for these ulcers to increase in size. This latter feature helps to differentiate them from both syphilitic ulcers and soft sores.

Treatment.—This is the same as for Herpes Simplex.

ERUPTIONS DUE TO ERRORS OF METABOLISM

XANTHOMA

Xanthoma forms an interesting link between the inflammations due to chemical toxins circulating in the blood and those due to bacteria, for in this condition lesions of a granulomatous nature are produced around a deposit of a chemical substance in the tissues. Apart from this condition, all the granulomata whose nature is known are produced directly by bacteria; tubercle, syphilis and lepra are the best known examples.

Three clinical varieties of xanthoma are recognised: (1) xanthoma tuberosum, (2) xanthoma diabeticorum, and (3) xanthoma planum.

Ætiology.—Xanthoma tuberosum and diabeticorum occur in patients who for some reason or other have some disturbance of lipoid metabolism, often shown by an excess of cholesterin in the blood serum. This is why one form is seen in diabetics. The cholesterin becomes deposited in the tissues and causes a reaction, chiefly among the fixed connective-tissue cells of the dermis, particularly the endothelial cells, and a granuloma not unlike that seen in tuberculosis is produced. Histologically the tumours of xanthoma consist of large cells, arranged around the vessels, containing droplets of a cholesterin-fatty-acid-ester and some fat. Around these cells a varying degree of connective-tissue hypertrophy may occur.

Symptoms.—*Xanthoma tuberosum.*—In this condition numerous discrete yellowish nodules appear in the skin. These increase in size and may form tumours as big as an orange. They are most commonly seen on the extensor aspects of the limbs, especially on the elbows and knees, where they may form large firm tumours, but they may be seen on any part of the skin. The bones, tendons, viscera and mucous membranes may also be involved. The colour varies from a bright yellow to an orange or red. The disease is usually seen in young adults. It does not generally affect the general health, but is occasionally associated with jaundice. The lesions are very persistent.

Xanthoma diabeticorum.—The lesions are usually smaller and more numerous; they are lentil-sized lesions and come out in crops, usually on the buttocks and extensor surfaces of the limbs. They disappear rapidly under appropriate treatment for diabetes.

Treatment.—In the diabetic cases, the underlying disease must be treated. For xanthoma tuberosum no definite treatment can be laid down, but a diet which contains as little fat as possible should be prescribed.

Xanthoma palpebrarum.—**Ætiology.**—This has been considered to be a fatty degeneration of the fibres of the orbicularis palpebrarum muscle, but in some cases an excess of cholesterin in the blood has been demonstrated.

Symptoms.—The lesions consist of flat, yellow, slightly raised patches, which are often symmetrically placed, on the eyelids near the inner canthus. They may be as small as a pin's head or may involve almost the whole eyelid. They produce no symptoms. They mostly occur in old people.

Treatment.—They can be destroyed by electrolysis or by caustics, or removed by excision.

C.—INFLAMMATORY DERMATOSES OF UNKNOWN ORIGIN

In this group are included certain dermatoses with well-defined characters which entitle them to be considered clinical entities, but whose ætiology is entirely obscure. The following diseases are included under this heading: psoriasis, parapsoriasis, pityriasis rubra pilaris, lichen planus, scleroderma and sclerema neonatorum. It must not be assumed that because these conditions are grouped together that they have any relationship to one another.

PSORIASIS

A very common condition characterised by the presence of red, scaly papules and patches of characteristic appearance on various parts of the body and unassociated with any disturbance of the general health.

Ætiology.—The disease frequently begins towards the end of the second decade, and is not infrequently seen in children from about 7 years of age and upwards, but is very rare in small children. Both sexes are equally affected. On the other hand, the first attack may occur in advanced age. It has been attributed to parasitic agencies, toxins of bacterial and metabolic origin, and to neuropathic causes, but there is very little evidence to support any of these views. There is no doubt that in some cases a strong family history can be made out.

Pathology.—Histological examination shows a great overgrowth of the epithelium, with downward growth of the interpapillary processes, and corresponding elongation of the papillæ. The horny layer is badly formed (parakeratosis), and collections of leucocytes can be found between the horny cells. There is a cellular infiltration around the papillary vessels and those of the subpapillary layer.

Symptoms.—The malady is a chronic one and may come and go throughout life. Usually attacks occur at quite irregular intervals, but in some cases they may appear at definite seasons—some appearing in the summer, others in the winter. The extent also varies greatly in different cases, some only having a few patches, others being covered with lesions.

The sites of predilection are the extensor aspects of the limbs—especially of the elbows and knees—the trunk—both back and front, but especi-

ally the waist region, the scalp and, more rarely, the face, nails and palms and soles.

The lesions begin as pinhead-sized papules, and are from their very beginning surmounted by a small silvery scale. The individual lesions usually spread centrifugally and may eventually attain great size. Usually, however, they join with other patches and so form plaques, which may, for instance, cover the whole back in one continuous sheet. The same type of scaling persists even in the largest patches, though in chronic treated cases the surface of these patches may appear to be highly polished; on scratching, however, with a sharp instrument the silvery scales are immediately apparent. The whole mass of scales can, with care, be removed in one continuous sheet, and underneath is found a shiny, dry red surface which, on examination with a lens, shows the dilated papillary vessels as tiny red points.

The arrangement of the lesions varies. In some cases the body and limbs are studded with lesions the size of a small pea or a threepenny-piece (psoriasis guttata); in others the lesions are larger (psoriasis nummulata); in some the centre of the lesions clears up, leaving rings (psoriasis circinata), and the rings may run together, forming gyrate figures (ps. gyrata). Occasionally the crusts are very thick (ps. rupioides), and this is especially the case on the scalp, where the hairs prevent the scales from falling off.

In some cases the lesions remain small and confined to the follicles (follicular psoriasis), and these may occasionally group into patches. They may also come out along scratches on the skin. When the nails are affected, either small pinhead-sized pits may be produced, or the whole nail may be forced up by lesions occurring in the nail bed, the nail eventually breaking up and thick masses of scales being found beneath it. The palms and soles are less frequently involved, but when they are affected circumscribed red patches form, associated with scaling and fissuring in the deep folds. In these regions also a pustular form of psoriasis has been described, consisting of sharply defined red patches studded with minute pustules, usually sterile, imbedded in the patches. The mucous membranes are not affected.

The lesions vary from a pale to a dark red in colour, and on clearing up usually leave little or no pigmentation, though in very chronic patches, especially on the legs, some pigmentation may remain for a time.

There are usually no subjective sensations, but occasionally itching is present. The general health is not affected.

Diagnosis.—This disease may resemble the secondary *papulo-squamous syphilide*. It differs, however, from this condition in the fact that the lesions are scaly from the start; that when the scales are removed no infiltration can be felt, and that the surface left is smooth, dry and studded with numerous small red points; that pigmentation is generally absent or little marked; that the lesions are mainly distributed on the extensor aspects of the limbs, and that the scalp may be extensively involved without loss of hair; and that other signs of syphilis, such as general adenitis and involvement of the mucous membranes, are not present. The Wassermann reaction and the effect of treatment will generally confirm a clinical diagnosis.

In *seborrhœic dermatitis* the scales are greasy, the patches spread by aggregation of follicular papules, and the scalp, face and centre of the chest and back are chiefly affected. The lesions respond quickly to sulphur, which is not the case with psoriasis.

In *eczema* itching is marked, when the scales are removed a moist surface is left, and the lesions are made up of aggregation of papules and papulo-vesicles.

In *pityriasis rosea* the scaling is usually in the form of a collarette, the lesions are of a pale pink colour, and the limbs are little affected, especially below the elbows and knees.

In *lichen planus* some typical papules can almost always be seen, the lesions have a characteristic lilac or purple colour, the flexor aspects of the limbs are most involved, and itching is generally intense.

Treatment.—Internal treatment is considerably employed, but it is difficult to estimate its value. Arsenic is the most valuable drug, and should be given in increasing doses up to the limit of tolerance, but should be entirely discarded if no effect is produced. Liquor arsenicalis, min. 3, t.d.s. and upwards, and pil asiatica are chiefly employed. Arsenic should not be given when lesions are coming out rapidly. In these cases salicin, gr. 15, t.d.s., and thyroid, gr. 1, t.d.s., have been recommended by Crocker and others.

Local treatment is the most efficacious, and chrysarobin gives the best results, but is messy, stains linen permanently, and is liable to set up a severe dermatitis if used carelessly. It is best applied in 5 per cent. to 10 per cent. ointment rubbed into the patches daily, after the scales have been removed in a hot bath with the aid of soft soap. Dithranol (derobin, cignolin), is a less messy chrysarobin substitute, and used as an ointment, in the strength of gr. ½ to the ounce, is a very efficient remedy. If this treatment is carried out thoroughly for 3 or 4 weeks the patches will disappear. This treatment is best carried out in hospital or in a nursing home.

Pyrogallic acid ointment 10 per cent., oil of cade ointment 20 per cent., or an ointment consisting of solution of coal tar 12·5, ammoniated mercury 6·25, salicylic acid 6·25, simple ointment to 100. If the patches become inflamed they are best treated temporarily with linimentum calaminæ. Isolated resistant patches may be treated by X-rays, but this cannot be often repeated. For the scalp, the scales should be removed with soft soap, and the patches painted with equal parts of solution of coal tar and industrial spirit. This latter solution is useful in psoriasis of the nails, after the nail has been cut away and the scales removed.

PARAPSORIASIS

This is a term applied to certain rare forms of resistant erythemato-squamous lesions which occur on the body. Three types are recognised: (1) parapsoriasis en gouttes, (2) parapsoriasis en plaques, and (3) parapsoriasis lichenoides.

Ætiology.—Nothing is known of the ætiology of these conditions.

Symptoms.—*Parapsoriasis en gouttes* occurs as pea-sized or slightly larger red spots, covered by fine branny scales, chiefly on the upper part of the trunk. In some cases necrotic lesions occur.

Parapsoriasis en plaques occurs as symmetrical patches, oval or linear, of pale yellow or red colour, with a shiny surface or covered by fine scales, and occurring chiefly on the legs, thighs and lower trunk.

Parapsoriasis lichenoides forms a reticular pattern, chiefly on the extensor

aspects of the upper limbs. The lesions are red or purplish in colour and the surface is either shiny or covered with fine scales.

Treatment.—These cases are very resistant to treatment, but should be dealt with on much the same lines as psoriasis.

PITYRIASIS RUBRA PILARIS

This is a rare disease characterised by the appearance of follicular papules, with horny spines, which tend to involve the whole cutaneous surface and eventually produce a generalised dermatitis resembling pityriasis rubra of Hebra.

Ætiology.—This is very obscure. It is thought by some observers to be a follicular form of psoriasis, but at present there is no conclusive evidence. The disease occurs in both sexes and at varying periods of life, but sometimes in the very young.

Symptoms.—The lesions are of two types: red follicular papules with horny spines, which are chiefly seen on the extensor aspects of the limbs, and especially on the dorsum of the hands and fingers; and red scaly plaques or sheets, which involve the scalp, face and trunk. Either of these types may predominate. Where the former type occurs the skin presents the appearance of a nutmeg grater. Hyperkeratosis of the palms and soles develops, with fissuring of the deeper folds, and the nails become pitted and brittle. Ectropion followed by conjunctivitis may occur. The mucous membranes usually escape. The malady does not seriously affect the general health, and subjective symptoms are usually absent.

Treatment.—No specific treatment is known. Thyroid has been recommended, but the results are very uncertain. Bran and alkaline baths, followed by inunctions of ac. salicyl., grs. 10, glycer. amyl., adip. lanæ hydros., āā gr. 240, seem to give the best results.

PITYRIASIS ROSEA

A widespread eruption of pinkish macules and papules of round or oval outline, with branny scaling, which does not usually extend to the periphery of the lesion.

Ætiology.—This is still obscure. It was originally thought to be of parasitic origin, probably owing to the resemblance of the lesions to ringworm, but no definite parasite has been discovered. It is possible that it may be of the nature of an acute exanthem, as it occasionally has a sudden onset with slight fever and malaise. One attack is said to confer immunity, though this is not absolute, and it seems to occur at times almost in epidemic form. It has been thought by others to be a toxic eruption. The disease occurs chiefly in children and young persons, but no age is exempt.

Symptoms.—The eruption usually comes out suddenly, and the onset may, though this is not usual, be accompanied by slight fever, malaise and sore throat. In some cases the general outbreak is preceded by the appearance of a single patch, the "herald" patch, which may appear a week or 10 days before the general eruption. The lesions are usually most profuse

on the trunk and central portions of the limbs, the distal parts of the latter escaping. The face, neck and scalp may be affected, but this is not common.

The lesions are pinkish macules or papules, mainly macules, which vary in size from a lentil to patches a couple of inches across. They tend to be arranged in lines parallel to the ribs, and the larger patches are oval. When the lesions reach the size of a pea, central scaling commences, and as the lesions grow the scales tend to form a collarette, with the free edge directed towards the centre. The colour of the portion within the scales changes to fawn and eventually returns to the normal skin tint. Sometimes pinhead-sized follicular papules of skin colour are seen among the lesions in considerable numbers. In rare cases vesicles and bullæ form.

Subjective symptoms are usually absent, but sometimes itching is a prominent feature. The rash usually lasts about 4 weeks and then disappears, but it may persist for several months.

Diagnosis.—Seborrhœic dermatitis is distinguished by its greasy scales and by its distribution; secondary syphilis, by the presence of other syphilitic lesions; and ringworm, by the small number of lesions, their asymmetry, and the presence of fungus in the scales.

Treatment —No internal treatment is known to affect the disease. In the early stages a simple coal tar and lead lotion can be used, as this allays itching if present. Once the rash is fully developed a daily warm bath, followed by the application of 3 per cent. salicylic acid in linimentum calcis, will usually cause the lesion to disappear. If there is fever the patient should be put to bed.

LICHEN PLANUS

An intensely itchy eruption characterised by the presence of angula papules of pinkish or lilac colour tending to be localised in special areas.

Ætiology.—The disease occurs chiefly in adult life and is very rare in young children. Two views are held as to its ætiology. By some it is thought to be of nervous origin, following shock, mental anxiety, worry, etc. It is true such a history is often obtainable, but Graham-Little has pointed out that it did not appreciably increase during the War of 1914–1918, which might have been expected if such was the main factor in its production. The other view is that it is of toxic origin, but there is no direct evidence on this score.

Pathology.—The microscopic anatomy of the papules is very characteristic. There is a circumscribed, dense, round-cell infiltration in the upper part of the dermis beneath the papule, and the epidermis is much thickened. The papillæ are flattened out. The granular layer is irregularly thickened and there is a hyperkeratosis, most marked at the orifices of the hair follicles and sweat ducts.

Symptoms.—The most common variety is the *localised type.* The lesions are chiefly found on the flexor aspects of the forearms and wrists, the inner aspects of the thighs near the knees, and on the front of the shins. The trunk, especially the lower part, the palms and soles, and the penis are also occasionally involved. The mucous membrane of the mouth is frequently attacked. The lesions on the skin are discrete, lentil-sized papules, raised

sharply from the skin, with polished shiny surface and usually of lilac colour. They have a curious and typical angular outline, due to the fact that they are bounded by the fine lines of the skin, and sometimes they are definitely umbilicated. Frequently the papules are arranged in lines along scratch marks. Occasionally patches are formed by the aggregation of papules and resemble rather closely patches of psoriasis. On the palms the lesions are generally circular, vary in size from a pea to a threepenny-bit, and the horny layer over them is much thickened.

In the mouth irregular dead white patches are found, usually on the tongue or inner aspect of the cheeks.

Several other types of lichen planus are seen. In one variety the lesions form rings and gyrate figures (*lichen planus annularis*), while in another atrophy occurs (*lichen planus atrophicus*). In a large number of cases the horny layer is much thickened (*lichen planus hypertrophicus*), and this is especially seen on the legs, where warty patches occur (*lichen planus verrucosus*). Occasionally the lesions are arranged in a single line, sometimes following the course of a nerve (*lichen planus linearis*), and very occasionally bullæ and vesicles may occur. Rarely cases are met with in which the papules are few in number, and very much hypertrophied, forming dome-shaped tumours, which itch intensely (*lichen obtusus*).

Another variety is an *acute generalised* type in which a large number of lesions are scattered diffusely over the trunk and limbs. In this type the papules are pale pink in colour and not so raised as in the chronic forms. Even in these cases the face and scalp almost invariably escape.

In association with the above-mentioned lesions small groups of follicular papules with horny spines may be found. The same condition is sometimes found independently of lichen planus and has been called *lichen pilaris* or *spinulosus*. Whether these latter cases have the same origin is still unsettled. Graham-Little has reported the association of this type with atrophic alopecia.

Lichen planus lesions are almost invariably accompanied by intense itching and often by marked neurotic manifestation, but otherwise the health remains good, though slight fever may accompany the acute cases.

The disease runs a very chronic course and is sometimes very resistant to treatment.

Diagnosis.—This is usually easy, as the lesions are very characteristic. The diagnosis from psoriasis has already been dealt with. From lichenification (lichen simplex chronicus of Vidal), which is produced by friction on the skin, the diagnosis is made by the fact that the latter only occurs in circumscribed patches, and that the typical discrete papules of lichen planus are absent.

Treatment.—In the acute generalised cases rest in bed is essential, and it is of the greatest service in chronic cases, materially shortening their course. Arsenic is looked upon as a specific, but may require to be pushed; arsphenamine (salvarsan) has been recommended by some authors. As in psoriasis, arsenic is not advised in cases in which the eruption is coming out, these cases doing best on mercury; liq. hydrarg. perchlor., min. 60, t.d.s. If the irritation is very bad, bromides or some hypnotic at night may be required, and for this symptom lumbar puncture has been recommended.

For local treatment anti-pruritic lotions and ointments are required; of these ichthammol, oil of cade, coal tar, phenol and menthol are most useful.

For the hypertrophic patches, ac. salicylic plaster, followed by X-rays or CO_2 snow, is the most satisfactory method of treatment.

SCLERODERMA

This is a condition of hardness and rigidity of the skin, caused by a degeneration of fibrous tissue, which is probably of inflammatory origin. It is met with in two forms—(1) Generalised scleroderma, and (2) localised scleroderma or morphœa.

Ætiology.—It is chiefly a disease of young adult life and is more common in women than in men. It has been variously attributed to a tropho-neurosis, to alterations in endocrine secretion, to an endarteritis, and to a primary hyperplasia of the fibrous tissue of the skin. Recent work by Dowling and Griffiths suggests that a relationship exists between this disease and thyrotoxicosis.

Pathology.—There is a degeneration of the fibrous tissue bundles in the dermis and subcutaneous tissue, with replacement of fat by fibrous tissue in the latter. There is also an exudation of cells around the vessels of the dermis, with some endothelial proliferation. The epithelium may be flattened by pressure and excess of pigment may be present. Degenerative changes may also be seen in the muscles in some cases.

Symptoms.—1. *Generalised scleroderma.*—This condition may appear rapidly or slowly. In both cases a disturbance of the general health, such as fever, joint pains, neuralgia or itching, may precede or accompany the attack. Stiffness of the parts involved is often the first symptom, and this may spread rapidly or slowly till it produces fixity of the joints, followed by progressive wasting of the muscles. Breathing may become difficult, owing to fixation of the skin of the chest, and taking of solid food may be prevented by the involvement of the cheeks and mouth. The skin appears swollen and glossy and is very hard; the deeper structures are fixed and the furrows of the skin disappear. The colour of the skin may be normal or waxy in appearance. The lesions are usually symmetrical and the mucous membranes may be affected. These cases may occasionally clear up spontaneously, but often end fatally.

Occasionally the disease begins in the hands. The skin is drawn tightly over the fingers, fixation of the joints occurs and atrophy supervenes, so that the fingers become pointed. This type is called *sclerodactylia*.

2. *Localised scleroderma* or *morphœa.*—In this type the lesions vary from the size of a pea to large patches involving almost all the back or front of the trunk. Patches may be pinkish in colour and raised, with a smooth polished surface and with a sensation of rigidity; or slightly depressed below the surface, very rigid and fixed, and often surrounded by a lilac border, and occasionally occurring in bands; or again they may be of dead white colour, with more or less irregular edges, and of normal consistence. This latter type is one of the forms of so-called *white-spot disease*.

These cases run a very chronic course, often of many years, and are resistant to treatment.

Diagnosis.—From sclerema neonatorum, by the age of the patient and the fact that this condition is confined to the subcutaneous fatty layer.

Treatment.—In generalised cases, the patient should be kept warm, and massage and hot air baths given. Cod-liver oil internally is of value. Thyroid is largely given in all varieties, but its action is very uncertain. In morphœa, local fibrolysin injections have been given with success. X-rays are claimed to be beneficial. Treatment, however, is unsatisfactory.

SCLEREMA NEONATORUM

This condition has no relationship to the foregoing. It occurs in newly-born infants, and is characterised by hardening of the subcutaneous fatty layer in certain parts of the body.

Ætiology.—It has been attributed to hardening of the fat, owing to lowering of body temperature, but this is certainly not an essential factor. There is evidence of a deposit of crystals in the tissues, and of a well-marked proliferation of the reticulo-endothelial cells in the neighbourhood of these deposits. This is probably due to a reduction in the olein in the fat, but how this comes about is not yet known.

Symptoms.—The affection usually begins within a day or two of birth. It occurs symmetrically and chiefly affects the calves, thighs, buttocks and back. The subcutaneous fat becomes very hard, and does not pit on pressure. The edges are well-defined. A certain number of cases die, but in the less severe cases the patches disappear in a month or two. A generalised hardening of the fat occurs all over the body in infants suffering from severe diarrhœa, but this condition appears to have no relation to that just described.

Treatment.—The child should be kept warm and given plenty of nourishment. Cod-liver oil is said to be very beneficial.

D—THE LYMPHO-GRANULOMATA

These cases form a bridge between the inflammatory dermatoses on the one hand and the new-growths on the other. The lesions in many ways resemble the granulomata produced by bacteria, and in other ways resemble sarcomata. The following conditions are included: (1) Sarcoidosis, (2) leukæmia cutis, (3) lymphadenoma cutis, and (4) mycosis fungoides.

SARCOIDOSIS

Synonyms.—Besnier-Boeck-Schaumann's Disease; Lympho-granuloma benigna (Schaumann).

Dermatologists have been familiar for many years with two conditions of the skin which from their histological characters have been thought to be tuberculous. The first, which consists of a symmetrical granulomatous condition affecting chiefly the nose, cheeks, ears and fingers, was described by Besnier in 1889 under the name "lupus pernio," and differentiated by him from lupus vulgaris and lupus erythematosus, with both of which conditions

it has some features in common. The second condition, described by Boeck in 1897, was characterised by the presence, generally on the face, of granulomatous swellings, single or multiple, of varying size and of a translucent appearance, often showing small yellowish points closely resembling the "apple jelly nodules" seen in lupus vulgaris. To these lesions Boeck gave the name of "cutaneous sarcoids." In 1917 Schaumann showed that these two conditions were only clinical types of the same disease, and he further showed that they were merely cutaneous manifestations of a pathological process which affected many other organs in the body, the lymphatic system, bone-marrow, lungs and other viscera. It is now recognised as a diffuse reticulo-endotheliosis, somewhat resembling, though clearly distinct from, Hodgkin's disease. Schaumann has suggested that the condition should be called "lympho-granulomatosis benigna," but at the present time the name "Sarcoidosis" has been tacitly adopted in this country.

Ætiology.—The condition is not very common in the British Isles but more frequent on the European continent, especially in the Scandinavian countries. It affects both sexes equally, and is most frequent between the age of 20 and 40. It is very rare before puberty but isolated cases have been described even in infancy.

There is much controversy as to the cause of the condition. The histological architecture, described below, has long suggested a tuberculous ætiology, but certain features have raised doubts on this point. The absence of caseation in the lesions; the fact that the vast majority of the cases give negative tuberculin reactions; that acid-fast bacilli have not been found in the lesions, except in one or two cases in which the clinical diagnosis was by no means certain; and the very indecisive results of animal inoculations experiments—these are points which make the acceptance of the tuberculous hypothesis difficult. Schaumann has obtained the bovine tubercle bacillus from the sputum of some patients suffering from this disease, and has pointed out that active tuberculosis sometimes develops in cases of sarcoidosis and that when this happens the characteristic lesions disappear. He holds the view that sarcoidosis is an indication of a particular phase of immunity to the bovine bacillus, and supports the view of Jadassohn that the high percentage of negative tuberculin reactions is not due to passive anergy, indicative of an absence of tuberculous infection, but is due to an active anergy occurring in a certain phase of this infection.

Certain South American dermatologists have noted the close resemblance of sarcoidosis to tuberculoid leprosy, and have suggested that it may be a form of leprosy. The geographical distribution of the two diseases, however, does not correspond, and this seems to rule out this hypothesis. Lastly other observers think that the disease is an entity due to specific organism not yet discovered. This theory is at present largely based on negative evidence. It is only possible at the present time to say that the ætiology of sarcoidosis is unknown, but that it is difficult to ignore certain similarities to tuberculous infections.

Pathology.—Although the pathological changes were first only described in skin lesions, it is now known that similar changes may occur in many organs of the body. They have been found in the mucous membranes, the lymphatic system, the lungs and other viscera, the bone-marrow and certain other structures. The lesions consist essentially of nodules of epithelioid cells,

often though not always showing a few giant cells in the centre, surrounded by dense bands of normal connective tissue. Sometimes a zone of lymphocytes is found around the epithelioid cells, but these are often very sparse. Fibrous and elastic tissue is entirely destroyed by these granulomatous deposits, and bone is absorbed when invaded. The nodules show no signs of undergoing necrosis or caseation, but in older nodules fibrous tissue infiltration may occur; in healing nodules the cellular structure is gradually replaced by fibrous tissue.

As is mentioned above a very high percentage of cases show a negative tuberculin reaction, a percentage higher than is found in a series of apparently healthy individuals, and this has suggested the possibility of an active anergy and is thought by Jadassohn to be due to the presence of excess of anticutins in the blood and indicative of a tuberculous infection.

The blood picture usually shows little abnormal, but a monocytosis has been described in some cases.

Symptoms.—*Skin.*—Skin lesions are of several types and can roughly be classified into (1) the small nodular sarcoid, (2) the large nodular sarcoid, and (3) lupus pernio. In the small nodular sarcoid the lesions come out more or less symmetrically, and are most common on the face but may be found, often in considerable numbers, on other parts of the body, especially the shoulders and upper limbs. The nodules vary in size from a pinhead to a pea, are smooth dome-shaped papules of yellowish-brown colour, translucent in appearance.

The large nodular sarcoids are often present singly or in small numbers, and are not always symmetrical in arrangement. Again, the face is the site of predilection, the forehead, nose and prominences of the cheeks being the usual sites, but they are found also on other parts of the body. The lesions vary in size from a pea to plaques an inch or so across. They are raised above the skin, smooth and shiny in appearance, reddish to purplish-brown in colour, and soft to the touch. On glass pressure they exhibit translucency, and often "apple jelly" nodules are visible. These differ from those of lupus vulgaris in not breaking down under pressure from a pointed match.

Both the small and large sarcoids can disappear spontaneously or as a result of treatment, and in this case some atrophy of the skin results. In the large variety annular lesions, with a pale atrophic centre and a flattened purplish margin, are sometimes met with.

In lupus pernio the lesions form less well-defined infiltrations arranged more or less symmetrically, the face again being most affected. The nose and cheeks show marked swelling with ill-defined outline and are of a dull purple colour, similar to that seen in chilblains, though the skin is warm and not cold. The ears are also swollen and purplish in tint, especially the lobules. In this condition the skin of the hands and feet are also frequently affected, similar ill-defined purplish swelling involve the fingers and toes, and dorsum of hands and feet; this infiltration may extend up the forearms and legs. Lesions of the large and small sarcoids may be present at the same time. In these cases infiltrations of the subcutaneous tissue are sometimes present, especially on the forearms and arms.

Rare cases of generalised erythrodermia have been described in sarcoidosis. The skin becomes red and scaly over considerable areas of the body, or the eruption may be universal. A similar type of eruption is some

times seen in lymphadenoma or leukæmia. Nodules and diffuse infiltration of the mucous membranes, chiefly in the nose, but also in the pharynx, larynx and mouth have also been described.

Lymphatic system.—Palpable enlargement of accessible lymphatic glands is often present, though this enlargement may be limited to certain glands, of which the epitrochlear are the most common. When examined microscopically these glands reveal the same changes as are seen in the skin. Enlargement of the peribronchial glands is even more common, and can usually be seen in a radiogram of the chest. Of other lymphatic tissue the tonsil is frequently affected, and biopsies of the tonsil are sometimes useful for diagnostic purposes.

Bones.—In many cases of lupus pernio, swellings of the fingers and toes suggestive of tuberculous dactylitis have been observed. These, however, never showed any signs of breaking down. Radioscopic examination has shown that these swellings are mainly due to deposits in the connective tissue surrounding the small bones of the fingers and toes, but it has also demonstrated that in the bones themselves areas of rarefaction and cystic spaces can be seen, sometimes so extensive that the surrounding compact bone of the phalanx may collapse. This change, which may occur in cases where the fingers look quite normal, affects mainly the phalanges and heads of the metacarpal and metatarsal bones, but may occasionally occur in the long bones and even the spine is known to have been affected. These changes are of considerable diagnostic importance.

Lungs.—Patients suffering from sarcoidosis rarely show any symptoms of pulmonary involvement, such as cough or expectoration. Since, however, radioscopic examination of the chest has become a routine, changes have been demonstrated which are more or less diagnostic of the condition. In addition to enlargement of the hilar glands, mentioned above, most cases reveal evidence of deposits of granulomatous tissue in the peribronchial regions. These changes take the form either of a diffuse mottling due to the presence of small nodules scattered along the bronchi, or a reticulation or marbling, showing a more diffuse infiltration along the bronchi. In no case is there evidence of cavity formation.

Other viscera.—Lesions in most of the viscera have been described. Of these the spleen is most frequently affected and may become much enlarged, reaching down to the iliac crest. The liver may also be enlarged but usually to a less degree. Lesions have also been found in the heart, stomach and kidneys. In the case of the last, albuminaria and hæmaturia may be present.

Nervous system.—Involvement of the peripheral nerves, giving rise to localised anæsthesia, paresis and muscular atrophy, has been recorded. Lesions have also been described in the brain and in the pituitary body.

Ocular lesions.—Small yellow nodules have been found on the conjunctiva but special interest attaches to lesions of the uveal tract. These may take the form of an iritis; of nodules on the iris; of exudate with the anterior chamber; and opacities in the vitrous. White patches have also been observed in the choroid. These eye changes may be found in association with infiltration in the salivary glands, especially the parotid, and the condition known as uveo-parotitis or Heerfordt's disease is now known to be a manifestation of sarcoidosis (see p. 532).

General symptoms.—Patients suffering from sarcoidosis generally appear

to be in remarkably good health. Fever is generally absent but in rare cases persistent fever is present. It is not usually high, about 100° F., but may continue without intermission for months. The pulse in these cases is scarcely raised and the patient's general condition is good.

It should be remembered that in most cases only a few of the lesions mentioned above may be present, and that although the skin lesions are the most prominent numerous cases are now on record in which skin lesions are absent.

Diagnosis.—In cases where skin lesions are present they are usually sufficiently typical to enable a diagnosis to be made, but a biopsy can be done to confirm this. The presence of characteristic lesions seen in radiograins of the chest and hands mentioned above are of further assistance, as is a negative tuberculin test. The absence of necrosis and caseation is a useful sign in differentiating from classical tuberculous lesions, while the absence of follicular plugging distinguishes these cases from lupus erythematosus. The diagnosis from syphilis can be made by a careful consideration of the characteristic symptoms of that disease, assisted by a positive Wassermann reaction.

Prognosis.—It is generally held that the milder types of the disease eventually clear up spontaneously. According to Schaumann, however, some cases eventually develop frank tuberculosis, and in these the symptoms of sarcoidosis disappear. Severe cases may die from involvement of vital organs.

Treatment.—The best results have so far been obtained by the administration of chaulmoogra oil preparations or sodium morrhuate. The latter drug is best given either intravenously or intramuscularly in a 3 per cent. solution: 1 to 3 c.c. being administered weekly. It may be necessary to give the drug over a considerable period of time. There can be no doubt that lesions gradually disappear under this treatment but there is some tendency to recurrence, just as there is in the treatment of leprosy by the drug. Milder cases seem to be cured, but it is not easy to say the same of the more advanced cases. Chaulmoogra oil preparations are administered in the same doses as for leprosy. Arsenic also appears to have some influence on the lesions, and is best given in the form of sulpharsphenamine intramuscularly, doses of 0·3 to 0·45 gm. being administered weekly in courses of 10 injections.

No local treatment has much influence on the lesions, but general arc-light baths appear to be of value.

LEUKÆMIA AND LYMPHADENOMA CUTIS

Symptoms.—In both these conditions itching may be a marked symptom; sometimes it occurs without any cutaneous lesions, while at other times very persistent urticarial or prurigo-like lesions are present. Hæmorrhages may occur into the skin, and in some cases exfoliative dermatitis is present.

The more characteristic lesions are, however, granulomatous infiltrations of the skin, which form tumours, either in certain localities or more or less all over the skin. In the former case the face is most affected, the tumours forming chiefly on the forehead, about the nose and on the cheeks, producing a leonine appearance. The lesions vary from a pea to an orange in size, and

are usually of a dull purplish-red colour. Most of the cases recorded occur in lymphatic leukæmia, but a few have been reported in the myeloid cases. They also occur in Hodgkin's disease, but there is great difficulty in distinguishing aleukæmic leukæmia from Hodgkin's disease, unless the glands have been examined microscopically.

Treatment.—This has been dealt with in the articles on Leukæmia and Hodgkin's disease (pp. 802 and 841).

MYCOSIS FUNGOIDES

A chronic inflammatory dermatosis with a tendency to form granulomatous tumours, which usually ends fatally.

Ætiology.—It is a disease of late middle life, and more common in men. Its cause is quite unknown, but it is probably an infective process and closely related to leukæmia, though no characteristic blood changes have been observed.

Symptoms.—In the early or premycotic stage the most frequent lesions are patches of redness and scaling, associated with intense itching. After a times these lesions become infiltrated and raised above the surface of the skin. Later, tumours appear in these patches, usually about the size of an orange, but not infrequently much larger. The epidermis over them gives way and a fungating mass is produced. These tumours are usually multiple.

Sometimes the initial lesion takes the form of an eczema, an urticaria or a dermatitis exfoliativa, but in all these cases itching is a prominent symptom. In other cases the tumours appear without any pre-existing dermatosis.

The course is slow, and the general health is affected first by loss of sleep and then by septic absorption. Practically all cases eventually terminate in death.

Diagnosis.—This may be very difficult in the premycotic stage. The itching and the persistence of the symptoms in spite of treatment, together with the age of the patient, will help in coming to a diagnosis.

Treatment.—The only treatment known to benefit these cases is X-rays or radium. Either of these will keep the lesions quiescent for a considerable time, but recurrence generally takes place sooner or later. Arsenic and antimony may also be given.

A. M. H. Gray.

V. TUMOURS OF THE SKIN

Tumours can be divided into epithelial and connective-tissue tumours, and each of these varieties into benign and malignant.

BENIGN EPITHELIAL TUMOURS

1. WARTS

These are benign epithelial tumours, characterised by an overgrowth of the prickle-cell layer, with or without hyperkeratosis, and produced by an

infective agent, which appears to be a filter-passing virus. The following types are recognised :

1. *Verruca vulgaris.*—This is the common wart which is so frequently met with on the back of the hands, but may occur on the face and other parts of the body. The lesions are raised tumours, varying in size from a pinhead to a filbert, and are usually discrete, but may group to form larger swellings. They have a rough surface, rise sharply from the surrounding skin, and are skin-coloured. Histologically they show great hypertrophy of all the epithelial layers, with downward growth of the interpapillary areas, and a corresponding papillary elongation. They occur chiefly in children. They are inoculable from one spot to another, and from one individual to another.

Treatment.—Isolated lesions are best removed by the application of CO_2 snow for from 15 to 40 seconds, according to their size. They may be burnt away with glacial acetic, trichloracetic, or nitric acid, silver nitrate or the actual cautery. When very numerous, evulsion with a sharp spoon or X-rays are most satisfactory.

2. *Verruca plana juvenilis* are pinhead-sized warts, seen chiefly on the face and hands of children, though they are met with in adults. They have smooth, flat tops, and are usually very numerous.

Treatment.—They are best treated by touching with the galvano-cautery, or by magnesium ionisation.

3. *Verruca plantaris.*—This is a wart which occurs on the sole of the foot, and has the appearance of a corn, because it is surrounded by a hyperkeratotic ring, and on account of the pressure on the foot does not stand up above the level of this ring. It is, therefore, often mistaken for a corn. It is usually extremely painful.

Treatment.—The most satisfactory treatment is by X-rays ; $1\frac{1}{2}$ to 2 skin units are usually required, the surrounding zone being carefully screened. These warts may also be removed by salicylic acid plaster, followed by touching with acetic acid, by CO_2 snow, or by evulsion.

4. *Verruca filiformis.*—These minute warts are usually about 1 mm. in diameter at their base, with long filamentous processes. They are sometimes found on the face ; but chiefly occur on the genitals, and around the anus. They frequently occur in very large numbers, forming cauliflower-like growths. They are often seen in cases of gonorrhœa, and are sometimes known as *gonorrhœal warts* ; but they may be present apart from this disease, and are probably due to some other infecting agent. In these warts there is very little overgrowth of the horny layer.

Treatment.—Locally antiseptic applications, such as 1 in 1000 perchloride of mercury in spirit painted on frequently, or silver nitrate 3 per cent. in sp. æth. nitros., will cause them to dry up, or they may be removed with the galvano-cautery, or painted with trichloracetic acid.

5. *Keratoma senile.*—These co-called senile or seborrhœic warts are commonly seen on the face, back and chest of old people ; but may occur in younger persons. They vary in size from a pea to a filbert, and are only slightly raised from the skin. They are soft to the touch, and have a slightly warty surface. Their colour varies from yellow to a deep black, and they may itch a good deal. The distribution is much the same as for seborrhœic dermatitis.

Treatment.—Washing with soap and water, followed by the application

of 10 per cent. ac. salicyl. ointment will often remove them. Failing this, painting with trichloracetic acid, freezing with CO_2 snow, or a skin unit of X-rays should be employed.

2. ACANTHOSIS NIGRICANS

This is a rare condition in which warty pigmented growths appear on the neck, axillæ, groins, umbilicus, and flexures of the limbs and on the face. These growths often fungate and suppurate, especially in moist areas. In addition areas of pigmentation and scattered warty growths may occur. The mucous membrane of the lips, cheeks and tongue may be affected. In a large proportion of cases abdominal malignant growths have been found; but in other cases no such complication exists. The nature of the condition is not understood.

Treatment.—No treatment is known to affect the condition.

THE DYSKERATOSES

1. MOLLUSCUM CONTAGIOSUM

In this condition small tumours appear on the skin which, like the warts, are infective and produced by a filter-passing virus. They differ from warts not only in clinical characters, but in the peculiar degenerative changes which occur in the process of horny cell formation.

Pathology.—The most striking feature in a section is the presence between the Malpighian and horny layer of large cells containing large transparent oval bodies. These are known as "molluscum bodies," and at one time were thought to be coccidial bodies, but are now considered to be degenerations of the cell protoplasm.

Symptoms.—The lesions consist of small lentil- to pea-sized bodies of a white or pinkish colour, with a smooth glistening surface. They may appear anywhere on the skin. They are dome-shaped, and have a central pit, in the floor of which the thickened horny layer can be seen. Not infrequently they become inflamed.

Treatment.—By taking a sharpened match, and introducing it into the central depression, the whole horny mass can be forced out, and if the cavity be painted over with pure carbolic acid a cure will result.

2. DARIER'S DISEASE

This is a very rare condition of the skin usually seen in young adults in which an eruption of follicular papules develops on the face, scalp, abdomen, back, and the flexor aspects of limbs. The lesions run together and form warty-looking masses. The disease is slowly progressive, and the lesions are resistant to treatment, but the general health is not affected.

Microscopic examination shows similar changes to those seen in molluscum contagiosum, namely, an irregular hyperkeratosis with formation of "psorosperms" in the region of the granular and Malpighian layers of the epidermis.

Treatment.—This consists of baths and the application of keratolytic agents, such as salicylic acid.

3. PAGET'S DISEASE OF THE NIPPLE

This is a chronic affection which usually develops around the nipple in middle-aged women, but has been described in other parts of the body and in men. It is seen as a sharply defined, red, oozing area involving the nipple, the areola, and the skin around for a short distance, and is almost always unilateral. The whole area has a distinct parchment-like induration. The nipple becomes retracted, and eventually disappears. The condition is associated with carcinoma of the breast, and whether it is primary or secondary is still a matter of dispute.

In this condition, as in the two diseases just referred to, "psorosperms" are seen under the microscope. The surface horny layer is mostly lost, and the deeper layers of the epidermis are much hypertrophied and œdematous, but show no obvious epitheliomatous proliferation.

Treatment.—Amputation of the breast is the only treatment that can be advised.

MALIGNANT EPITHELIAL TUMOURS

1. RODENT ULCER

A slowly growing epithelioma usually single, but sometimes multiple, which may cause considerable local destruction of tissue but does not form metastases.

Pathology.—This variety of epithelioma is usually described as a basal-cell epithelioma. In section epithelial processes are seen penetrating into the underlying dermis and subcutaneous tissue; but the processes are bounded by a regular basal layer of cubical cells, and although degeneration cysts may form in these processes no cell-nests are formed.

Symptoms.—The lesions chiefly occur in old people; but this is not always so. They also rarely begin anywhere but on the face, and then chiefly in the neighbourhood of the eye, or on the nose or cheek. At first a small raised white nodule appears, with small vessels coursing over it. Then, as it spreads, an ulcer forms in the centre, but the raised intensely hard white border persists. If not treated a great deal of tissue destruction occurs; the nose may be destroyed, or the antrum perforated, and the whole of the nasal cavities opened up. In advanced cases practically the whole face is destroyed. Some cases, however, remain superficial, spreading slowly, the older parts healing as the lesion spreads. Multiple lesions are not very rare.

Benign forms are also recognised. In one the lesions are pea-sized or slightly larger nodules, scattered over the face, and of the same type as the early lesions referred to above. Sometimes they undergo cystic change. They were described by Brooke under the name of *epithelioma adenoides cysticum*. Another benign type is seen in which multiple walnut-sized tumours form on the scalp (*Spiegler's tumours*). A third type occurs in the form of multiple psoriasiform patches on the trunk, and has been named by Graham-Little *erythematoid benign epithelioma*.

Diagnosis.—This can always be made in cases of doubt by microscopic examination.

Treatment.—Excision is the best treatment when possible ; but excellent results are obtained by radium, or X-rays. CO_2 snow has been advocated for early cases, and the results obtained are excellent. In advanced cases, which are unsuitable for surgical treatment, diathermy is useful.

2. SQUAMOUS EPITHELIOMA

In this condition rapidly growing tumours form, which ulcerate and cause local destruction of tissue, and also cause secondary glandular involvement. It is chiefly a disease of old age.

Pathology.—Sections show an irregular proliferation of the Malpighian layer, with the formation of cell-nests, and the limiting basal layer is absent.

Symptoms.—The lesions begin as nodules, much like those of rodent ulcer, but they spread much more rapidly and either form irregular deep cut ulcers, without the characteristic edge seen in rodent ulcer, or else they become raised and form mushroom or cauliflower-like growths. The glands may be involved, and general dissemination may occur. The condition may sometimes supervene on pre-existing non-malignant conditions. It may commence in a keratoma senile, in the warty conditions which occur in cases of atrophy of the skin due to exposure to tropical sun, on an old lupus scar, on X-ray dermatitis, in xeroderma pigmentosa, in arsenical keratoses and in tar molluscum.

Treatment.—This is purely surgical, and consists of erasion of the local growth and of the glands draining the area concerned. Radium is now extensively used in treating these growths. In the case of epithelioma complicating lupus vulgaris, however, secondary glandular involvement does not appear to occur, and local destruction with arsenic paste, or by diathermy, gives even better results than excision.

TUMOURS OF THE APPENDAGES OF THE SKIN

1. MILIUM

In this disease pinhead-sized yellowish-white bodies are seen in the skin of the face, chiefly on the cheeks, eyelids and forehead. They are often very numerous. They can be shelled out, and are found to consist of a whorl of epithelial cells. Their origin is unknown, but they are probably derived from the lanugo hair follicles.

Treatment.—These tumours can be destroyed by electrolysis.

2. SEBACEOUS CYSTS

These are painless cystic swellings chiefly found on the scalp, face, ears, back and scrotum. They vary in size from a pea to an orange. When incised they are found to be filled with cheesy matter. They are either due to blocking of the sebaceous duct, or according to some authorities they are of embryonic origin. True *dermoid cysts* of the skin are also found.

Treatment.—Excision is the most satisfactory method of treatment.

3. ADENOMA SEBACEUM

A symmetrical eruption of pinhead-sized, bright red papules, of congenital origin, on the face. It commences very early in life, and is often associated with mental defect—in fact, cases are most often seen in asylums. The lesions are distributed chiefly over the nose and cheeks, and consist of hypertrophied sebaceous glands and numerous capillary vessels.

Treatment.—The lesions can be destroyed with the galvano-cautery, by electrolysis or by diathermy.

Tumours of the sweat glands and ducts are so rare as to need no description here.

CONNECTIVE-TISSUE TUMOURS

1. KELOID

This is a fibrous tumour developing in a scar. The mere overgrowth of a scar is sometimes referred to as a *hypertrophic scar*, while the term keloid is limited to those cases in which the tumour extends beyond the original limits of the scar. In this latter condition processes often grow out in all directions like tentacles, and also in some cases the condition appears to start spontaneously from the normal skin; but there can be little doubt that some small abrasion was present. Small keloids often appear after acne vulgaris, varicella and other dermatoses which lead to scarring. There can be little doubt that this fibrous overgrowth is due to some chronic bacterial infection of the wound—probably a staphylococcal infection.

Treatment.—The best results are obtained by radium and X-rays.

2. FIBROMA—MOLLUSCUM FIBROSUM

Hard fibromata of the skin are rare, and usually occur in pear-sized nodules scattered about the skin. Soft fibromata are common, and are met with as small pedunculated tumours, chiefly on the trunk. They may occur in large numbers, and are then described as molluscum fibrosum. In this condition the tumours vary in size from a small pea up to several inches in diameter. Not only the skin but the mucous membranes may be the seat of these tumours. At times they form huge dependent unshapely masses, which completely disfigure the part from which they arise; this condition is called *dermatolysis*. Not all the tumours are pedunculated—as some are sessile—but all have the same softness. Some definitely surround nerve trunks, and it has been thought that they all develop in connection with the nerve fibres; hence they are often called *neuro-fibromata* or *plexiform neuromata*.

In some cases true neuro-fibromata and molluscum fibrosum lesions occur in combination with pigmented spots about the body. This syndrome is called *Recklinghausen's disease*, and is sometimes associated with mental disturbance.

Treatment.—Nothing can be done except surgical removal of the tumours, and this is only occasionally necessary.

3. LIPOMATA

These are soft freely movable lobulated tumours in the subcutaneous tissue, and may be single or multiple. One variety is very painful and associated with general adiposis, and is referred to as *Dercum's disease* (p. 1480).

Treatment.—Excision is the only treatment.

4. MYOMATA

Small multiple tumours of the size of a pea are sometimes found which have the structure of leiomyomata, and arise from the arrectores pilorum muscles. The lesions are often numerous, grouped and painful.

Treatment.—The cautery, or excision, is the only treatment.

5. MULTIPLE IDIOPATHIC SARCOMA OF KAPOSI

This is a curious condition chiefly seen in old people, and generally in the natives of Eastern European countries; but cases have arisen *de novo* in this country. The lesions occur chiefly in the region of the ankles, but have also been found on the hands and on the trunk. They are irregularly shaped red plaques raised from the skin, and of firm consistence. Histologically they consist of an overgrowth of fibrous tissue with dilated blood spaces. Whether this condition is of inflammatory origin, or is a species of nævus is as yet undecided. The condition does not affect the general health.

Treatment.—No treatment is known to affect the condition.

6. SARCOMATA

Both round- and spindle-celled sarcomata have been found arising in the skin, but are rare. They may be single or multiple, of any size, sessile or pedunculated, and are usually of a purplish-red colour. They tend to break down and produce fungating ulcers, and run a rapid course ending in death unless removed in the early stages.

Treatment.—This is purely surgical.

7. NÆVI

This term should be applied only to certain new formations of congenital origin; but in practice certain other conditions have been included. They fall into four classes: (1) Vascular nævi; (2) lymphatic nævi; (3) pigmented nævi; and (4) hyperkeratotic nævi.

Vascular Nævi.—There are two chief varieties, the capillary and the cavernous nævi.

Capillary nævi.—These nævi are essentially dilatations of the capillary vessels of the papillary and subpapillary layers of the dermis. They form flat red patches of varying size. They may be small pea-sized lesions, or they may practically cover the whole body, including the mucous membranes. When they occur in large patches they are called *port-wine stains*.

The lesions are usually not raised and not infiltrated, the only change being in the colour of the skin, which is red or purple in the affected areas.

Sometimes, however, thickenings occur irregularly throughout the patches. On examination with a lens the capillaries can often be seen. These nævi are either present at birth or appear shortly afterwards. They tend to get paler as age advances, but rarely disappear.

Treatment.—These cases are very difficult to treat, especially the more extensive ones. CO_2 is useless, unless the application is sufficiently long to destroy the skin. Radium, though sometimes successful in removing the nævus, is inclined to produce atrophy and telangiectases in its place. The best hope in disfiguring cases rests with excision and plastic surgery, though some fair results have been obtained with diathermy.

Cavernous nævi.—These are soft or hard tumours, which appear as bright red sharply defined swellings raised above the level of the skin or as purplish indurations in the skin and subcutaneous tissue. The blood can usually be squeezed out of them by pressure. They consist of a fibrous stroma surrounding irregular blood spaces, the whole being more or less encapsuled. The tumours vary much in size and extent, some being as large as a cricket-ball or larger. Any part of the body may be affected, but they are frequent on the face and scalp, the lips and eyelids often being attacked.

Treatment.—Small tumours are best treated with CO_2 snow, one exposure of 15 to 30 seconds being sufficient to remove them. Larger tumours may be dealt with by repeated applications of snow, but they do better with multiple punctures with a fine galvano-cautery at dull red heat. In some situations excision is the best treatment, while radium can often be used with success. Electrolysis was formerly much employed, but is slow and has been superseded by the methods mentioned above. It is often advisable to abstain for a time from active treatment, as there is a tendency for the tumours to disappear spontaneously.

Stellate nævi.—These are not strictly nævi at all—that is, they are not congenital growths. The cause is not clear, but they may be degenerations or possibly traumatic dilatation of venules. The lesions consist of a central pinhead-sized dilatation of a venule, with a stellate arrangement of dilated vessels running into it. They are seen chiefly in children on the face, but also occur in adults. It has been thought that insect bites may be a determining cause.

Treatment.—If the central vessel is destroyed by a fine galvano-cautery or by electrolysis the lesion will disappear.

Lymphatic Nævi.—**Synonym.**—Lymphangioma Circumscriptum.

This occurs as a raised circumscribed patch of skin colour, which on close examination is seen to consist of closely grouped vesicles, varying in size from a pin's head to a lentil. There may be a few discrete vesicles surrounding the main patch. In some cases, too, the surface is warty. The patches appear at or soon after birth, but may come out later. Microscopic examination shows dilatation of the lymphatic vessels of the dermis, with or without epidermal hypertrophy.

Treatment.—Excision, cauterisation or treatment by radium are the three methods applicable.

Pigmentary Nævi or Moles.—Nævi of this class are very numerous and vary considerably in type. They may consist of pigmented patches of varying size and various depth of colour from a pale yellow to a deep black. These may be associated with hairy growths. In other cases smooth lobulated

pigmented tumours may occur on any part of the skin. Some cases have a rough, warty surface, while others are hairy. They may be quite small, no larger than a pea, or may cover large areas of the body, and have a distinct tendency to occupy segmental areas. They may appear at or soon after birth, or may occasionally develop later in life. The histological picture is characterised in all types by the presence of masses or columns of round embryonic cells in the dermis and also in the deeper layers of the epidermis. There is excess of pigment in the cells of the basal layer, in the adjoining Malpighian layer, and also pigmented wandering cells in the upper part of the dermis. The epidermal changes vary with the type of nævus.

There is a slight tendency for these pigmented moles to undergo malignant transformation into *nævo-carcinoma*, which has a high degree of malignancy, giving rise to rapidly generalised metastases.

Treatment.—It is best to leave pigment moles alone unless some definite indication for treatment is present. Free excision with grafting or plastic procedures is indicated in some disfiguring lesions, or in those liable to irritation from friction. CO_2 snow, diathermy or electrolysis may be used in the case of the smaller tumours.

HYPERKERATOTIC NÆVI.—**Synonyms.**—Linear Nævi; Ichthyosis Hystrix.

In this type of nævus the lesions are arranged in lines or bands, usually on the limbs, and often appear to follow the course of certain nerves. They are frequently unilateral, though in the ichthyosis hystrix type they are frequently symmetrical. The lesions consist of thick horny plugs, which can be pulled out from depressions in the skin, and are closely packed together; sometimes great horns protrude from the skin. On microscopical examination an irregular hyperkeratosis is found, with alternating depressions and elevations.

Treatment.—This is very unsatisfactory. Salicylic acid plasters may be used to soften and remove the horny masses, and small areas can be excised or cauterised.

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VI. OTHER MORBID CONDITIONS OF THE SKIN

ANOMALIES OF PIGMENTATION

Pigmentation may be produced by the deposit of blood pigment in the skin, by the excessive production of melanin—the normal pigment of the skin, or by the deposition of such substances as silver, seen in poisoning by that substance.

Blood pigment is found after hæmorrhages have subsided and in congestive conditions.

Increase in melanin occurs in the pigmentary nævi already referred to; in certain internal diseases, such as Addison's disease, diabetes and exophthalmic goitre; and in pregnancy; after the ingestion of arsenic; and locally, after certain inflammatory conditions of the skin, such as sunburn, erythema ab igne, lichen planus and syphilis. It also occurs in a curious condition named vitiligo, the ætiology of which is obscure.

1. LENTIGO

This is the name given to *freckles*, which occur on parts of the body exposed to the sun in certain individuals. The lesions are so well known as to require no description.

Treatment.—This is purely preventive. The application of a greasy preparation, such as lanolin, to the skin before exposure to the sun will protect the face from an erythema; sunshades and veils, especially red or brown, are also useful.

2. CHLOASMA UTERINUM

This is a peculiar yellowish-brown pigmentation which occurs chiefly about the face in women who are pregnant, or suffering from some uterine disturbance. It occurs in ill-defined patches, chiefly on the forehead and on the abdomen. It disappears after the termination of pregnancy, or when the pelvic condition is rectified.

3. VITILIGO

This condition, also known as *leucodermia* and *melanodermia*, may occur at any age or in either sex. The ætiology is quite unknown, both toxic and tropho-neuritic theories having been invoked to explain the phenomenon, but very little evidence is at present forthcoming in favour of either view. It consists of patches of a dead white colour appearing in various parts of the body; they may be quite small, or may in rare cases completely cover the body. The edge of the patches is sharp, and the surrounding skin is hyperpigmented; the texture remains normal. In the white areas pigment is entirely absent, but no other histological changes can be observed. The patient's health is in no way affected, nor can any derangement of any of the organs of the body be made out in the majority of cases.

Treatment.—The only treatment which appears to have any effect is the repeated application of ultra-violet rays, either by the Kromayer lamp or by arc-light baths.

4. ALBINISM

This is a congenital condition in which there is complete absence of pigment in the skin and other epidermal structures. The hair is white, the eyes pink from absence of pigment in the iris, and the skin fails to pigment, even when exposed to the strongest sun.

ATROPHIES OF THE SKIN

Various conditions may cause atrophy of skin, particularly local inflammations, but under this heading certain atrophic conditions are dealt with that have not been considered elsewhere.

1. SENILE ATROPHY

Generalised atrophy of the skin occurs in old age. The skin becomes thin and loses its elasticity; irregular pigmented spots, small telangiectases

and vascular cysts (de Morgan's spots) appear, especially on the face and trunk; wrinkles are very numerous; and the skin develops a yellowish colour. A generalised pruritis may occur. Senile warts are frequently found, and these may be the seat of a localised pruritus. They occasionally become transformed into squamous epitheliomata.

Treatment.—This is purely symptomatic.

2. STRIÆ ATROPHICÆ

These are bands of atrophic skin which develop in areas where the skin has been much stretched. They are seen best on the abdomen, breast and hips of women who have borne children. The lines when first formed are red in colour and about ½ inch in diameter, but as they get older they become greyish-white. It is thought that they are produced by damage to the elastic fibres of the skin by stretching.

No treatment is required.

3. XERODERMA PIGMENTOSA

This is a rare condition of the skin which is hereditary. The ætiology is quite unknown, but there is no doubt that light-rays play a part in the production of the lesions. The affection begins in infancy, and is characterised by the appearance on the face and backs of the hands of macules of yellow and brown pigmentation. The disease is slowly progressive, and in addition to pigmentation other signs of skin degeneration appear, namely, atrophic patches, telangiectases and warty growths. Later, ulceration occurs and epitheliomatous tumours appear on the warty growths.

Treatment.—The patient should be protected from the sun's rays as much as possible. The warty growths can be removed and the ulcer treated antiseptically. Epitheliomatous growths can be checked by radium, but the cases always end fatally.

CONGENITAL CONDITIONS OF THE SKIN

Most of these, such as ichthyosis, the nævi and xeroderma pigmentosa, have been already considered. There still remains one condition which has not been alluded to, namely, epidermolysis bullosa.

EPIDERMOLYSIS BULLOSA

This is a congenital defect of the skin which renders it extremely sensitive to the slightest injury. In those affected, the slightest knock is sufficient to produce a blister. The disease is hereditary, and can often be traced to a considerable number of members of a family. The lesions usually appear first in early infancy, but occasionally they have occurred for the first time later in life. They vary much in degree. In some cases the lesions are slight and cause very little inconvenience, and no disturbance to the general health. In other cases the lesions are numerous, almost all parts of the body being affected at one time or another; teeth and nails develop badly, septic com-

plications are often severe, and these cases usually do not live to adult age.

Treatment—Nothing can be done except by prevention of sepsis and the antiseptic treatment of the lesions when once formed.

DISEASES OF THE HAIR

1. ALOPECIA

Loss of hair occurs in many diseases. It may fall out after acute illnesses, such as influenza and typhoid fever, in inflammatory conditions of the scalp, in secondary syphilis, and in dermatitis exfoliativa. It is also lost locally in scarring conditions, traumatic or inflammatory, as seen in lupus erythematosus or tertiary syphilis. A progressive loss also occurs in senile atrophy of the skin; this, however, may occur prematurely.

ALOPECIA PREMATURA.—**Ætiology.**—The disease is essentially one of the male sex, and usually begins at about the age of 20. The ætiology of the disease is not clear. Two factors appear to be present, heredity and seborrhœa of the scalp. It is quite clear that the latter condition by itself does not always produce baldness, but it appears to accelerate the loss of hair, as might be expected. Heredity seems to be important, especially in those cases where complete baldness occurs at an early age, and there is no doubt that fine hair is more liable to fall out early than is stouter hair.

Symptoms.—This gives rise to a very characteristic type of hair loss which is familiar to every one. The hair gradually gets thin on both temples and on the vertex, and by slow progression these thinned areas eventually meet, leaving the top of the head entirely bald or only covered by a fine down, while the sides and back of the scalp are covered normally. The progress varies very considerably in different individuals, some becoming completely bald in a year or two, while others still have a good crop of hair at 50.

Treatment.—This has mainly to be directed to curing the seborrhœa, and the methods for doing this have been dealt with under that heading. Apart from this, avoidance of tightly fitting hats, and gentle massage with the fingers are the most appropriate remedies. Certain drugs such as pilocarpine, have been thought to have a stimulating effect on hair growths, and rubefacients, such as cantharides, are also much employed. The general health should receive attention.

ALOPECIA AREATA.—In this condition the hair falls out in patches, leaving smooth, shiny, bald areas. There is a general tendency for the hair to grow again.

Ætiology.—The malady affects both sexes and generally occurs in early adult life. It is probable that the disease is an inflammatory condition, but the nature of the irritant is unknown. A somewhat similar loss of hair can be produced by the administration of thallium salts, which lends support to the toxic theory. It was at one time thought to be due to an external parasite, but there is no evidence to support this view. It has also been thought to be of nervous origin, as damage to nerves has produced bald patches over the areas sup

Symptoms.—The disease may start suddenly or slowly. In some cases a large circular patch of baldness may occur in a single night, and in these cases the skin may be tender and reddened. Generally, however, a small bald patch appears, which spreads slowly, and other patches may subsequently arise, causing considerable loss of hair and a curious patchy condition of the scalp. Not only the scalp hairs but those of the beard, the eyebrows, axillæ and pubes may be affected, and in severe cases all the hairs of the body, including the eyelashes, may fall out. In one type a band of hair may be lost extending from ear to ear around the margin of the scalp, either in front or behind the head or even in a complete circle.

In the patchy form, the individual patches are characteristic. The centre is usually completely bald and shiny, though new downy hairs may be seen. Around this a row of stumps may be observed. These are club-shaped, like a note of exclamation, being very thin as they enter the scalp and thicker above. When pulled out, a shrunken hair bulb comes out and the hair does not break as in ringworm. The zone outside the zone of stumps looks normal, but if the hairs are pulled upon many loose hairs may be detached.

Course.—This varies in different cases. Usually new hair grows fairly rapidly, and the patches cease to spread. The new hair is usually white when it first appears, but pigments later. In some cases, however, the patches progress as new hairs grow and this may continue for many months. In the band-form hair growth is usually much slower. In the generalised cases the prognosis is not so good, a large proportion losing the hair permanently.

Diagnosis.—This has to be made from ringworm and is generally easy. In ringworm the patch is scaly and covered by stumps, which break easily and have an irregular fractured end. Under the microscope the fungus can be seen.

Impetigo contagiosa of the scalp sometimes gives rise to bald patches. They are numerous, small and usually red in colour, and no stumps are seen.

Treatment.—The general health must be looked to and all possible sources of irritation removed. The teeth must be attended to, tonsillar sepsis treated, and errors of vision corrected. General tonic treatment should be prescribed, and rest from overwork and worry ordered. Thyroid extract has been recommended, but in the writer's experience has sometimes made the condition worse.

Local applications which cause hyperæmia are of most value. Painting the patches with pure phenol, iodine or blistering fluid, or rubbing in oil of turpentine is useful. Various antiseptic lotions, such as perchloride of mercury and resorcinol, have been used with success. High frequency current and ultra-violet rays have given good results when other means have failed. If seborrhœic dermatitis is present it should be treated.

Cicatricial Alopecia.—In this condition, also known as *pseudo-pelade* or *folliculitis decalvans*, progressive loss of hair takes place, and the scalp shows signs of atrophy or scarring. There is a progressive patchy loss of hair occurring over considerable areas of the scalp, and on examination inflammatory lesions are often present round the hair follicles. The denuded areas show obvious scarring, and hair does not regrow on the patches. The disease occurs chiefly in young adults, and though it does not usually lead to complete baldness, very disfiguring patches remain.

Treatment.—This consists in the application of antiseptic ointments and lotions, perchloride of mercury, resorcinol and sulphur being the most useful, but no treatment is very efficacious.

2. HYPERTRICHOSIS

This is the term applied to an excessive growth of hair. It is usually confined to those cases in which a growth of stout hairs occurs in sites usually covered with lanugo hairs, such as the face in women. This may sometimes be very excessive, and the " bearded woman " and the " dog-faced man " are extreme examples, though the latter are often cases of hairy moles. The only conditions that the medical practitioner is likely to have to deal with are those in which stout and dark hairs occur on the chin and upper lip in women. The treatment consists in removal of the hairs by electrolysis, but considerable judgment is often required to decide whether a case is suitable for treatment. Electrolysis consists in passing a current of about 1 milliampere for a quarter to half a minute into the hair bulb by means of a fine needle attached to the negative pole of a galvanic battery. The hair then loosens and can be removed. It is important not to remove hairs too close to one another at the same sitting, or troublesome scarring will supervene.

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VII. TROPICAL SKIN DISEASES

In the tropics many skin diseases occur which are met with in Europe; in addition, there are certain conditions peculiar to hot climates, and it is with these that the present section deals. At the same time it must be realised that skin diseases may be modified by racial immunity, social custom and skin pigmentation. Leucodermia has, for instance, a peculiar and sinister significance, not only on account of the great disfigurement it produces in dark-skinned people, but also because of its superficial similarity to the depigmented patches of nerve leprosy. Again, native custom may modify such conditions as keloid, which may assume a magnitude never experienced in Europe, owing to the fact that primitive people often purposely irritate wounds to produce tribal marks of a keloid nature.

CRAW-CRAW

A West African native name (Kra-kra) applied to any itchy, papular or pustular eruption of the skin. It originates as a papular dermatitis.

Ætiology.—O'Neill found filarial embryos in an eruption resembling scabies, but they were probably *Microfilaria streptocerca*, which Scott Macfie has since commonly found in the skin of West African negroes.

Symptoms.—The papules are hard and horny, occur chiefly in the limbs, and are very itchy: scratching and secondary infection lead to a pustular dermatitis with enlargement of adjacent lymph glands.

Diagnosis.—The condition must not be confused with scabies or coolie itch: no acari are obtained and no burrows seen.

Treatment.—Pustules are opened, ulcers scraped and crusts removed, then disinfected with 1 in 1000 sublimate solution and subsequently dressed with boric acid ointment. Carbolic lotion improves some cases.

PRICKLY HEAT

A form of miliaria associated with excessive sweating in hot climates.

Ætiology.—The condition quickly disappears in cold weather, and is possibly purely a mechanical process due to blocking of the sweat glands with sodden, inadequately cornified cells of the stratum corneum. Bacteria and yeast-like fungi have been incriminated, but these are probably secondary invaders.

Symptoms.—The red eruption consists of small, watery vesicles and inflamed, red papules which feel like grains of sand and may involve the trunk, limbs, forehead or almost any part of the body. The pricking sensations and great itching may be sufficient to prevent sleep.

Treatment.—The underclothes should be frequently changed (twice daily), and antiseptic soaps used in bathing. After a warm bath the application of corrosive sublimate solution (1 in 1000) containing eau-de-cologne is helpful. McLeod recommends the following lotion: ℞ acid. salicyl., grs. xxx., hyd. perchlor. grs. ii., sp. vini rect. ʒ ii., aq. dest. ad ʒ vi. After this has dried a dusting powder such as zinc oxide, boracic acid and starch in equal parts, or boracic acid and menthol should be employed.

VELDT SORE

This is a chronic, septic, ulcerated sore met with in the tropics and subtropics, generally involving the exposed hairy parts of the body.

Ætiology.—The disease has a widespread geographical distribution in hot, dry, sandy or desert country, being known as barcoo rot in Northern Australia, and veldt sore in South Africa: during the war it became known as desert sore, and affected troops in the Near East, especially in Sinai and Mesopotamia. Vitamin deficiency may be a predisposing factor, for there is often a history of living on tinned foods and an absence of fresh fruit and vegetables. Organisms isolated from the lesions include streptococci and diphtheria bacilli; staphylococci are also present, but these are probably surface contaminants. Horse manure may constitute a source of origin for the infecting organism.

Symptoms.—The lesion commences as a painful vesicle, containing yellowish fluid, on exposed parts of the skin, especially the dorsum of the hand, forearm, elbows, knees and occasionally the face. Rupture follows, and the condition ultimately results in a punched-out, circular or oval ulcer with a tough, dirty grey base and thick, bluish indurated edges; it may take many months or even years to heal, leaving a thin scar. Typical diphtheritic paralysis of the limbs and palate was noted in some of the Sinai cases associated with Klebs-Loeffler bacillus (Craig) in the sores.

Diagnosis.—The condition must be distinguished from ulcus tropicum and Leishmanial sores; cultures may reveal the causative organism, which, in some cases at least, is the diphtheria bacillus.

Treatment.—PROPHYLACTIC.—Adequate dietary, protection of exposed parts and antiseptic treatment of abrasions should help. *Curative.*—The only specific treatment is anti-diphtheric serum (4000 units); dramatic cure may follow in certain cases. The lesions themselves must have sterile protective dressings: ammoniated or nitrate of mercury ointment often does good. Iron and arsenic tonics and a high vitamin diet should be given, and autogenous streptococcal vaccines are worth a trial in intractable cases.

PEMPHIGUS CONTAGIOSUS

A contagious skin eruption, known also as *Pyosis mansoni*, due to coccal infection, characterised by inflammatory vesicles and bullæ which ulcerate and scab.

Ætology.—The disease is common in the humid tropics such as Ceylon and Malaya, also in parts of Africa. European children are specially affected. Culture generally shows *Staphylococcus aureus* or *albus*; streptococci may be isolated.

Symptoms.—The condition begins as a minute red speck which is transformed first into a vesicle, then a bulla and later a pemphigus-like blister. The fluid content, which is at first clear, later becomes purulent and, after bursting, the lesions generally dry up, desquamate and heal, sometimes leaving pinkish, slightly glazed spots on the skin. The eruption is mainly confined to the axilla and crutch, but in children may be spread more widely by auto-infection, the whole body, except the face, being sometimes involved (Smith). Constitutional disturbances are minimal.

Diagnosis.—The condition is allied to impetigo contagiosa and may need to be distinguished from early small-pox, chicken-pox and ringworm.

Treatment.—Cleanliness is all-important and auto-infection must be avoided. The parts should be washed with perchloride of mercury (1 to 1000) followed by a dusting powder of zinc oxide, boracic acid and starch (equal parts). Ammoniated mercury ointment is often useful. Sulphapyridine preparations (M. & B. 693) in full dosage is worthy of trial.

TROPICAL ULCER

Ulcus tropicum or tropical sloughing phagedæna is a gangrenous ulceration of the skin and subcutaneous tissues of unknown ætiology, resulting in the formation of sloughing ulcers of great chronicity.

Ætiology.—In contradistinction to veldt sore, this disease is met with in damp, steamy jungle in the tropics. The lower limbs are generally involved, and a history of preceding trauma is the rule. It is common in debilitated and diseased populations, may affect people of any age and either sex, and has occasionally assumed epidemic proportions, as amongst coolies in the tea plantations of Assam. Some regard it as a dietetic deficiency. Fusiform bacilli and a spirochæte named by Prowazek, *Treponema schaudinni*, are commonly present in the ulcer: various cocci, fungi and diphtheroids have also been found. The condition is directly transmissible by inoculation of ulcer material from man to man (Smith).

Symptoms.—Phagedænic ulcers generally affect the dorsum of the foot and the front of the legs, and more rarely the hands and forearms. The disease originates as a serosanguineous bleb which soon ruptures, leaving a dirty grey slough. This process rapidly extends, forming a foul sloughing ulcer, which may attain several inches in diameter, giving rise to pain, and sometimes fever, and occasionally involving deeper structures like muscles, tendons, blood vessels, nerves, periosteum, and even joints. Three stages are recognisable: (1) spreading sloughing ulceration; (2) a stage of tissue equilibrium when destruction and growth of granulation tissue are equalised; (3) healing. Generally these ulcers persist for months, a factor delaying healing being inadequate epithelial proliferation, even after a healthy granulation tissue base has formed. Many cases show a decrease in blood calcium.

Diagnosis.—In the humid tropics diagnosis is generally easy, though varicose ulcers, yaws, syphilitic and blastomycotic ulcers and oriental sore may need differentiation.

Treatment.—Protection of the legs with puttees is very advisable. Curative treatment varies with the stage of the ulcer. Rest, a nutritious diet, calcium, cod-liver oil and general vitamin reinforcement by multivite pellets (B.D.H.) are advised. In the rapidly ulcerating stage sloughs should be removed and ensol dressings or lotions of carbolic or permanganate applied. Good results have been reported following curettage of the ulcers and daily dressing with B.I.P.P. Cod liver oil dressings have also been favourably reported on, and local treatment with tar spread on lint and changed every three days has been found suitable for mass treatment of natives. The application of iodoform powder may be followed by firmly bandaging with elastoplast which is left undisturbed for a week; septic dermatitis sometimes complicates this treatment. Probably the most effective procedure in the chronic stage is complete excision, followed by skin grafting. Rarely in the acute stage of fulminating cases, with rapid sloughing and gangrene, amputation is necessary to save life; even more rarely has it to be done in chronic cases.

TINEA

Ringworm infections abound in the tropics, some being confined to special regions, while others are much the same as in temperate climates. The chief ones are: (1) *Tinea cruris* or dhobie's itch; (2) Hong-Kong foot or ringworm of the foot; (3) *Tinea unguium*; (4) *Tinea imbricata.* The first two are due to the *Trichophyton, Epidermophyton inguinale*: they are not peculiar to warm climates and are described elsewhere (p. 1436).

Tinea Unguium.—A mycotic infection of the nails affecting Europeans from the Far East: it may last for years and be associated with ringworm elsewhere. The nail-bed is involved, leading to brittleness, ridging and opaqueness of the nail. Diagnosis is made by demonstrating *Epidermophyton inguinale* in scrapings mounted in liquor potassæ. In severe cases the nails may have to be removed before cure is effected.

Tinea Imbricata (Tokelau).—A form of ring-worm mainly indigenous in the Eastern Archipelago and South Pacific, and characterised by non-inflammatory raised brown spots, giving rise to flaky tissue-paper scales which are free centrally, but attached at their peripheral bases, producing

a rosette-like appearance. These circles are about ¼ inch in diameter and as adjacent ones form they cause a characteristic festooned appearance. The fungus, *Endodermophyton concentricum*, is readily demonstrable in the scales: it affects the face, trunk and limbs, but the palms, soles, scalp, axillæ and crutch generally escape.

Pityriasis Versicolor or Tinea flava is common in the tropics, producing pale, yellowish-brown, scurfy patches on the pigmented negroid skin, especially on the face, neck, arms and chest. Castellani holds that the yellow patches met with in his Ceylon cases differed from the brownish patches long recognised as being caused by *Microsporon furfur* in the European disease, and has named the tropical variety Tinea flava and the causal fungus *Malassezia tropica*; the black variety, which is caused by *Cladosporium mansoni*, Castellani calls Tinea nigra.

PINTA

This is a group of dermatomycoses associated with coloured patches of pigmentation in the skin.

Ætiology.—The disease, also called caraate or mal de los pintos, is found in tropical America, is contagious and attacks either sex at any age. A variety of fungi are implicated, including *Penicillium*, *Aspergillus* and *Monilia*.

Symptoms.—Patches of pigmentation are first noted on the back of the hands or face, from which they spread elsewhere: they are somewhat rough, dry and raised, and vary in colour with the fungus, red, violet, white and black types all being encountered. The skin may be offensive and itchiness marked. When the scalp is involved the hair may become white.

Diagnosis.—Microscopic examination of material scraped from the pigmented areas reveals the fungi. The patches are not anæsthetic like leprosy, while leucodermia, which the white variety may resemble, fails to show fungi.

Treatment.—As for ordinary ringworm.

PIEDRA

Trichosporosis or Piedra is a disease common in Colombia and British Guinea in which hard, gritty nodosities form around the hair of the scalp; it is caused by the *Trichosporon giganteum* and may be confused with ordinary Trichomycosis nodosa.

CREEPING ERUPTION

Synonyms.—Larva migrans, Myiasis linearis, Hautmaulwarf.

Definition.—A peculiar linear, slightly raised red eruption, gradually creeping forward in a sinuous or straight line, the posterior end fading away.

Ætiology.—The condition may be produced by *Gastrophilus* or other fly larvæ wandering under the skin, but more commonly it is due to nematode larvæ of animals which have accidentally invaded man. The following species have been implicated: *Ancylostoma braziliense*, *A. caninum*, *Uncinaria stenocephala* and *Gnathostoma hispidum*.

Symptoms.—The symptoms vary in different individuals and include smarting pain and intense itching along the raised line which first shows red spots, and later hard round red papules 2 to 5 mm. in diameter; pustulation may occur. Unless treated the condition persists for a long time.

Treatment.—Freezing the anterior end of the line where the larva is located, with an ethyl chloride spray for 2 minutes, is suitable for the type due to canine ancylostomes. Multiple lesions may be treated with collodion ethyl acetate or salicylic acid, and blisters and pustules with mercurochrome solution. An injection of pure carbolic an eighth of an inch in front of the spreading spot may kill the larva, or if the condition is due to the larva of *Gastrophilus*, this may be cut down on and removed. Recently oleum chenopodii applied locally either pure or diluted with three parts of castor oil has been favourably reported on.

CERCARIAL DERMATITIS

Definition.—An inflammatory condition of the skin due to the passage through it of different species of cercariæ.

Ætiology.—In 1928 Cort in Michigan described a form of dermatitis due to the passage of *Cercaria elvæ* through the skin and Taylor and Baylis have also found this in England.

Symptoms.—The skin at the site of entry of the cercariæ becomes intensely itchy and smarts, then red spots or urticarial wheals appear, these being followed by papules which sometimes go on to pustulation.

Treatment.—No specific treatment is known. The part should be kept clean and dusted with boracic and zinc powder. Calamine lotion combined with lead acetate may reduce the itching.

ULCERATING GRANULOMA

Synonyms.—Granuloma venereum; Granuloma inguinale; Granuloma inguinale tropicum; Ulcerating Granuloma of the Pudenda; Serpiginous Ulceration of the Genitals.

Definition.—A very chronic ulcerating condition of uncertain ætiology occurring in the tropics, involving the genitals, perineum and groins.

Ætiology.—The disease occurs in the West Indies, Guiana, Brazil, Porto Rico, parts of India and Africa, the Pacific Islands and Northern Australia. Both sexes are affected, but not before puberty, and all races are susceptible. Spirochætes have been reported, and Donovan and many other observers have found a short, oval bacillus specially located within the mononuclear cells; it is a non-motile, capsulated bacterium of the rhinoscleroma group, but though found with frequency in the lesions there is still doubt as to its real ætiological significance. The disease itself is probably contracted during coitus.

Pathology.—The condition resembles an infective granuloma, and microscopic section of the nodules situated at the edge of the sore shows infiltration with plasma and round cells containing poorly staining nuclei in which phagocytosed bacilli may occur in clumps. The granulomatous tissue is very vascular, while in the older areas fibrosis and scarring are marked. Spread is by direct continuity and the lymphatic system is never involved.

Symptoms.—The disease begins on the genitals as a flat papule which desquamates, leaving a red granulation-tissue surface which bleeds easily: this superficial ulceration extends serpiginously producing offensive pus. As the process advances the older areas cicatrise, but this scar tissue readily breaks down again. The disease is auto-inoculable so that adjacent parts such as the scrotum and thighs, or the surfaces of the labia become infected. Ultimately the whole of the penis, scrotum and groins in the male, and the clitoris, vulva, labia, vagina, perineal and perianal region in women become involved, and, if unchecked, the urethra and rectum as well. Though skin ulceration extends slowly over a period of many years, the process accelerates once the mucuous membranes are involved, and here there is little tendency to heal. Until the terminal phase the general health remains good and the local lesions give rise to a minimum of pain and discomfort.

Complications.—These include recto-vaginal fistula, urethral stricture, septic cystitis and pyelitis.

Diagnosis.—Ulcerations due to syphilis, tubercle or lupus vulgaris may be confused, and where the glans penis is involved with fungating granuloma, epithelioma may be suspected.

Prognosis.—This has greatly improved by modern treatment; formerly the condition was hopeless, lasting for life.

Treatment.—Illicit intercourse, especially with native women, should be avoided. Surgical excision of the early lesions is curative, especially as the ulceration does not extend deeply, but in more advanced cases is not feasible. The modern treatment consists of intravenous injections of tartar emetic which is a specific. This drug is given as in schistosomiasis (p. 311) only a longer course of injections and a greater total dosage, *i.e.* 50 to 60 grains, is generally necessary; in extreme instances as much as 150 grains have been given. Certain pentavalent preparations of antimony, such as stibosan and stibenyl, are reported to be more efficacious, a total dosage of 3–4 g. being necessary to obtain complete cure. Protein shock produced by the intravenous injection of T.A.B. vaccine starting with 50,000,000 per c.c. and gradually increasing to 300,000,000 per c.c. may be employed in addition to antimony: sometimes it stimulates healing in a remarkable fashion.

In certain chronic cases unaffected by antimony, gauze soaked in an aqueous solution of zinc oxide (40 per cent.) is an effective dressing, especially if non-hæmolytic anærobic streptococci be present in the ulcer. Sulphapyridine therapy (M. & B. 693) is still under trial.

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SECTION XX

DISEASES OF THE NERVOUS SYSTEM

AFFECTIONS OF THE CRANIAL NERVES

INTRODUCTION

AFFECTIONS of the cranial nerves may be due to their involvement: (1) by purely local disease at some point between their central origin and their peripheral distribution; (2) by some general toxic or infective disease of the whole nervous system; as, for example, by alcoholic or diphtheritic poisoning; (3) by multiple local lesions of the central nervous system, as, for example, by syphilis or disseminated sclerosis; and (4) in some systemic neurone degeneration, as in progressive muscular atrophy.

In the case of local lesions within the brain stem, the presence of one or more cranial nerve palsies may have considerable localising importance in diagnosis. In their peripheral course, both inside and outside the skull, these nerves may be involved by a great variety of inflammatory processes, by hæmorrhage, or by compressing tumours.

THE OLFACTORY NERVE AND TRACT

The sense of smell includes the appreciation of all flavours, and in its absence taste is reduced to the appreciation of bitter, sweet, salt and sour. The view that only readily oxidisable substances are appreciated by the sense of smell, formerly expressed in these pages, cannot be sustained. Benzene, for example, has a powerful smell yet is chemically very stable. The same is true of chloroform and carbon tetrachloride, both substances with a strong odour. The gas phosgene is a final example. Most conditions of anosmia are due to affections of the nasal mucosa, or occur in such general diseases as syphilis or influenza. More important is unilateral anosmia, which indicates the involvement of one olfactory tract by the pressure of a tumour. Bilateral anosmia is a not uncommon sequel of head injuries in which the olfactory filaments are torn as they traverse the cribriform plate.

OPTIC NERVE

The optic nerve, from its origin at the back of the eyeball to its termination in the optic chiasma, is liable to injury from the pressure of tumours within the skull, or at the back of the orbit, and from inflammatory conditions of

the bone and periosteum as it passes through the optic foramen. It may be affected by a primary thrombosis of vessels, or from thrombosis of the ophthalmic artery in the condition known as carotid hemiplegia. These conditions result in blindness of one eye, which may be partial or complete, and with a varying visual field, according to the degree of the lesion and the manner in which the pressure falls upon the optic nerve. On account of the cutting off of the light-reflex path, the pupil will be moderately dilated and insensitive to light. Notwithstanding the fact that the nerve cells which control the nutrition of the optic nerve fibres are situated in the retina, lesions of the optic nerve of any long duration produce atrophy of the optic disk.

Retrobulbar Neuritis

Inflammatory and other local lesions in the substance of the optic nerve between the globe and the chiasma are of very common occurrence. According to their severity they give rise to partial or complete blindness, which often recovers wholly or in part. The central part of the optic nerve is the seat of election for these lesions and, therefore, the visual defect appears commonly in the form of a central scotoma. According to the degree of the visual defect, the pupil tends to be dilated, and to react poorly to light, and dilate badly to shade. These conditions of retrobulbar neuritis are very often followed by optic atrophy of varying degree. When the inflammatory lesion occurs far forwards and impinges upon the optic papilla, papillœdema occurs, and, as this region is sensitive, whereas the optic nerve is not, there is usually pain on movement of the eyeball. The prognosis in this condition varies with the causes, which are as follows :

1. *Syphilis.*—The lesion is a diffuse gumma of the nerve, and sometimes there is thrombosis. It is commonly unilateral, and often recovers, if treated early and energetically, but in severe untreated cases, and when thrombosis occurs, it not uncommonly ends in complete blindness. It is the common cause of complete blindness confined to one eye in tabes, and in other syphilitic conditions.

2. *Disseminated sclerosis.*—Plaques in the optic nerve tracts and chiasma are very common in this disease. When they first form they are swollen œdematous pink patches and cause pressure, and on their subsequent shrinking, this pressure is removed, and the nerve fibres recover to a great extent, and never become completely destroyed. This condition is the cause of the very common transient amblyopia or blindness, which may come on very suddenly. Though the plaques often occur in the tracts and chiasma, yet the visual defect always indicates a lesion of the optic nerve, and therefore it is possible that it is determined by the swelling of the optic nerve as it passes through the optic foramen and is compressed against the bony canal. It may be unilateral or bilateral, and may recur several times. It always causes some degree of optic atrophy ; but is never followed by complete blindness.

3. *Local septic conditions.*—Before the general recognition of disseminated sclerosis as the common cause of retrobulbar neuritis in young adults, the chief rôle in its production was attributed to local infection, or suppuration in the sphenoidal or other accessory sinuses in the neighbourhood. The natural restoration of vision that marks the subsidence of the retrobulbar neuritis was accordingly often ascribed to the operative procedures designed

to deal with the local infection. It is probable that such local infections are but a rare and exceptional cause of retrobulbar neuritis.

4. *Diabetes.*—In this malady a form of retrobulbar neuritis occurs. It commences with a central scotoma for colour, and the failure of vision may progress to blindness, with optic atrophy.

5. *Other causes.*—Tobacco, if over indulged in, may cause a curable form of retrobulbar neuritis, commonly called "tobacco amblyopia," of which the chief sign is central scotoma, and the symptom mistiness of central vision. It recovers rapidly on the removal of the cause. Alcoholic indulgence, and especially taking of wood spirit and many other poisons such as arsenic, lead, bismuth and quinine, may cause retrobulbar neuritis. A large proportion of cases of retrobulbar neuritis are without discoverable cause; there is evidence that some of these are dependent upon local œdematous reactions within the optic nerve of an allergic nature.

The expansion of the optic nerve within the globe of the eye is visible on ophthalmoscopic examination, and the pathological changes therein occurring afford important indications which cover the whole realm of medicine. Among these changes the most important in connection with diseases of the nervous system are: syphilitic choroiditis, as an indication of the presence of syphilis, papillœdema, which is fully described in the section on intracranial tumours, and optic atrophy.

Optic Atrophy

Optic atrophy is recognised, on ophthalmoscopic examination, by a peculiar opaque whiteness and flatness of the disk, with a very high contrast at the edge of the disk between disk and surrounding retina, both as regards colour and limitation. The lamina cribrosa—the sieve-like cross-latticing of the strands of the sclerotic through which the bundles of optic nerve fibres pass—becomes visible as a stippling of the temporal region of the disk. The vessels of the retina become atrophied, and are seen to be unduly small. In many atrophies the edge of the disk is sharply cut; but when atrophy follows papillœdema the edge is apt to be fluffy, like that of torn cotton-wool. Optic atrophy may be of three kinds—(1) Primary optic atrophy results from an original devitalisation and death of the nerve cells of the retina with their processes, which constitute the fibres of the optic nerve. This is a primary neuronic degeneration, analogous to that of the anterior-horn cells in progressive muscular atrophy. (2) Secondary or retrograde optic atrophy results from lesions of the optic chiasma and optic nerve, and is the constant result of long-continued pressure upon these structures. (3) Consecutive optic atrophy follows the more severe grades of papillœdema and papillitis, in proportion as these are of long standing, and proportional to the amount of exudate, and is due to strangling of the optic nerve fibres by the œdema in the first place, and by the cicatrisation subsequently. Severe degrees of papillœdema may, if pressure be relieved, recover perfectly without atrophy or impairment of sight. It may be that there is another factor in the atrophy following papillœdema, and that is the long-continued pressure of a distended infundibulum upon the optic chiasma.

Ætiology.—1. It is of frequent occurrence in familial, hereditary or

congenitally installed diseases in which primary degeneration of neurones occurs, as in cerebral diplegia, amaurotic family idiocy, and hereditary cerebellar atrophy where it is characteristic of Marie's type, and sometimes occurs in Friedreich's type. It is the chief feature of the familial optic atrophies, of which Leber's type, appearing about the twentieth year, is one. It occurred in several members of a family with peroneal atrophy under our observation.

2. It is one of the common manifestations of syphilis of the nervous system, and may occur alone, but much more usually as part of the syndrome of tabes and general paralysis. It is not rarely met with in congenital syphilis. It is commonly associated with local lesions of the chiasmal region, pituitary neoplasms being the most often met with. The optic atrophy of disseminated sclerosis is not a primary optic atrophy, but is secondary to retrobulbar neuritis.

3. It may follow the exhibition of certain drugs, and noticeably the injection of the earlier used arsenic preparations, such as atoxyl, soamin and orsudan. In rare cases it has followed the use of quinine.

4. Optic atrophy also occurs in connection with diabetes, malaria and arterial disease. It is common as a primary condition in later life. Its occurrence in glaucoma from increase of the ocular pressure requires no explanation.

Prognosis.—This is uniformly bad in primary atrophy. When once the degenerative process is installed, the atrophy proceeds to complete blindness, sometimes slowly, sometimes quickly, and seems entirely uninfluenced by any form of treatment.

Secondary optic atrophy is frequently arrested, with the recovery or removal of the cause; but some defect of vision usually remains. Consecutive atrophy from neuritis may be of any degree of severity, from the slightest, which allows of $\frac{6}{9}$ths vision, to the most complete with utter blindness and loss of light reflex.

OCULO-MOTOR NERVES

The third nerve supplies the two internal muscles of the eye, and all the external muscles of the eyeball, except the superior oblique, which is supplied by the fourth nerve, and the external rectus, which is supplied by the sixth nerve. Complete paralysis of this nerve produces a dilated and inactive pupil with complete ptosis, a downward and outward strabismus and complete loss of upward, downward and inward movements. There is often no diplopia complained of by the patient, because of dropping of the lid. When diplopia is present it is a crossed diplopia, because the strabismus is divergent. There is secondary deviation of the sound eye, and false projection in the visual field.

The fourth nerve supplies the superior oblique muscle. Paralysis produces no obvious strabismus, but in looking outwards or downwards there is a wheel movement of the globe which can be detected by observing the conjunctival vessels when the eye moves. The diplopia is most discomforting, and occurs in every position of the eyes, except on looking up. The diplopia is uncrossed, and the false image is lower than, and with its top tilted toward, the true image.

The sixth nerve supplies the external rectus muscle. Paralysis produces a convergent squint and an uncrossed diplopia. In the case of the skeletal musculature, we are accustomed to distinguish between upper and lower motor neurone paralyses; the essential difference being that in the former case we are dealing with loss of co-ordinated movements, in the latter with paralysis of individual muscles. Disorders of ocular movements may usefully be considered on the same basis of classification. Thus we may contrast the loss of conjugate deviation of the eyes to the right—an upper motor lesion—with paralysis of the left internal rectus the result of a lesion of the lower motor neurone. In the former case, the internal rectus muscle acts normally on convergence, but does not act on attempted conjugate deviation to the right. In the latter case—a lesion of the peripheral nerve supply—the muscle is paralysed in all movements of the eye.

We may thus classify paralyses of ocular movement under the following headings: (1) paralyses of ocular movements, conjugate and supranuclear; and (2) paralyses of ocular muscles, nuclear, stem and root palsies.

1. Paralyses of Ocular Movements.—Conjugate palsies consist in the loss or impairment of co-ordinated ocular movements in one or more directions. Since both eyes are equally and simultaneously involved, there is neither squint nor diplopia. The commonest form is that in which there is loss of conjugate movement to one or other side. The lesion in such a case is so situated as to interrupt the association path between the sixth and third nerve nuclei, probably where this path lies in the dorsal longitudinal bundle. If a lesion in this situation be a coarse one (*i.e.* not a simple nerve cell degeneration), there will probably be an associated nuclear or stem palsy, in which case there may be diplopia and squint. Possibly a lesion lying just oral and ventral to the sixth nerve nucleus is capable of causing a pure paralysis of conjugate deviation to the side.

Lesions involving the corpora quadrigemina cause loss of vertical (upward) movement of the eyes, sometimes with dilatation and immobility of the pupils. This combination of signs may be seen in pineal tumour.

Supranuclear ocular palsies differ from conjugate palsies in that with the latter a given movement is totally lost, while in the former, whether or not the movement occurs will depend upon the particular stimulus in action. Thus, in a supranuclear palsy the patient may be unable to deviate his eyes to order, but deviation may be elicitable by labyrinthine stimulation. Or again, the gaze may be unable to follow a moving object, but if the object be still and the head slowly rotated passively, the gaze may remain fixed on the object, and the eyes thus come to take up a position of deviation.

2. Paralyses of Ocular Muscles.—The lesion in this case may be in the brain stem (nuclear or stem palsies), or in the peripheral course of the nerve (root palsies). Further, the lesion of the peripheral part of the nerve may involve the nerve between its point of origin from the brain and the point of entry into the orbit; that is, in its intracranial course; or in the region of the sphenoidal fissure; or, finally, within the orbit.

Within the orbit lesions of any of these nerves or of their branches may occur from perforating wounds, blows upon the eyeball or from local syphilitic lesions of a gummatous nature. Injury to the lenticular ganglion, with resulting complete internal ophthalmoplegia, not uncommonly results from a blow on the eyeball. A lesion, confined to the nerve to the inferior oblique,

occurs in rare cases from syphilis, and produces a peculiar attitude of the head, for, since the resulting diplopia occurs only above the horizontal level of the eyes, the patient constantly throws back his head, and looks down his nose to avoid the diplopia.

Lesions at the back of the orbit may involve one or more of the oculomotor nerves, and since the first division of the fifth nerve passes through the sphenoidal fissure with these nerves, and the second division of the fifth nerve is entering the infra-orbital canal at the apex of the orbit, both these nerves are commonly involved in the same lesion. New-growths, including those of the bone, periosteal inflammation and subperiosteal hæmorrhages arising from fracture of the skull are the common lesions. A not infrequent clinical picture may be described. It has been attributed to a periostitis of the orbital bones in the region of the sphenoidal fissure. There is, however, no pathological confirmation of this view, which remains speculative. It has been thought, too, that the condition is closely allied to the common facial palsy from exposure to cold, but here also proof is lacking. It may occur at any age from puberty onwards. The serum reactions for syphilis have always shown that this infection is absent. The condition may arise from exposure to cold or from septic conditions of the nose and its accessory sinuses, and sometimes without obvious cause. The malady commences with pain in the orbit, which is often severe and long lasting. Soon after some proptosis is evident, and there is tenderness on pressing the globe backwards. This is soon followed by signs of involvement of the nerves which pass through the sphenoidal fissure. The sixth nerve is the first and sometimes the only nerve involved, but usually the paralysis of this nerve is followed by that of the fourth, the first division of the fifth, the third, and the second division of the fifth nerve in that order. The final result usually is that of a total ophthalmoplegia with anæsthesia of the upper two divisions of the fifth nerve, unilateral proptosis and tenderness of the eyeball, and often excruciating and lasting pain. When the sixth nerve is involved alone, and there is no spread to the divisions of the fifth nerve, there may be little pain, and the proptosis and tenderness may be little marked. Under treatment with mercury by inunction, salicylates in full doses, warm applications to the eye and counter irritation, the condition commonly recovers in a few weeks in the milder cases, to a few months in the more stubborn ones. It is in their intracranial course that the oculomotor nerves are most frequently involved by disease-processes, or by injury; thus, by acute or chronic meningitis, by toxic or infective neuritis, by compression from tumour, aneurysm, hæmorrhage or fracture of the skull.

Fractures of the skull, may involve the orbit, or the middle fossa of the skull, thus producing ocular palsies. Sometimes a blow on the skull without fracture is followed by an ocular palsy. It is possible that in this instance small hæmorrhages in the brain-stem involving the nuclei may be responsible.

In subarachnoid hæmorrhage, the effused blood in the region of the interpeduncular space may compress the cranial nerves, thus producing ocular palsies. These may also occur in the course of an acute lepto-meningitis. In association with middle ear disease, there is occasionally a localised meningitis at the tip of the petrous bone, which gives rise to a unilateral sixth nerve palsy and to pain on the side of the head and face from fifth nerve involvement. This is the condition known as *Gradenigo's syndrome.* It is

usually seen in children; and a mastoid operation may be necessary before it clears up.

Formerly, one of the commonest causes of ocular palsies was a gummatous infiltration of the nerves of the base of the brain in neurosyphilis. In some cases of tabes dorsalis, however, it is probable that the lesion underlying the defects of ocular movement (squint, diplopia, ptosis) may be due to primary degeneration of nerve cells in the nuclei.

In some cases of alcoholic and diphtheritic multiple neuritis, paralysis of one or more ocular muscles may occur, and also an isolated sixth nerve palsy has been known to follow the spinal administration of stovaine.

In some elderly subjects with atheroma and high blood pressure a sixth or third nerve palsy may develop, and recover after some two or three months. It is probable that in such not infrequent cases one or other of these nerves has been compressed by a tortuous and rigid artery. Thus, during its passage forwards the sixth nerve lies in close contact with the middle cerebellar, the basilar and the internal carotid arteries; the fourth nerve crosses the posterior cerebral artery; and the third nerve lies between the last-named vessel and the superior cerebellar artery.

Stem palsies, in which the lesion is in the brain-stem, are usually recognisable from the presence of associated signs due to involvement of other structures. These may be the long projection paths, sensory or motor, association nuclei and reflex centres, or other cranial nerve nuclei. Thus, a lesion in the crus will produce a homolateral third nerve palsy, with a crossed hemiplegia (Weber's syndrome). A lesion in the region of the red nucleus will cause a homolateral third nerve palsy, with tremor of the crossed limbs (Benedikt's syndrome). A pontine lesion will produce associated sixth and seventh nerve lesions on the side of the lesion.

Nuclear palsies may result from a number of inflammatory processes within the brain stem: *e.g.* epidemic encephalitis, disseminated sclerosis, acute poliomyelitis, botulism, chronic alcoholism (Wernicke's encephalitis hæmorrhagica superior acuta). Barbiturate poisoning, diphtheria and diabetes may also be associated with ocular palsies of nuclear origin. Finally, there is the rare condition known as *chronic progressive nuclear ophthalmoplegia*, in which there is a primary degeneration of the third, fourth and sixth nuclei. The course of this malady, which is related to progressive muscular atrophy, is slowly progressive, and finally all the extrinsic ocular muscles are paralysed.

Pathological Conditions of the Pupil and of Accommodation.—Myosis or unusual smallness of the pupil is a common sign of syphilis of the nervous system. It is an important sign of paralysis of the cervical sympathetic. It occurs in lesions of the pons below the third nerve nucleus, is often met with in advanced age without pathological associations, and is also a symptom of the morphine habit.

Eccentricity of the pupil and deviations of its form from the circular are important signs of nervous syphilis, and these signs occur also in lesions of the foremost part of the third nucleus.

Inequality of the pupils occurs in connection with all nuclear and peripheral ocular paralyses, and with cervical sympathetic paralysis. It accompanies all defects of vision from lesions of the visual path between the eye and the external geniculate bodies, provided the appreciation of light be unequal in the two eyes. It may be congenital or associated with inequalities

of the refraction of the two eyes, and then has no pathological significance. It is commonly a sign of nervous syphilis.

The Argyll Robertson pupil (reflex iridoplegia) as originally described includes loss of the light reflex, myosis, inequality and irregularity of the pupils. Atrophic changes in the stroma of the iris have also been described. These are best seen in blue-eyed persons in whom the stroma is not concealed by pigment, and they impart a fineness of texture and a pale, washed out tint that, in association with myosis, gives the eye of the tabetic so characteristic an appearance.

The iridoplegia may be due to a lesion in the region of the posterior commisure and the aqueduct of Sylvius, and it is here that some believe the essential lesion of the Argyll Robertson pupil to lie. But the Argyll Robertson pupil of neurosyphilis is almost constantly associated with the other pupillary phenomena noted above, and it is difficult to see how a central lesion could produce any of these. In short, the pathogenesis of this familiar phenomenon still remains obscure.

When reflex iridoplegia is met with apart from neurosyphilis—which is but rarely—it is not accompanied by myosis, or irregularity of the pupils, and the absence of these signs is of diagnostic importance.

It has been said to occur in disseminated sclerosis and in epidemic encephalitis, but the statement is one to be accepted with reserve.

The Myotonic Pupil.—During the past fifteen years a number of writers (Foster Moore, Holmes, Adie) in this and other countries have described a pupillary phenomenon which has the following components: There is no reflex contraction to light, and there is a very slow contraction on convergence, followed by an extremely slow relaxation and dilatation. In some patients this condition is associated with a total loss of all tendon jerks. The patient is more commonly a young woman in normal health, the phenomenon being discovered usually in the course of a routine examination of the eyes. It constitutes no disability. Serological examination of the blood and cerebro-spinal fluid is always negative, and the condition is not related to neurosyphilis or tabes, with which, however, it may be confused if a complete examination of the nervous system be not made.

Total internal ophthalmoplegia is met with in lesions of the anterior part of the third nucleus, and in lesions of the lenticular ganglion in the orbit.

Wernicke's hemianopic pupil phenomenon is a test for the position of a lesion causing hemianopia. If the lesion is situated upon the visual path where that path contains the light reflex path, the pupil does not react when light is thrown on the blind side of the retina. In other words, this sign is present if the lesion is involving the visual path between the eye and the external geniculate body. When the lesion is between the geniculate body and the visual cortex in the occipital lobe, the pupil reacts equally well from the blind and from the seeing field.

PARALYSIS OF THE CERVICAL SYMPATHETIC

Synonym.—Horner's syndrome.

So far as the eye and orbit are concerned, the sympathetic is the tonic retractor of the lid, the tonic protruder of the eyeball, and the tonic dilator of the pupil, and stimulation of this mechanism results in retraction of the

lid or widening of the palpebral fissure, exophthalmos and wide pupil, while paralysis of the cervical sympathetic produces narrowing of the palpebral fissure (cervical sympathetic ptosis), and a small pupil. It is customary to include enophthalmos amongst the components of cervical sympathetic palsy, but it is extremely doubtful that this is ever present. The excitation condition is seen in Graves's disease; the paralytic condition is of common occurrence in nervous diseases. The cervical sympathetic is also the tonic vaso-constrictor and secreto-motor nerve of the head generally, but disturbance of the mechanism does not often give rise to characteristic or important clinical phenomena. A curious lack of expression is, however, sometimes observable in the face on the side of the lesion. Cervical sympathetic paralysis occurs in the following clinical associations: (1) In all lesions of the cervical cord, especially when the last cervical and first dorsal segments or roots are damaged. It is common in syringomyelia. (2) In lesions of the cervical sympathetic trunk by trauma, pressure, growths, etc. (3) It is very common in tabes and nervous syphilis generally, where it appears as partial bilateral ptosis with small pupils. It appears to be a primary neuronic degeneration in this condition and never improves.

THE FIFTH OR TRIGEMINAL NERVE

Symptoms of Lesions of the Fifth Nerve.—Pain over the sensory distribution of this nerve occurs from irritating lesions and reflexly, if its periphery is irritated. With organic lesions in any part of its course, the pain is followed by sensory loss, corresponding with the part involved. The initial expression of this sensory loss in a progressive lesion of the fifth nerve: *e.g.* compression by an eighth nerve tumour, is loss of the corneal reflex. The peculiar disease, neuralgia, of which the pathological basis has not been as yet discovered, is practically confined to the distribution of this nerve. Herpes zoster over the distribution of this nerve is common, and results from a lesion by a virus infection in the Gasserian ganglion, and is in every respect comparable with that occurring in the distribution of the spinal nerves from similar lesions in the posterior root ganglia. It produces bad scarring, and when affecting the cornea is apt to produce ulceration, very destructive to the eye. It is accompanied by severe pain, which may be persistent for months. It should be borne in mind that the sensory supply to the cornea is entirely from the naso-ciliary branch, via the long ciliary nerves, and that herpes zoster of the cornea is usually accompanied by a small group of vesicles only at the tip of the nose on the same side.

Taste.—It has frequently been argued that loss of taste over the anterior two-thirds of the tongue follows destruction of the Gasserian ganglion and proximal portions of the fifth nerve. Cushing has, however, investigated this subject upon a series of cases of complete Gasserectomy, and has found that in every case the sense of taste was preserved. The path of taste thus seems proved. It is from the glossopharyngeal nucleus via the fasciculus solitarius, portio intermedia, facial nerve, chorda tympani and lingual nerve to the tongue.

Trophic changes.—Lesions of the first division of the fifth nerve are often productive of serious corneal deterioration and ulceration, which may be followed by septic panophthalmitis. These changes, however, have been

proved to be the result of mechanical damage upon the insentient surface. If, for example, after destruction of the fifth nerve for neuralgia, the eye be carefully protected either by covering or sewing it up, these changes do not occur. After a little while, the anæsthetic cornea becomes much less vulnerable, and will stand the wear and tear of ordinary life without disturbance.

Paralysis of the motor function of the fifth nerve occurs in lesions of the nucleus in the pons, or of any part of the peripheral course of the motor division. The signs of such paralysis are not apparent to the patient, who experiences no difficulty in mastication, provided the lesion be unilateral. To the observer, the jaw deviates to the side of the paralysis on opening the mouth, on account of the action of the unopposed external pterygoid of the sound side. The masseter, as felt by the finger on its anterior edge, does not harden on biting, nor do the temporal muscles harden. The floor of the mouth does not stiffen on the paralysed side on forcibly opening the mouth.

Bilateral involvement of all the muscles supplied by the fifth nerve is the rule in all cases of progressive muscular atrophy where the bulbar nuclei are affected.

THE SEVENTH OR FACIAL NERVE

This nerve supplies all the facial muscles of expression. In the petrous bone, it gives off a branch to supply the stapedius muscle. One quarter of an inch above the stylomastoid foramen, it gives off the chorda tympani, which enters a small foramen, the iter chordæ posterius, which leads it to the tympanum, where it crosses the long process of the malleus and enters the temporal fossa by a canal, the iter chordæ anterius, and subsequently joins the lingual, by which it is conveyed to the anterior two-thirds of the tongue and to the submaxillary and sublingual glands.

1. BELL'S PARALYSIS

Synonym.—Common facial palsy.

Definition.—A common variety of peripheral paralysis of the facial nerve, sometimes of uncertain ætiology and sometimes a sequel of herpes of the geniculate ganglion. The paralysis almost invariably recovers, but if the recovery is slow, a very peculiar spasm or facial contracture may accompany or follow the recovery.

Ætiology.—Facial paralysis is rare at the extremes of age and it is most common in early adult life. The sexes are equally affected. Many different views have been held as to the pathogenesis of Bell's palsy, as, for example, that it is the result of a local inflammation of the fibrous tissue forming the deep part of the sheath of the parotid gland, from which a process in the form of a sheath accompanies the facial nerve into the Fallopian aqueduct, and along which the inflammation extends and compresses the facial nerve in that canal. The proofs adduced in favour of this view are, that facial paralysis is so often accompanied at its onset by pain in the stylomastoid region and behind the mastoid process and by tenderness on pressure, and that in some cases there is very considerable swelling of the deep part of the parotid gland. Moreover, it might be thought that the pathological process begins outside, and subsequently spreads up the facial canal, since the loss of taste in the anterior two-thirds of the tongue, from involvement

of the chorda tympani, is so often not present when the palsy first appears, and develops in the course of a few days, as the inflammatory process spreads up the facial canal, and reaches the region where the chorda tympani leaves the facial trunk. However, it is apparent that this can be no more than speculation, lacking pathological confirmation. On the other hand, it is clear that a proportion of cases of Bell's palsy are a sequel of herpes of the geniculate ganglion. There is also, in the experience of the present writer, a curious periodicity in the appearance of cases of Bell's palsy in the late autumn and early spring. While this may perhaps be attributed to cold weather, it is perhaps more strongly indicative of an infective origin and suggests that geniculate herpes may be responsible for a greater proportion of cases of Bell's palsy than is commonly believed.

Symptoms.—The onset is usually rapid and sometimes even sudden. Pain of a neuralgic character below the ear, behind the mastoid process, or referred to the occipital region, is common, but it does not last more than a few days, and sometimes pain is entirely absent. On deep pressure upon the styloid region behind the ramus of the jaw on both sides, one can almost always elicit the fact that there is tenderness on the paralysed side, and sometimes obvious swelling of this region may be felt. The first sign of the facial paralysis is that the patient feels the face to be stiff when he attempts to move it. Subsequently, the paralysis appears rapidly, and the face is drawn over to the opposite side. The paralysed side is motionless, according to the degree and distribution of the paralysis, if incomplete, and, if complete, is expressionless. The eye cannot be closed, and there is epiphora from paralysis of the tensor tarsi. The paralysis at the corner of the mouth causes difficulty in articulation and escape of fluids on drinking, but the patient soon learns to dodge these disabilities. When the paralysis is partial it is nearly always the lower part of the face which is the most affected. The facial muscles soon become hyperexcitable to mechanical stimuli. In nearly all the severe cases, there is loss of taste over the anterior part of the tongue. It should be remembered that the sense of taste is confined to a very small area on the lateral edge of the tongue, some half an inch behind the tip.

There is never any pain in the distribution of the facial nerve. After a time, which may vary from a few days to two years, the paralysis begins to recover, and invariably this recovery appears in the upper facial region first, and in almost every case becomes complete. We have seen perfect recovery follow complete paralysis lasting 21 months. Bilateral Bell's palsy is not so rare as is supposed. When seen, there is usually a lapse of 4 or 5 days before the second nerve shows signs of paralysis. The paralysis may become complete on both sides, or upon one only. Perhaps less common is recurrent Bell's palsy. The writer has seen several cases of the kind, including one in which the patient has three separate Bell's palsies, two on the right and one on the left side of the face. All recovered.

Treatment.—Those who believe in a fibrositic ætiology of Bell's palsy will base their treatment on this hypothesis. Salicylates and iodides are given internally and mercurial inunction (3 grs. rubbed in over the mastoid region daily for 2 weeks). The local application of warmth and of such a counter-irritant as tincture of iodine may also be used. The patient is probably best kept in the house for the first week and instructed to massage the face gently using olive oil for 5 to 10 minutes daily. In cases which show

early signs of recovery this is adequate, but when after a month or 6 weeks no evidence of recovery is seen, undue stretching of the paralysed muscles may be minimised by "splinting" the face. For this purpose a silver wire, rubber covered where it turns round the lip, may be bent so as to hook round the lip at one end and over the ear at the other, so that the mouth is kept symmetrical during facial movements. Gentle massage may also be continued. In such cases it has been customary to give galvanic stimulation to the paralysed muscles. Since the present writer abandoned this practice many years ago, he has satisfied himself that recovery proceeds as quickly and completely without it, and the distressing facial contractures that are sometimes seen do not occur. In other words, electrical stimulation has no place in the treatment of Bell's palsy. When geniculate herpes is in question, the vesicles and the swollen pinna require the local treatment suitable for this condition.

Facial paralysis from caries of the temporal bone rarely makes any recovery, and it is almost always complete and permanent. To remedy the unsightly and permanent distortion of the face, union of the peripheral trunk of the facial to the central end of the divided spinal accessory or preferably the hypoglossal nerve, has been performed, and with considerable success. Section of the hypoglossal with consequent hemiatrophy and hemiparalysis of the tongue produces no disability with speech, mastication or swallowing. It is not so much that reunion of this nerve restores volitional power to the face, but associated movement does return and also some after-contracture, which restores to some degree the symmetry of the face.

Facial Paralysis from herpes of the geniculate ganglion.—Among the not infrequent causes of facial palsy must be numbered geniculate herpes. Attention was first drawn to this cause by Ramsay Hunt. The herpetic vesicles, preceded by local pain, appear in the external auditory meatus and adjacent parts of the pinna, and sometimes also just behind the pinna and on the soft palate and anterior pillar of the fauces. When the innervation of the last named derives fibres from the geniculate ganglion, the clinical picture of geniculate herpes is apt to be a misleading one if it be not thought of. The patient complains of pain in the ear, and in the throat on the same side. As the eruption develops the fauces on the affected side are red and injected, and several small ulcers (ruptured vesicles) may be seen. At the same time, the vesicles appear in the ear, rupture, and give off a watery discharge which may be mistaken for otorrhœa. The pinna may then swell very considerably. After some days, during which the patient may feel ill and be feverish (temperature of 100° to 102° F.), a facial paralysis almost invariably develops and becomes complete within 12 hours. In milder cases there may be only initial pain in the pinna and the appearance of herpetic vesicles on the pinna without much swelling. It is in the severe cases that an erroneous diagnosis of middle ear disease with otorrhœa may be made and hazardous and unnecessary steps be taken to deal with this. According to Ramsay Hunt facial palsy always follows geniculate herpes, and undoubtedly many cases of this kind, where the herpetic eruption is minimal, escape accurate diagnosis.

Diagnosis.—Care in diagnosis is necessary lest peripheral facial palsy of very unfavourable prognosis should be mistaken for it. The facial palsies which result from lesions of the nerve in the temporal bone, from caries and

from tumour, those due to lesion of the nerve within the skull and from pontine lesions, rarely make any recovery. To this rule the following exceptions must be made: In the peripheral facial paralysis of poliomyelitis, lethargic encephalitis, tetanus and diphtheria recovery always occurs, if the patient survives.

Facial contracture.—In cases of long duration when recovery commences, the face goes into a condition of persistent spasm which causes often a very unsightly distortion of the face, which is very disappointing to the patient, who after waiting many months for improvement, now finds the place distorted in the opposite direction and to a more severe degree than at the onset. No adequate explanation of facial after-contracture has ever been put forward, and no similar condition occurs after the lesion of any other peripheral motor nerve, so far as we are aware. It recovers slowly in the majority of cases. Patients should be warned from the first about the occurrence of after-contracture so that disappointment may be obviated, and at the same time encouraged as to the probability of complete recovery.

The diagnosis is not difficult, and mistaken diagnosis means faulty examination. In disease of the temporal bone, the facial palsy is accompanied by signs of such disease, which should be carefully sought, namely, deafness, perforation of the drum, discharge from the ear, and signs of long-standing otitis.

Lesions within the skull are apt to co-involve the auditory nerve, the fifth nerve of the cerebellum, and the characteristic signs of tumour of the lateral recess are common. In the pons, hemiplegia, hemiataxy and hemianæsthesia are likely to coexist.

Course and Prognosis.—Recovery is so usual that it should be promised in every case. The date of recovery is often difficult to forecast. If at the end of a week after the onset there is the slightest trace of any voluntary power in the orbicularis palpebrarum, which is the "ultimum moriens" of the facial muscles, or if any trace of faradic excitability to bearable stimuli remains, then it may be confidently said that recovery will be complete and rapid within 3 months, and that there will be no contracture. Cases in which no complete paralysis occurs in any region of the face usually recover in a fortnight. In complete cases, with complete reaction of degeneration in the muscles, it is difficult to say when recovery will occur or when the effect of contracture will be at an end. Cases which show no loss of taste and, therefore, in which there is no great extension of the inflammatory process up the facial canal, usually recover rapidly. Traumatic facial paralysis from blows upon the side of the face, and obstetrical facial paralysis from the pressure of forceps during delivery, always recover and leave no sequelæ.

2. PERIPHERAL FACIAL SPASM

Synonym.—Facial hemispasm.

Definition.—A unilateral malady of the facial nerve, in which intermitting spasm of the facial muscles occurs, exactly like that caused by faradism of the facial trunk. Rarely it is associated with a slowly oncoming facial paralysis, and may follow a facial paralysis due to injury.

Ætiology.—This malady occurs in adults, and the onset is usually in-

sidious and without known cause. It is most often seen in middle-aged women. It is certainly due to a lesion of the peripheral facial nerve trunk, and this lesion seems to be of such a nature as to irritate, and not in most cases to destroy; but in rare cases partial destruction, with the appearance of partial facial paralysis, does occur.

Symptoms.—It commences with twitching of some part of the facial musculature, which occurs at first at rare intervals, and subsequently becomes more and more frequent, so as in some cases to be almost continuous. Commencing locally, it tends to spread so as to involve the whole face in a sudden and hideous contortion. We have seen cases in which the attacks of peripheral facial spasm at first glance almost exactly resembled a Jacksonian fit of the face. The spasms may be so severe and continuous as to keep the eye closed for long periods together, and to interfere greatly with the work and enjoyment of life. The malady is associated with no other symptoms. Cases exist in all degrees of severity, from the mildest, in which an occasional flicker of the face occurs, to the most severe and incapacitating and unsightly malady.

Course and Prognosis.—Some of the cases recover spontaneously, and others under treatment; but when the malady becomes severe and the spasm hardly remitting, it is practically intractable, except by operative interference.

Treatment.—In the milder cases, measures calculated to subdue chronic inflammation, such as mercury, iodides and salicylates, are said to be of benefit. In severe cases, the only remedy which affords relief is the injection of alcohol into the facial nerve either at the stylomastoid foramen, or as it crosses the ramus of the jaw half an inch below the external auditory meatus, or when one division of the nerve only is affected, in any part of the pes anserinus.

THE AUDITORY AND VESTIBULAR NERVES

Lesions of the cochlear nerve produce deafness, and in addition pathological changes in its peripheral termination are productive of tinnitus. Except from direct involvement of this nerve or of its terminations in the cochlea, deafness is practically unknown as a symptom of disease of the nervous system. In other words, lesions of the central auditory paths are not as yet recognisable by any known symptoms.

Nerve deafness may be produced by any lesions of the cochlea and cochlear nerve, and is confined to diseases of the temporal bone and labyrinth, lesions of the intermeningeal part of the eighth nerve by tumours, meningitis or pressure, and lesions of the lateral side of the medulla. The deafness is the same wherever the lesion may be, and the position of the lesion is to be deduced from the associated involvement of contiguous structures. Nerve deafness, which characterises lesions of the cochlea and its nerve, is distinguished from deafness due to middle-ear disease by the facts that hearing both by air conduction and by bone conduction is diminished or lost, while in middle-ear deafness the hearing by bone conduction is increased. If a tuning-fork in vibration be applied to the forehead until it is no longer audible, and then presented to the ear, it will not be heard aerially in middle-ear disease, since the aerial conduction is impaired in that condition. But in nerve deafness it is either not heard through the bone when the tuning-fork

is applied, or if heard, when it has ceased to be audible to bone conduction, will still be audible when presented to the ear. This is known as Rinne's test, and it is a reliable one. Weber's test for nerve deafness consists in the application of a tuning-fork to the forehead in the middle line, the patient being asked which ear the sound comes to most. In middle-ear deafness the sound is heard best on the deaf side, and in nerve deafness it is best heard on the sound side. As a symptom of nervous disease, nerve deafness is met with in disease of the lateral region of the medulla, in tumours of the cerebello-pontal angle growing from the eighth nerve, following epidemic meningitis, and in syphilis of the nervous system, especially congenital syphilis.

1. TINNITUS

Ætiology.—Tinnitus or the occurrence of persistent recurring noise referred to the ears may be produced by wax in the ear, by otitis media, or by any other condition of vascular congestion, or by inflammation in the region of the auditory mechanism. It occurs in those who work exposed to deafening noise, as in boiler-makers and riveters, and may be produced by the administration of quinine and salicylates. It is much more frequently indicative of intractable disease of the cochlea, which often ends in complete deafness. Persistent tinnitus is a malady of adult life, the earliest cases occurring after puberty. It is rare for the malady to commence in old age. It begins insidiously, and as a rule without cause, but debilitating influences may precede its onset.

Diagnosis.—The diagnosis of tinnitus presents no difficulty. A careful examination of the ears will discover and cause to be removed any local trouble in the external auditory meatus and tympanum. Moreover, these conditions do not give rise to persistent tinnitus with nerve deafness.

Symptoms and Course.—The sounds commence faintly and often intermittently, and at first may be only perceived in stillness and silence at night, and later become louder and more persistent, and are often absolutely continuous. The slight sounds may be low pitched, a low rumble like a distant wagon, or a faint murmur such as may be heard when a shell is held to the ear. The loud sounds are never low in tone. They may be humming, hissing, rushing or bell-like noises. The common simile used by the patient is that of a hissing kettle, of a gas jet, of a threshing machine, of a steam-engine, or of a room full of machinery. The same patient may have several sounds, sometimes successive and sometimes heard all at once. When the sounds are rhythmical they are usually synchronous with the pulse. In some of the cases labyrinthine vertigo occurs, and the attack may be heralded by an increasing intensity of the sound. The condition of hearing in patients suffering with tinnitus may vary in each case, and from time to time in any one case. In many cases hearing is perfectly normal, and may remain so for years, in spite of increasing tinnitus. One of my patients retained perfect hearing for over twenty years, with increasing tinnitus; but the hearing rapidly declined afterwards. In many cases, however, there is some degree of nerve deafness on one or both sides. In the course of time the deafness increases even to absolute deafness, and in a few of them the noises persist in spite of absolute deafness. As a rule, the noises decrease as deafness becomes severe.

Prognosis.—The prognosis is very uncertain, and in most cases unfavourable. In many cases the noises persist in spite of all treatment, sometimes treatment secures considerable relief, and not infrequently the symptom is removed by treatment.

Treatment.—In the early stages the disease may be much benefited by the exhibition of salicylates and iodides. As a symptom, tinnitus is more affected by bromides than by any other drug, and these should be given in doses of from 10 to 20 grains twice or three times daily. The effect of the bromide is sometimes increased by the addition of from 5 to 10 minims of tincture of belladonna.

2. VERTIGO

Definition.—The word "vertigo," which by derivation means a "turning," is used to designate any movement or sense of movement or unsteadiness either in the individual himself (subjective vertigo) or in external objects (objective vertigo) that involves a defect, real or seeming, in the equilibrium of the body. It is a sensation of involuntary movement, either of subject or of external objects. It always involves a slight interference with consciousness, which, in severe vertigo, is often momentarily lost.

Ætiology.—Vertigo is always the result, direct or indirect, of disturbance of the labyrinth, vestibular nerves or cerebellum. It is commonly associated with vomiting and with vasomotor and secretory phenomena, such as "cold perspiration." The disturbance of the vestibular mechanism which results in vertigo may be set up by multitudinous causes, among which may be mentioned toxic states as in specific fevers, and from the administration of alcohol, anæsthetics and morphine, irregularities of blood supply as in fainting, loss of blood, cardiac feebleness, Stokes-Adams' disease, and sudden alterations of position and in arterial disease; from visual or bodily disorientation as in diplopia, dancing, swinging, sea-sickness and train-sickness; in anæmic states; in migraine, and as an aura in epilepsy; in diseases of the tympanum, labyrinth and semicircular canals; in diseases of the vestibular nerve and cerebellum, and in conditions of raised general intracranial pressure.

Diagnosis.—The vestibular mechanism is closely connected functionally with the cerebellum, and the symptoms which result from its disturbance are almost identical with those resulting from lesions of the lateral lobe of the cerebellum, and comprise nystagmus to the side of the lesion, vertigo, forced movements, hemiataxy and hypotonus on the side of the lesion. There are two points which serve to separate the two conditions. In the first place, vestibular lesions are usually associated with nerve deafness, which is absent in cerebellar lesions, and secondly, the cerebellar symptoms are only marked in vestibular lesions when the condition is acute, or during acute exacerbations.

Tests for vestibular lesions.—1. Barany's caloric test is made by irrigating the external auditory meatus with either hot or cold water or air. With an intact vestibular mechanism this causes irritation of the vestibular apparatus with the appearance of nystagmus or lateral deviation of the eyes to the side of the irrigation. When the vestibular mechanism is impaired this test fails relatively or completely.

2. If the patient be rotated either by placing him in a special rotating chair, or by turning him round several times in the standing position, lateral

conjugate deviation of the eyes immediately after the rotation will show nystagmus in the opposite direction to the rotation, if the labyrinth on that side is intact. It will not appear if the functional activity of the vestibular mechanism is deficient.

3. MÉNIÈRE'S DISEASE

Synonym.—Labyrinthine vertigo.

Definition.—A malady in which paroxysmal attacks of severe labyrinthine vertigo occur at irregular intervals, associated with tinnitus and progressive deafness, and due to disease of the labyrinth of a chronic nature.

Ætiology.—The cause of this symptom-complex has always been obscure, and this is not surprising since until a recent careful pathological examination of the labyrinth in two cases of typical Ménière's syndrome by Hallpike nothing was known of its underlying morbid anatomy. Ménière's original hypothesis was that hæmorrhage into the labyrinth as the responsible factor, but is inherently improbable and lacks pathological support. According to Hallpike the essential lesion is a gross distension of the endolymph system together with degenerative changes in Corti's organ and the presence of albuminoid coagula throughout the endolymph spaces. He regards these changes as incompatible with an infective origin, and as probably primarily degenerative in nature.

The correlation of these changes with the paroxysmal character of the vertigo can at present only be surmised, but Hallpike believes that the attacks are probably due to rapidly induced bouts of asphyxia of the labyrinthine end-organs caused by rapid rises of fluid pressure in response to small volume increases in the endolymph.

Symptoms.—The attacks set in suddenly with a buzzing noise in the ears, followed immediately with intense vertigo, both subjective and objective. The vertigo may be so intense that the patient feels he is hurled to the ground. He often falls as if shot; sometimes he has time to assume the sitting or lying position, before the vertigo reaches its height. Consciousness is often lost, or seriously impaired, for a few moments only. Spontaneous nystagmus occurs to the side of the lesion, and unilateral cerebellar signs on the side of the lesion. The patient becomes nauseated, and often vomits repeatedly. The skin is pale and covered with a clammy sweat. The patient lies perfectly still, and in terror lest the least movement should bring on more vertigo. The duration of the attack and the time taken in the recovery from an attack vary from a few minutes to 24 hours. Sometimes the attacks are excited by some sudden movement, such as coughing or sneezing, but they are usually without any such antecedent. They may occur during sleep, and wake the patient. The recovery from the attack is usually perfect, the vertigo disappearing; but in some cases slight persistent vertigo remains between the attacks. When Ménière's disease is persistent a slow onset of nerve deafness and signs of slow vestibular destruction follow, and as these signs deepen the attacks become less and less severe, and finally cease when the functions of the labyrinth become destroyed.

The **Diagnosis** of Ménière's disease presents no peculiar difficulty, for the symptoms are highly characteristic, and although the attacks vary in the degree of their severity, from a slight momentary giddiness to a sudden falling, with the most acute cerebellar symptoms, yet the first attack is usually

severe. The rapid disappearance of the symptoms is striking. Vertiginous attacks from all other causes must be excluded. In epilepsy consciousness is usually lost. In Ménière's disease it is momentarily impaired, and there is no convulsion. In acute cerebellar lesions the symptoms are very like those of labyrinthine vertigo, but they are not transitory in a few hours. A careful search of the nervous system for signs of organic nervous disease should in every case prevent any mistake.

Prognosis.—The outlook in Ménière's disease is uncertain. Some cases go from bad to worse in spite of treatment, and progressive deafness ensues with disappearance of the attacks. Many cases, however, recover perfectly with little or no impairment of hearing.

Treatment.—The salicylates seem to have a definite specific effect upon the morbid process, and should be given in doses of 20 grains thrice daily. In the form of aspirin they may be even more beneficial from the sedative effect of the latter drug. The bromides have a wonderful effect in relieving the symptoms, and in averting the attacks, to the extent that it may be said that labyrinthine vertigo may be almost diagnosed by the beneficial effect of bromides upon it. They should be given in doses of from 10 to 20 grains three times a day. Syphilis must be excluded, and if present, treated. Counter-irritation of the mastoid region has been recommended, and can certainly do no harm.

THE NINTH OR GLOSSOPHARYNGEAL NERVE

Lesions of this nerve involve loss of taste over the posterior one-third of the tongue with some unilateral paresis of the pharynx. It is rarely involved alone; but, with the other nerves taking origin in the neighbourhood, by tumours of the lateral region of the medulla.

THE TENTH OR VAGUS NERVE

This nerve is a mixed nerve. The motor fibres supply the voluntary muscles of the soft palate (except the tensor palati), pharynx and larynx in conjunction with the accessory fibres, and the non-striped muscles of the respiratory and alimentary tracts.

The sensory fibres of the vagus supply the respiratory tract, the pharynx and œsophagus. Its visceral fibres supply the lungs, heart and abdominal viscera. No sensibility seems to be supplied to the abdominal viscera by this nerve, since with division of the spinal cord above the offshoot of the splanchnic nerves all sensibility in the abdomen is lost.

Lesions of the Vagus.—The important signs of lesion of this nerve and its nuclei are pharyngeal and laryngeal paralysis and loss of sensibility. Symptoms indicative of lesions of its complicated and mysterious visceral supply are neither well marked nor well understood, and in unilateral lesions seem to be entirely absent; they are therefore not considered.

Lesions of the vagus in the medulla are common. Syringomyelia, when affecting that region, usually involves the nucleus ambiguus, causing unilateral palsy of palate, pharynx and larynx. Thrombosis of the posterior inferior cerebellar artery which supplies that region of the medulla containing the nucleus ambiguus is likely to produce vagus paralysis of the same side. Pro-

gressive muscular atrophy, in the form of progressive bulbar paralysis, may affect its cells, as do often polyneuritis and lethargic encephalitis and rabies. Lesions of the nerve roots often occur from tumours of the lateral region of the medulla, and growths outside the medulla from nerve roots and meninges, and here the lesion of the vagus roots is associated usually with those of the glossopharyngeal, spinal accessory and hypoglossal. In the neck perforating wounds and growths may implicate the nerve, and in the thorax tumours, particularly aneurysms and new-growths, are apt to cause paralysis of the muscles supplied by its recurrent branches.

Unilateral pharyngeal paralysis.—This is characteristic of all unilateral lesions of the vagus high up. It is recognised by the low-lying motionless palate and the loss of sensibility of one side of the pharynx, with loss of the pharyngeal reflex on that side. There is no impairment whatever of deglutition.

Bilateral pharyngeal paralysis.—This results from nuclear lesions of the nucleus ambiguus on either side, and is common in diphtheria, polyneuritis, myasthenia gravis and progressive muscular atrophy. The whole palate is low and paretic or paralysed, the voice is nasal, there is nasal regurgitation of liquids, the cheeks cannot be forcibly blown out, and there is difficulty in pronouncing final "b" and "g," the words "rub" and "egg" becoming "rum" and "enck."

Total unilateral laryngeal paralysis.—Since the superior laryngeal nerve which supplies the cricothyroid muscle, which is the chief tensor and adductor of the vocal cords, is given off high in the neck from the ganglion of the trunk of the vagus, it follows that total paralysis of the larynx on one side can only result from a lesion of the vagus, between the ganglion of the trunk and the nucleus ambiguus in the medulla. The vocal cord on the paralysed side is motionless in the cadaveric position—that is, midway between abduction and adduction. The larynx is insensitive on the same side. There is some loss of tone of voice but no stridor.

Unilateral abductor paralysis or recurrent laryngeal paralysis.—This occurs from all lesions of the trunk of the vagus below the ganglion of the trunk, and from lesions of the recurrent laryngeal branch. The vocal cord on the side of paralysis lies close to the mid-line. It fails to abduct on taking a deep breath. There is no change of voice; but there may be slight stridor on inspiration—the sensibility of the larynx is not affected.

Bilateral abductor paralysis.—This condition is most commonly seen in the earlier stages of nuclear laryngoplegia, and is most often met with in tabes, sometimes in bulbar paralysis, and we have seen it in disseminated sclerosis. It occurs also in bilateral lesions of the recurrent laryngeal nerves in the thorax, which may occur from aneurysm and new-growths. It is the most dangerous form of laryngeal palsy, as the vocal cords cannot be abducted from close to the middle line, and they tend to open during expiration, but to suck together during inspiration, and for this reason may cause death from asphyxia, or necessitate laryngotomy.

THE ELEVENTH OR SPINAL ACCESSORY NERVE

This nerve may be caught with the vagus by lateral lesions outside the medulla, or by lesions in the region of the jugular foramen; but it is more

often damaged by injuries to the neck, and by operations for the removal of cervical glands. The spinal accessory nerve, as it crosses the posterior triangle of the neck, is very liable to injury, either from blows or from sudden strains, and most of the isolated trapezius palsies are due to local neuritis of the nerve trunk, so arising. Paralysis and wasting of the sternomastoids is conspicuous in most cases of myotonia atrophica. That of the trapezius is often conspicuous in the facio-scapulo-humeral type of myopathy. Both muscles are commonly affected in progressive muscular atrophy.

When the sternomastoid is paralysed there is neither weakness complained of, nor deformity, nor peculiar attitude of the neck, other muscles compensating for its paralysis. The muscle does not harden when turning the head to the side opposite the paralysis, and its reaction to faradism is diminished or lost.

Paralysis of the trapezius, on the other hand, causes great disability in raising the arm above the horizontal level of the shoulder and also difficulty in shrugging the shoulder or approximating the scapula to the middle line behind and therefore also in carrying the extended arm backwards. It produces a very ugly deformity, for the scapula unsupported by the trapezius rotates so that the superior internal angle appears as a hump in the slope of the neck above the clavicle, and there is also winging of the angle of the scapula with the axillary border of that bone horizontal. This paralysis of the trapezius may be confused with that of the serratus magnus, for in both winging of the angle of the scapula is marked. In trapezius palsy, however, the deformity is much more marked, the scapula is farther away from the spine, and is much more rotated. Tests for the movements of these two muscles and the faradic excitability should prevent any confusion.

COMBINED LESIONS OF THE NINTH, TENTH, AND ELEVENTH NERVES

No account of the glossopharyngeal, vagus and accessorius nerves is complete which does not consider their clinical interrelationships. Not only are they closely associated in part of their peripheral course, but their central origins are very intimately connected. It is therefore not surprising that in both central and peripheral nervous lesions two or more of them may be involved. A number of characteristic syndromes have thus been observed and described. We may classify these according to whether the causative lesion is intramedullary, or extramedullary (at the base of the skull, or in the neck).

Intramedullary lesions include thrombosis, nerve cell degeneration (chronic bulbar palsy), and syringobulbia; and its component symptoms (*syndrome of Avellis*) are unilateral paralysis of the palatal, pharyngeal and laryngeal muscles, with a crossed hemianæsthesia of syringomyelic type (for pain and temperatures).

At the base of the skull injuries or new growths involving the jugular foramen may give rise to *Schmidt's syndrome*: unilateral paralysis of pharyngeal, laryngeal, palatal, sternomastoid and trapezius muscles; or to *Jackson's syndrome*, in which a hypoglossal palsy may be added to those of the above syndrome.

Injuries high in the neck may produce *Tapia's syndrome* (first described

in bull fighters from penetrating wounds caused by the bull's horn), which consists in unilateral paralysis of the vocal cord and tongue, the palate being intact.

THE TWELFTH OR HYPOGLOSSAL NERVE

The nerve supplies all the muscles of the tongue, both intrinsic and extrinsic.

Unilateral lesions of the hypoglossal nerve are usually the result of tumours in the lateral region of the medulla, or local lesions just lateral to the medulla, and catching the nerve roots. Hemiatrophy of the tongue is perhaps more commonly seen in tabes than in any other condition. A hemiatrophy also occurs in cases of facial hemiatrophy, where the lower distribution of the fifth nerve is the region affected; but this variety does not involve paralysis of the tongue. Spastic paralysis of the tongue, with well-marked dysarthria and dysphagia, occurs in double hemiplegia and amyotrophic lateral sclerosis. Atrophic paralysis of the whole tongue, with exactly similar defects of articulation and swallowing, occurs when the hypoglossal nuclei are affected, and is commonly seen in progressive bulbar paralysis and sometimes in polyneuritis and myasthenia gravis. The sole physical sign of a lesion of one hypoglossal nerve is atrophic paralysis of one side of the tongue with loss of faradic excitability. The affected side of the tongue shrinks and comes in the end to consist solely of mucous membrane, fibrous tissue and glands. The tongue becomes sickle-shaped, with the concavity on the paralysed side. There is little impairment of movement, and no defect of articulation from a unilateral lesion.

The treatment is that of the condition causing the paralysis.

TRIGEMINAL NEURALGIA

Synonym.—Tic Douloureux.

Definition.—A disease of the fifth cranial nerve, in which no definite morbid changes in the nerve have been discovered, and in which no loss of function, either motor or sensory, occurs in the distribution of the nerve. The chief feature of the malady is the occurrence of pain of varied intensity which tends to be paroxysmal, and is often excruciating. Tenderness over the branches of the fifth nerve is always present during the bouts of pain, and when the third division of the trigeminal nerve is affected there is conspicuous unilateral furring of the tongue when pain is present.

Ætiology.—The malady is first met with at the age of puberty; it is not seen in childhood. In the earlier years of adult life it is often a mild and curable condition, though notable exception to this rule may occur; but as age advances, and especially after the age of 50 years, it tends to be increasingly severe and intractable by any measures save those for the destruction of the affected branch of the nerve, or of the Gasserian ganglion. No causal factors can be adduced. The sexes are equally affected. It is much more common in cold and damp climates than in southern and dry countries. Any debilitating influences, such as overwork, general ill-health and specific fevers, especially influenza, may preceded the onset of the malady.

Symptoms.—The chief feature of the malady is pain, which may be general throughout the area of distribution of the nerve, but which is more commonly confined to one of the three divisions of the nerve and often to one branch of a division. It is characteristic for the pain of neuralgia to commence locally, and subsequently to spread in each attack and gradually, in the course of the disease, permanently to invade a larger area. Two different kinds of pain occur, the sharp and paroxysmal, and the dull and continuous pain. The paroxysmal pains are sudden in onset and in cessation. They have a lightning-like character, and are described as piercing, knife-like, or as if the affected region were penetrated by red-hot wires. Often quite spontaneous, these pains may be brought on by touching the surface, by a cold draught, by movement of the face and jaw, or by the act of swallowing, and in this last condition mastication and deglutition may become so difficult as to render feeding the patient a matter of great anxiety. When the paroxysms are occurring in a severe case the patient remains for a period, which may be from a few minutes to several hours, paralysed under the fear of the pain, unable to move a muscle lest a spasm more dreadful then the last should occur. The paroxysmal pains are usually followed, if severe, by a more lasting dull continuous pain often of a boring character, and sometimes such pain becomes absolutely continuous. The skin over the affected region is sore and tender after the paroxysm, and the patient may be unable to bear brushing the hair or shaving the face. The pain may be of every degree of severity, from mild momentary starts to continuous incapacitating pain, interrupted only by excruciating attacks of agony which render life a piteous burden. The distribution of the pain may be anywhere or everywhere in the distribution of the trigeminal nerve. The lightning-like onset of the agony often causes convulsive spasm of the face and of the body and limbs, and from this feature the names "tic douloureux," "spasmodic neuralgia," and "epileptiform neuralgia" arose. The tender points of Valleix are constantly present during the attack, and for some little time after. When the first division is affected, the tender points are found above the supra-orbital notch, over the external angular process, on the upper outer aspect of the nose, and on the globe of the eye. When the superior maxillary division is affected the chief tender point is over the infra-orbital foramen, while other points may be found over the points of exit of the temporo-malar nerves and in the roof of the mouth. When the third division of the nerve is involved, the chief tender points are over the mental foramen, the side of the tongue, and just in front of the external auditory meatus. When the third division is affected, unilateral furring of the tongue, which always occurs when the pain is present and which does not seem to occur with organic lesions of the fifth nerve, nor constantly in any other malady except neuralgia, is seen. Vasomotor and secretory disturbances are common. During the paroxysms, tears and saliva may flow in abundance. The trophic changes which have been described in the skin are usually the result of rubbing during attacks of pain, or of the application of heat or liniments. Local greying of the hair, however, does undoubtedly occur. The clinical picture of trigeminal neuralgia is completed with varying degrees of general physical ill-health, mental apathy and depression, which occur in proportion to the frequency and severity of the attacks, the presence of continuous pain, the ability to

take food and to sleep, and the possibility of taking any interest in life. It is surprising in England how few of the sufferers from severe neuralgia become habitual drug-takers.

Course.—In patients under the age of 40 years the malady is often transient and is completely and permanently recovered from, though even at this age cases occur which are only amenable to surgical interference. But when the malady commences after the age of 40 years, it is the rule for it to become progressively worse. The paroxysms become more severe, and occur at shorter and shorter intervals, continuous pain sets in, sleep and the taking of nourishment become difficult, and useful life becomes more and more restricted.

Diagnosis.—There should be no difficulty in making a correct diagnosis if proper care be taken. In the first place, all local cause for pain in the peripheral distribution of the trigeminal nerve should be excluded. The teeth should be most carefully examined and the jaws skiagraphed for any concealed disease, which should be put right if present. Organic disease of the fifth nerve can be excluded by the facts that such disease cannot long exist without signs of loss of function, which never occur in neuralgia. Diminution of sensibility, which is first marked perhaps by increased tolerance of the conjunctiva and cornea to touch, and weakness of the musculature with deviation of the chin on opening the jaw, and diminution of taste are certain signs of a local organic lesion. Moreover the pain of neuralgia, with its lightning onset and cessation, is hardly imitated by any pain of organic origin. Ocular conditions, such as glaucoma, which may give rise to agonising pain, can hardly be mistaken for neuralgia.

Treatment.—Having in the first place seen that all possible causes of local irritation in the region of distribution of the fifth nerve are absent, or, if present, adequately dealt with, it is essential to improve the nutrition and general physical health with tonic, dietetic and hygienic treatment, and such remedies alone will often cure slight cases. It is important to remember that in its early stages, the malady shows complete remissions of long duration. These remissions do indeed tend to become shorter after some years, but their occurrence suggests that in planning treatment it is essential to consider the circumstances of each individual case. Thus, if a patient who may be expected to enjoy a long period of freedom from pain can be tided over the present attack by medical means, it is clearly not wise to give an alcohol injection. This confers a long period of "cover" from pain which the patient will probably not require, and the premature recourse to injection means that in the end more injections may be called for than would otherwise have been needed.

With this qualification, treatment may be undertaken on the following lines: Tr. gelsemii in doses of from 10 to 20 minims thrice daily is an admirable remedy, and arsenic is a useful adjuvant. All the analgesic antipyretics of the coal-tar series are of great value, not only as immediate relievers of pain, but also as curative agents, and among these aspirin is most important. In cases where malaria has been recently present, quinine should never be omitted. In very severe cases, and when operation is to follow, morphine is an invariable temporary relief to the pain. But if persisted in, the beneficial effects of moderate doses soon disappear. In every case except in old subjects, a thorough trial of the above treatment should be made over a

sufficient period to make a competent judgment of its efficiency or inefficacy, as the case may be. When failure is met with, and in old subjects, who will be found to respond little if at all to such treatment, operative relief should be sought. In the first place, the injection of alcohol should be performed, and if this fail, as it sometimes does, on account of anatomical peculiarities of the individual, recourse should be had to the operation for dividing the fifth nerve proximal to the Gasserian ganglion. The permanence of the effect of alcohol injection varies, sometimes lasting relief is obtained; more often, after a period which varies from months to years, some return of the pain occurs. It is, however, a most difficult procedure for the operator, and requires great skill and experience. While absolutely devoid of risk in skilled hands, alcohol injection should never be undertaken by one who has not special training in its performance. The radical operation produces final cure.

GLOSSOPHARYNGEAL NEURALGIA

Definition.—A comparatively rare form of neuralgia within the distribution of the glossopharyngeal nerve. It is strictly comparable with trigeminal neuralgia in the quality and severity of the pain, its paroxysmal incidence, the remissions in its course, its provocation by special stimuli, and finally by the absence of any discoverable lesion in, or loss of function of, the nerve.

Ætiology.—Nothing is known of its ætiology. It is most frequently seen in middle-aged or elderly males. A symptomatic neuralgia of the same distribution is occasionally found in cases of carcinoma of the tongue in which the growth invades the faucial region.

Symptoms.—When fully developed, the malady consists in paroxysms of shooting pain of great severity in the region of the throat and ear. The exciting stimulus is commonly the act of swallowing. But just as in trigeminal neuralgia the pain may at first be confined to a single branch of this nerve, so in glossopharyngeal neuralgia, the pain may for long be confined to the tympanic branch, the pain being felt deep in the ear. This pain does not spread to the pinna. In other cases, pain in the faucial region predominates, the pharyngeal branches being affected. As in trigeminal neuralgia, the patient may enjoy long intervals of freedom from pain. During a paroxysm the patient screws up his face and may hold his head in his hand as does the subject of trigeminal neuralgia.

Diagnosis.—The presence of neuralgic pain of great severity, provoked by the act of swallowing, and in its general characters and behaviour resembling the very familiar and characteristic paroxysms of trigeminal neuralgia, but differing from these in its restriction to the ear and throat, occurring also in the absence of objective signs of a lesion of the cranial nerves: these together are the features which make a diagnosis of glossopharyngeal possible and easy.

Treatment.—In the early attacks, the same forms of medication employed in trigeminal neuralgia may be employed. If the pain does not respond to these, then surgical measures are called for. The tympanic branch of the nerve leaves the main trunk within the skull, so that when pain in the ear is present an intracranial section of the glossopharyngea

nerve is necessary. On the other hand, when pain is confined to the distribution of the pharyngeal branches, division of the nerve high in the neck is adequate. But intracranial section appears to be the operation of choice.

FACIAL HEMIATROPHY

Synonym.—Parry-Romberg syndrome.

Definition.—A peculiar malady confined to some part of the distribution of the trigeminal nerve, or rarely extending from thence on to the area of sensory distribution of the upper four cervical nerves. It is characterised by a progressive atrophy of all the tissues, skin, subcutaneous tissue, muscle and bone, without sensory loss or paralysis. It comes to an arrest after a few years. No pathological condition has been discovered to account for the atrophy.

The disease may commence in childhood even as early as the second year, but it is most commonly started in early adult life. Females are much more often affected than males.

Symptoms.—The atrophy may be distributed over the whole area of the supply of the trigeminal nerve, or, as is more usual, may be confined to one or more of its branches. In general atrophy, a gradual diminution in the bulk of the whole side of the face is the first indication of the disease. When the disease is confined to one of the three great divisions of the nerve, the atrophy usually commences in one spot, commonly on the cheek just below the malar bone, where the skin becomes thin and pale from loss of pigment, and the down falls out. The submalar fat disappears, leaving an unsightly hollow. The atrophy spreads to the side of the nose, where the cartilages and bones become gradually smaller. The jaws gradually decrease in size upon the affected side, until they are too small to hold the teeth, which are actually pushed out by the decreasing size of the tooth sockets. The half of the tongue upon the affected side decreases in size, and thereby is rendered sickle-shaped. Even the eye may be remarkably lessened in size. The upper part of the first division of the fifth does not seem so liable to involvement, for it is rare to see any diminution of the size of the forehead, or dropping out of the hair of the scalp. The atrophy not uncommonly affects the ear. The skin in the end becomes very thin and parchment-like.

Treatment.—The only treatment is cosmetic, to improve somewhat the appearance of the face, by the injection of semisolid paraffin, to replace the fat and fill the unsightly submalar hollow.

THE SIGNS OF LOCAL LESIONS WITHIN THE SKULL AND BRAIN

Owing to the complete inaccessibility of the central nervous system to direct examination by any method comparable with those in use in the case of the viscera, the clinical localisation of disease within that system must necessarily depend upon the study and interpretation of disorders of function in tissues innervated by the nervous system. Many bodily functions have a localised representation in the brain and in the spinal cord. It must be remembered, however, that in clinical diagnosis we are concerned not directly with the localisation of functions within the nervous system, but with some-

thing rather different, namely, the localisation of symptoms of lesions. A simple example will serve to make this distinction clear. In a case of unilateral ataxy of movement, our object is to locate the lesion which by damaging some part of the nervous mechanism has allowed ataxy to develop. We may decide from our examination that this lesion is within the cerebellum, and we conclude that a destructive lesion of this organ is followed by ataxy. This ataxy is clearly produced by the activity of the intact remaining parts of the brain, working without the co-operation of the cerebellum. In this instance we have not localised any "function" of the cerebellum; we have simply localised the symptom following a lesion of this organ. Nor can we conclude that one of the functions of the cerebellum is to prevent ataxy, the fact being that the functions of this organ are still very imperfectly understood. Nevertheless, the localisation of symptoms of cerebellar lesions can be performed with reasonable accuracy.

This brings us to a brief consideration of the ways in which lesions within the nervous system may disturb its functions. The functions of a region of the brain that is directly involved in a disease-process may be deranged in either of two ways. They may be stimulated to overaction, or they may be impaired or destroyed. We may thus speak of "*irritative*" *or excitatory symptoms* on the one hand, and of *paralytic symptoms* on the other. A Jacksonian fit is an example of the first; a hemiplegia of the second. Further, although there is some measure of localisation of topographical and of functional representation within the brain, normally this organ works as a whole and derangement of the functions of one region may derange the functions of the whole, as we have already seen illustrated in the case of cerebellar ataxy. There is another way in which such general disturbance may follow a local lesion, and that is by what is known as diaschisis or shock. We see this mode of disorder in the coma which accompanies a cerebral hæmorrhage. In this state the cerebral hemispheres are for the time being out of action, even those parts that are not actually damaged by the lesion. Such *shock symptoms* are necessarily transient. A final group of symptoms are those we speak of as "*release symptoms.*" When the coma of the hemiplegic subject has passed off, he is left with paralytic symptoms, namely, the hemiplegia. In a few weeks the paralysed limbs become spastic, their tendon jerks increase, and clonus makes it appearance. These symptoms of persistent overaction of nervous mechanisms freed by the lesion from the normal control of higher mechanisms, are what we refer to when we speak of release symptoms. Such symptoms may persist for years and may in some instances entirely dominate the clinical picture. But the practical task of localising lesions is sometimes even more complicated than this analysis of disorders indicates. The degree of disturbance of function produced by any lesion depends also on temporal factors. A suddenly arising lesion, such as an arterial occulsion or a hæmorrhage, or a direct injury is apt to produce a much more severe and widespread disorder of brain function than a slowly developing lesion. Thus, the intracranial cavity may come to accommodate a large new growth which compresses and markedly deforms the brain without giving rise to any subjective discomforts or disabilities, or to any abnormal physical signs discoverable on examination. Again, it is known that a chronic cerebral or cerebellar abscess is commonly present for some weeks before it reveals its presence by signs or symptoms. This is its period of clinical latency. Finally,

a tumour within the brain, while it may give rise to symptoms of a general rise of intracranial tension, such as headache, papillœdema and sickness, may yield on examination no localising signs, and this not necessarily because it is in what is known as a "silent area" of the brain. Or, it may cause but a minimal disturbance of local function even when large regions of known and specific function are directly involved. Finally, we have to take into consideration that space-occupying lesion within the skull or brain may come ultimately to produce indications of local disorder of function in parts of the brain remote from the lesion. These may be spoken of as false localising signs.

From what has been said it will be apparent that at least two factors determine the symptoms associated with disease within the brain, namely, (i) the localisation of the lesion, and (ii) the nature of the lesion. The latter determines its rate of development, its stimulating or paralysing effects upon the nervous tissue, and its capacity for producing remote effects.

Hence it is that the localisation of a lesion within the brain (the topographical diagnosis) and the determination of its nature (the pathological diagnosis) are frequently something more than a simple essay in applied anatomy and physiology, and that complete diagnosis calls also for a knowledge of the natural history of the different disease-processes, that is, for clinical experience. In this chapter we must be content with a brief consideration of the signs upon which we depend for the localisation of symptoms. We may take first the various regions of the brain, and secondly, since we have to deal not only with lesions within the brain, but also with all lesions within the skull, that may be outside the brain, we will consider the symptomatology peculiar to lesions in the three cranial fossæ.

The Cerebral Hemispheres

General lateralising signs.—A lesion within or involving one hemisphere may reveal by the signs it produces whether it is right- or left-sided without affording further localising information. Such signs are unilateral diminution or absence of the abdominal reflexes, a unilateral extensor type of plantar response, and a just perceptible unilateral paresis of movements of the lower part of the face.

The frontal lobes.—These include that part of the hemisphere anterior to the ascending frontal convolution. The lesions to be met with in this region include tumour, abscess and thrombosis of the anterior cerebral artery, the last named being comparatively rare.

The syndrome of the anterior cerebral artery consists of spastic weakness of the crossed lower limb with the appropriate changes in the reflexes, sometimes a slight degree of weakness of the crossed face and arm, sometimes forced grasping and groping in the arm of one or both sides, and apraxia of the left arm. There may also be some mental obfuscation.

The syndromes of frontal lobe tumour vary according to the rapidity of development of the tumour and under other factors not fully understood. As a rule an early, if not the initial, symptom is a change in the patient's mental state. He becomes apathetic and lacking in initiative. The association and flow of ideas tends to fail. He sits about idly. He is apt to permit the unhindered passage of urine and even of fæces, and to be totally indifferent to and unaware of the social embarrassments such conduct involves. This

form of "incontinence" is in fact a diagnostic symptom of great value in frontal lobe lesions. Rarely, the patient develops an abnormal facetiousness and euphoria—the so-called "Witzelsucht." Movement is disordered by the development of apraxia, and sometimes by that of forced grasping and groping, another useful sign of frontal lobe involvement, though it must be admitted one occasionally seen in lesions elsewhere in the cerebral hemispheres, as in a case under the care of the present writer in which bilateral grasping and groping and forced sucking were prominent features, the lesion being found at necropsy to be a bilateral degeneration of the thalamus. Nevertheless, this sign is an important one. It has been analysed by Walshe and Robertson into two components: (1) Volitional grasping movements made by the conscious patient when some object is felt by him in his palm or is seen by him to approach his hand. These movements wane and cease when consciousness is failing, or when attention is defective. (2) A true tonic reflex grasp of any object held in the hand, if this object be so pulled away by the observer (or by the patient with his other hand) so as to put the flexors of the fingers on the stretch. The flexors tighten as the pull is maintained and may become of great force, so strong indeed that sometimes the patient can be pulled out of the bed by this involuntary grasp which he is unable voluntarily to relax. This reflex may persist even though consciousness be lost. If the orbital lobule be involved, there may be bilateral anosmia and even direct pressure upon one optic nerve. These two symptoms will be further considered in connection with the syndrome of the anterior fossa of the skull. The tumour being an expanding and space-occuping lesion may when in this situation lead to the appearance of slight crossed hemiparesis, and when left-sided may be accompanied by motor or "expressive" aphasia. When, in the case of tumour, the corpus callosum is involved, the patient becomes completely apathetic and silent and immobile, displaying no initiative of any kind.

Syndromes of the central region (region of the "motor cortex.")—Hemiplegia is the characteristic paralytic manifestation of a lesion, Jacksonian fits of an "irritative" lesion. Such a fit may be followed by transient hemiparesis, and in the case of tumour by a slowly progressive and permanent hemiplegia. Local involvement of some part of this region will affect face, arm or leg predominantly according to its situation.

Conjugate deviation of the head and eyes may be met with, away from the side of the lesion, if this be irritative, as at the commencement of an apoplexy, or of a local fit, or towards the side of the lesion if the lesion be paralysing. The two forms of conjugate deviation often follow the one after the other, from the same lesion which is at first exciting and afterwards paralysing. Conjugate deviation of the head and eyes is seen with acute lesions rather than with those of slow development. The more deeply the lesion extends into the sublying white matter, the more does it tend to produce an extensive hemiplegia, since the pyramidal fibres converge from the cortex towards the capsule. Loss of localisation to sensory stimuli is not infrequent from simultaneous involvement of the neighbouring post-central convolutions.

Parietal lobe.—A characteristic series of sensory disorders may mark the presence of a lesion in this region. These include defective localisation of tactile stimuli, defective appreciation of two simultaneous contacts (Weber's compass test), defective appreciation of three dimensional space

(*i.e.* of size and form). There is, in addition, defective power of differentiating varying intensities of stimulus (painful or thermal), and a ready fatigue of sensory functions. The simple recognition of painful and thermal stimuli may be relatively intact. It will be seen that the defects in spatial discrimination which result from these modes of sensory loss lead to that inability to recognise and identify objects held in the hand, or to describe their size, shape or texture, which is known by the name of astereognosis. The appreciation of active movement and passive position is apt to be faulty, and some ataxy may result therefrom. Trophic changes may be observed in the periphery of the limbs, and lesions in this situation seem to be responsible for the arrest of growth which is seen in cases of infantile hemiplegia. Jacksonian attacks, consisting of a peripheral sensory aura, sometimes followed by convulsions, occur. These localising signs are confined to the opposite side of the body.

Occipital lobes.—Lesions of the cuneus and region of the calcarine fissure on the mesial aspect of the occipital lobe result in hemianopia of the opposite field, but central vision escapes. Gordon Holmes has found that if the lesion is limited above the calcarine fissure a quadrantic hemianopia of the lower field results, and if the lesion is below the calcarine fissure the quadrantic hemianopia resulting is of the upper field. Since central vision is represented at the posterior pole of the hemisphere, a lesion of the posterior pole causes central hemianopic scotoma, vision in the periphery of the field remaining intact. Consequently a bilateral lesion of both posterior poles will result in bilateral central scotoma, and a bilateral lesion of the calcarine region will produce blindness of both peripheral fields, central vision remaining intact. If the lesion extends deeply into the occipital lobe so as completely to sever the optic radiation to the occipital cortex, complete hemianopia, affecting both the central and peripheral part of the visual field, will occur. The hemianopias resulting from lesion of the occipital lobe are distinguished from those due to lesion of the optic tract by the fact that in the former the pupil reacts to light thrown on to the blind part of the field (Wernicke's hemianopic pupil phenomenon). On the outer surface of this lobe, a lesion extending deeply on the left side may sever the connection of the visual centres with the speech centres, and so produce word-blindness. Such a lesion is usually situated at the junction of the left occipital and temporal lobes. Jacksonian attacks are often of great value in occipital localisation, and take the form of visual hallucinations, often accompanied by transient hemianopia.

Temporal lobe.—The uncinate and hippocampal regions of this lobe are the cortical seats for taste and smell, and the localising symptoms which are rarely absent when lesions in this region exist are Jacksonian attacks in the form of hallucinations of taste and smell, nearly always of an unpleasant nature. The hallucination is often immediately followed by a "dreamy stare," during which smacking movements of the lips, or champing movements of the jaw, or spitting may occur. Experience seems to prove that all highly organised hallucinations, whether auditory, visual or psychic, when occurring from organic lesion of the brain, point to a lesion in the uncinate region. The senses of taste and smell are not lost from a unilateral lesion of this region, since they are bilaterally represented in the cerebral hemispheres. The outer surface of the temporal lobe is concerned with hearing, but from

the complete semi-decussation of the auditory path, unilateral lesions never produce detectable deafness. On the left side, however, the temporal lobe is concerned with speech, and destruction results in serious disorder of speech functions. Inasmuch as lesions of this region are situated far forward toward the insula, they result in " verbal aphasia," or towards the centre of the convexity of the temporal lobe, in amnesia, or lack of recall of words and " word-deafness," while if towards the posterior limits of the lobe they produce " word-blindness " from severance of the visual path to the speech region. Deeply seated lesions isolating the speech region from the incoming auditory path produce jargon aphasia. Jacksonian attacks, consisting of auditory hallucinations, which may or may not be followed by aphasia or by convulsions, may occur. Extensive lesions of the left temporal lobe cause much mental impairment. On account of the wide excursion which the optic radiation makes into the deep part of the temporal lobe in its course from the thalamus to the cuneus, homonymous hemianopia, especially of the upper quadrants, is very common in deep-seated lesions of the temporal lobes. The occurrence of incontinence of sphincters of a mental type is occasionally seen in some cases. When lesions extend deeply there may be a paresis of the opposite face for emotional movements, out of all proportion to the loss of volitional movements.

Internal capsule.—In this region, the chief motor tract is condensed into a small space, and is situated immediately in front of a narrowly localised sensory tract, while not much farther, posteriorly, the visual path enters the thalamus. Lesions of this region therefore produce severe and widely-spread hemiplegia of the opposite side, often associated with hemianæsthesia and not infrequently with hemianopia of the opposite side. From the proximity of the thalamus and corpus striatum, there is often involvement of these structures in a capsular lesion, with appearance of the characteristic, spontaneous involuntary movements and sensory loss.

Basal Ganglia

Optic thalamus.—A very characteristic clinical picture results from destruction by thrombosis of this structure which is termed the " thalamic syndrome " of Dejerine and Roussy ; there is hemiparesis with spontaneous involuntary movements of the opposite side, which may be of the nature of tremor, intention-tremor, choreic, athetotic, dancing or irregular movements. Most post-hemiplegic involuntary movements are due to a lesion of the thalamus. In addition, there is hemianæsthesia, often with a characteristic hyper-sensitivity to aggressive stimuli, such as tickling, cold water, etc., which may produce agonising distress. Sometimes spontaneous, constant and unrelievable pain occurs on the opposite side. Emotional movement of the opposite face may be impaired much more than is volitional movement. The thalamic syndrome is not invariably, or even commonly, seen when the lesion is a tumour. In this case, as Smyth and Stern have pointed out, the symptom-complex varies according to whether the growth primarily arises in this structure or invades it from its lateral aspect. In the former case they arise in the sub-ependymal glia and spread laterally. They are characterised by early mental deterioration, with conjugate ocular palsies. Sensory changes are absent or only terminal in appearance. In

the case of tumours secondarily invading the thalamus from its lateral side, sensory changes of the order described under the "thalamic syndrome" of Dejerine and Roussy, Head and Holmes, are seen.

Corpus striatum.—Little is certainly known of the symptomatology of focal lesions of this structure, and the various syndromes (tremor-rigidity, athetosis) which have been described are associated with diffuse lesions involving other parts of the cerebral hemispheres in addition to the corpus striatum. However, a local lesion (thrombotic) in a neighbouring mass of grey matter, the corpus subthalamicum, or corpus Luysii, is followed by violent unilateral choreiform movements, the so-called *apoplectic chorea.*

Region of the falx cerebri.—Lesions of this structure are likely to affect both hemispheres equally. Tumours opposite the paracentral lobules cause bilateral crural monoplegia, and those in the posterior region of the falx, bilateral hemianopia. Thrombosis of the superior longitudinal sinus produces widely spread bilateral softening of the hemispheres, with double hemiplegia.

Corpora quadrigemina.—The oculo-motor nuclei lie on either side of the aqueduct of Sylvius, and lower down on either side of the middle line, in the floor of the upper part of the fourth ventricle, and lesions of this region cause nuclear ophthalmoplegia—that is, paralysis of both eyes in terms of the conjugate movements upwards, downwards or laterally. From before backwards, lesions of this column of oculo-motor nuclei will produce reflex iridoplegia, paralysis of accommodation, paralysis of upward, downward and lateral movements respectively. Immediately ventral to the oculo-motor nucleus and decussating beneath it, lie the superior peduncles of the cerebellum, involvement of which causes bilateral ataxy of limbs and trunk. Lesion of the dorsal part of the quadrigeminal layer produces a characteristic syndrome of nuclear ophthalmoplegia with bilateral ataxy, which is termed Nothnagel's syndrome. The pyramidal fibres for the face leave the pyramidal tract in this region of the tegmentum and may here be involved alone, causing bilateral spastic paralysis of the face. In the ventral portion of this region of the brain stem are the crura cerebri with the third nerve, perforating each crus to emerge upon its inner side, and the optic tract running round the crus from the geniculate bodies to the optic chiasma. A lesion of one crus will cause hemiplegia of the opposite side, and paralysis of the third nerve on the same side. This pathognomonic localising combination is known as Weber's syndrome. Situated a little more dorsally, a lesion of the crus will produce ophthalmoplegia of one eye with tremors and inco-ordination of the opposite limbs. This is known as Benedikt's syndrome. Extension of a lesion outwards from the crus will cause tract hemianopia, in which the half-fields are completely involved, with no light reaction from the blind fields. Interference with the fillet may cause hemianæsthesia.

Pons and Medulla

In these regions the motor and sensory tracts, the cerebellar peduncles, the cranial nerve nuclei, and the outgoing cranial nerves are closely packed together, and the signs resulting from destruction of these will be varying combinations of spastic paralysis, ataxy and sensory loss—from interference with the long conducting tracts—in the body and limbs, with

nuclear and peripheral nerve palsies and anæsthesia in the region of the face. If the lesion is unilateral the body and the face will be affected on opposite sides, causing the " crossed paralyses " or " alternate paralyses " of lesions of the brain stem, of which facial palsy with contralateral hemiplegia, trigeminal palsy and sensory loss, and vagal palsy with contralateral hemiplegia are usual varieties. From the smallness of the brain stem lesions most often involve both lateral halves of this structure, and bilateral symptoms result. Lesions of the brain stem below the oculo-motor nuclei, cause small pupils (pontine myosis) from cutting off those nuclei from the spinal cord, whence the tonic dilator of the pupil—the cervical sympathetic system—emerges. Glycosuria may occur from interference with the vasomotor centre, and involvement of the respiratory centre is frequent. The common lesion involving the medulla is softening of the lateral region following thrombotic occlusion of the posterior inferior cerebellar artery, the so-called cerebellar apoplexy (see p. 1602).

Cerebellum

When lesions of this structure develop suddenly they are apt to produce more striking disturbances of movement than when they develop gradually, a point which it is important to remember when the presence of an abscess or a tumour within the cerebellum is suspected. Further, it is well to regard the several different components of cerebellar ataxy not so much as special disorders of different cerebellar functions, but as expressions of a single disorder, which owe their varying appearance to the varying nature of the clinical tests employed. The current nomenclature of cerebellar symptoms is redundant and complicates description, but it is universally employed and so is here adopted, but with no conviction of its scientific value.

Nystagmus.—In unilateral lesions there is a coarse nystagmus on deviation of the eyes to the side of the lesion, with a finer and more rapid movement on deviation away from the side of the lesion. In extensive lesions, there may even be considerable difficulty in deviation to the side of the lesion, and in this condition a true nystagmus may be present only on looking to the opposite side. In bilateral lesions the nystagmus may be symmetrical, but it may be entirely absent. Rarely—usually after acute lesions—such as gunshot wound or operative interference—the phenomenon of " skew deviation " may appear temporarily; the eye on the side of the lesion being displaced down and in, the opposite eye upwards and outwards.

Hypotonia.—This is usually seen in acute lesions rather than in chronic ones, and consists of a marked flaccidity and extensibility of the limb muscles, and leading to the " pendular " form of knee jerk.

Dysdiadochokinesis.—This is a clumsiness and slowness in the performance of rapidly alternating movements (pronation-supination), although the single movement can be normally performed. In carrying out this test, it is common to see adventitious movements of the limb occur, the whole limb being in movement.

Dysmetria.—When the patient is asked to extend the arm to pick up some object, such as a glass, the limb is shot forwards with undue haste and force and may overshoot the mark.

Tremor.—This is not a resting tremor, but an unsteadiness which develops

during movement, and in purposive movements tends to increase in range and severity as the climax of the movement is reached. It is an "intention tremor." Similarly, if the arms be horizontally extended, they may show a tendency to droop, which is corrected by a series of jerks which thus gives the form of a tremor.

Excessive rebound.—This diagnostically valuable sign may be present when more striking components of the cerebellar syndrome are absent. If the arms be horizontally extended by the patient, and the observer smartly strikes them downwards somewhere in the region of the hand, the arm on the normal side is quickly brought to rest in its original position with a minimum of recoil. On the side of the lesion, however, the hand and arm "bounce" freely, and may swing two or three times before being brought to rest.

Gait.—In bilateral lesion the gait has a reeling, tottering character, and in strictly unilateral lesions there may be a tendency to sway and deviate to the side of the lesion. The disorder may vary in severity from a slight unsteadiness to a complete inability to stand or walk unassisted. There is a tendency to walk with the legs abnormally separated, to raise the legs unduly, and to stamp them down heavily (manifestations of dysmetria).

Numerous other defects may be elicited by special tests, but one only calls for special mention, that is the defective movement of the articulatory musculature in speech. The defect is known as "scanning" or *staccato* speech. It consists in a slowness of articulation, and a tendency to say each syllable of a word as though it were a separate word. In polysyllabic words the syllables are not normally run together.

The cerebellum forms part of the non-sensory afferent nervous system. It is not a sensory organ and there is no disturbance of any form of sensibility in cerebellar lesions (Holmes).

The Anterior Fossa of the Skull

The lesion commonly found in this region is meningioma arising from the olfactory groove. The signs are unilateral anosmia from pressure upon the olfactory bulb and tract; primary optic atrophy and visual loss on the side on which the tumour develops; and crossed papillœdema as an expression of the general rise of intracranial tension. Aneurysm of the anterior cerebral artery may give rise to a similar syndrome, papillœdema in the crossed eye being absent.

The Middle Fossa of the Skull

A rich variety of lesions may arise in or invade this fossa, and the syndromes also vary according to the situation, mesial or lateral, of the lesion.

The lesions in the midline include pituitary adenomata, tumours of the pituitary stalk, and meningioma of the sellar diaphragm. In the lateral parts of the fossa, passing from the mesial to the lateral extremity, we have to consider cerebral aneurysm, meningioma arising from the sphenoidal ridge, and growths invading the base of the skull and either occluding its foramina and thus producing cranial nerve palsies, or actually invading the

cranial cavity. Epithelioma of the naso-pharynx is the common lesion of the last-named type.

(i) *Region of the optic chiasma and the pituitary body.*—The most common lesion in this region is pituitary tumour, which involves the optic chiasma, at first in the middle line posteriorly, and subsequently advancing forwards. Three sets of symptoms are likely to arise: (1) Those due to dyspituitarism, such as acromegaly or gigantism if there is hyperpituitarism, or Fröhlich's dystrophia adiposo-genitalis, or Lorain infantilism if there is hypopituitarism. Adenomata of the pituitary body produce hyperpituitarism if they contain eosinophil cells, and hypopituitarism if such cells are absent. (2) Those due to the pressure upon the optic chiasma, which commence as bitemporal paracentral scotomata, which enlarge as the compression extends until a complete bitemporal hemianopia results. It cannot be too strongly impressed upon the reader that the pattern of the visual field defect is determined by the position of local pressure upon the visual paths, and that any variety of defective field may occur. While bitemporal loss is the most usual, yet when the pressure is far forward, uniocular hemianopia, blindness of one eye, and central scotoma are all of common occurrence, and when the pressure is farther back than usual homonymous hemianopia is frequently seen. And (3) those due to the general effect of the tumour, namely, headache and vomiting. Optic atrophy is the rule, as the result of the direct pressure, and not papillœdema. It is to be remembered, that all pituitary cases are prone to headaches and subject to fits. We have seen also (p. 1593) that cerebral aneurysm may be productive of this syndrome, or at least of the chiasmal component thereof.

(ii) *Lateral region of the middle fossa; syndromes of the sphenoidal ridge.*—The dural sinus which runs along the sphenoidal ridge (sinus sphenoparietalis) is one of the sites of election of the development of meningioma. From the point of view of localising diagnosis this ridge may be divided into three parts, namely, outer, middle and inner (or clinoidal).

A meningioma arising from the *outer end* of the ridge may produce as its localising syndrome unilateral exophthalmos without squint, some fullness of the temporal fossa with local tenderness on pressure, together with the general signs of raised intracranial tension.

Meningioma of the *middle part of the ridge* may remain for long without clear localising indications, and radiography (including ventriculography) may be necessary. Meningioma of the *inner or clinoidal part of the ridge* commonly gives rise to a striking and characteristic syndrome which in addition to the general signs of raised intracranial tension, unilateral failure of vision due to primary optic atrophy, unilateral exophthalmos, crossed papillœdema, more or less complete ophthalmoplegia on the side of the lesion and finally symptoms referable to pressure on the temporo-sphenoidal lobe (uncinate fits, hemiparesis, personality changes). It will be remembered that internal carotid aneurysms also arise in this neighbourhood and may produce a similar symptom-complex, papillœdema, however, being commonly absent. The syndrome of naso-pharyngeal tumour when the skull is invaded also closely resembles this. In other words, this syndrome, in partial or complete form, should arouse in the observer's mind the possibility of one or other of these three varieties of lesion—meningioma of the inner end of the ridge, cerebral aneurysm, and naso-pharyngeal tumour invading the skull.

THE POSTERIOR FOSSA OF THE SKULL: SYNDROME OF THE LATERAL RECESS

Lateral recess.—The angle formed by the posterior surface of the petrous bone and the tentorium is a common situation for neurofibromata which grow usually from the eighth nerve, but occasionally from the seventh and from the fifth nerve, and press into the lateral lobe of the cerebellum. A highly characteristic clinical picture results, of slowly oncoming nerve deafness, unilateral signs of cerebellar involvement and some peripheral facial spasm, to which are sometimes added facial weakness and tinnitus. Such tumours are not of great size, and therefore headache and papillœdema are often absent or occur late.

INTRACRANIAL TUMOURS

Under this heading are grouped all new formations which encroach upon the intracranial space, and which produce the familiar pressure symptoms and local symptoms of tumour, though some of these are not, strictly speaking, neoplasms.

Ætiology.—The brain is one of the commonest seats of new growth in the body. Further, new growth is one of the commonest forms of structural disease of the brain—vascular lesions naturally not being included under this heading. Thus, out of a total of 1309 patients admitted to the National Hospital in 1928, there were 163 cases of intracranial tumour, 132 of disseminated sclerosis, and 113 of neurosyphilis.

Age.—Cerebral tumour may occur at any age, but it is relatively uncommon in the very young and in the very old. It seems to be somewhat more common in the female sex. The relation between head injury and the first appearance of symptoms of cerebral tumour, is one which occurs much too often to be ignored, though it is likely, in some of the cases in which this relation exists, that the blow on the head has simply served to bring a pre-existing tumour into symptomatic prominence, either by causing œdema or hæmorrhage in its substance, or vicinity. It must be remembered in this connection that a cerebral tumour may exist for long periods without definite symptoms.

Pathology.—The pathological classification of intracranial tumours has a practical importance, for when the nature of a new growth can be determined clinically, some idea of its future behaviour can be formed, and the surgeon can make his plans to meet the special problems which each variety of tumour presents.

The chief varieties of intracranial tumour are as follows:

Tumour of the brain substance—Glioma.
Tumour arising in the meninges— { Meningioma. / Auditory nerve tumour.
Tumour of the pituitary body and stalk.
Secondary carcinoma.
Infective granuloma—Tuberculoma, Syphiloma.
Blood vessel tumours.
Parasitic cysts.

It is not possible to indicate the relative incidence of all these different types of tumour, but it is possible to state that glioma constitutes 40 per cent. of all intracranial tumours, and meningiomas and pituitary tumours together from 20 to 30 per cent. Formerly, the incidence of secondary carcinoma was said to be about 6 per cent., but a recent estimate by Elkington places the figure at 20 per cent., and there can be no doubt that as greater precision in diagnosis is reached the frequency of this complication of visceral carcinoma will be more fully recognized.

As its name implies the *glioma* is a tumour arising in the glial or supporting tissue of the brain, but within the limits of this term are included growths of varied cytological type and modes of growth. Some are richly cellular, highly vascular, rapidly growing and fairly circumscribed tumours. To these the name *glioblastoma* is given. Others are diffuse infiltrating tumours, invisible to the naked eye except where degenerative processes have occurred in them, very extensive and often bilateral. To this type the name of astrocytoma is given. They are prone to cyst formation and grow more slowly than the glioblastoma. In childhood a variety of glioma known as the *medulloblastoma* is common. It is a richly cellular, highly malignant growth of the fourth ventricle.

Very many other types of glioma have been described, but these classifications are ephemeral and largely artificial, for each type may be represented within a single tumour, and changes from one type to another—from astrocytoma to glioblastoma—may occur in a given growth. Scherer has shown that none of these types is capable of extirpation, the astrocytoma because it is diffuse and largely invisible, the glioblastoma because death follows attempt to remove it. Thus, there is no such thing as a benign glioma. The best that can be said is that the astrocytoma recurs in some cases relatively slowly. Recurrence is invariable in all who survive partial extirpations. The glioma is not always a single tumour, contrary to what has been believed in the past.

Meningioma and auditory nerve tumours. — These tumours of the meningeal sheaths which insulate the ectodermal nervous system occur next in order of frequency to the gliomas. The meningioma, or endothelioma as it is sometimes called, grows from the endothelial cells of the arachnoid villi where these penetrate the walls of the dural venous sinuses. It is therefore found in the neighbourhood of the various sinuses, especially the superior longitudinal, the spheno-parietal and the petrosal sinuses. The meningioma does not invade the brain, but compresses and displaces it, and may become imbedded in it. It may also develop outwards and invade the skull, appearing externally as a rounded boss on the top of the head. The auditory nerve tumour may be single, or may appear as part of a generalised neurofibromatosis, in which case it may be bilateral on the eighth nerve. It grows in the lateral recess, where it compresses and stretches the fifth, seventh and eighth nerves, and also compresses and displaces the cerebellum and gives rise to internal hydrocephalus.

Secondary carcinoma is probably more common than is generally realised. It is a frequent event in pulmonary cancer, and the presence of a secondary involvement of the brain may first bring the patient to notice. Indeed, in all adult cases presenting the signs and symptoms of intracranial tumour the possibility of carcinomatous metastasis should be explored, especially

in a patient who is losing weight. Secondary carcinoma gives rise to numerous deposits in the brain, of various sizes, and may also produce a fine infiltration of the pia-arachnoid, with or without macroscopic masses in the brain. When this "meningitis carcinomatosa" occurs alone its diagnosis may be difficult. Secondary growths may follow primary carcinoma of the breast, stomach, uterus, or prostate, as well as of the lung.

Cholesteatomata.—Sometimes called "mother of pearl" tumours, on account of their glistening appearance, are found in connection with the basal meninges. Their origin is uncertain. They are either of slow growth, or run a symptomless course. They consist of a greasy, greyish, friable and more or less laminated mass, made up of layers of a closely packed mosaic of flat polygonal cells. The tissue is necrotic, and contains no blood vessels.

Among the rarer tumours of the brain may be mentioned dermoid tumours, teratomata, chordomata, which arise from rests of the anterior end of the primitive notochord and are found below the base of the brain, lipomata, fibromata, neuromata, neuroblastomata, consisting actually of undifferentiated nerve cells, enchondromata, angiomata and psammomata.

Cysts.—Cysts of the following nature may occur—(1) Congenital interpeduncular or pituitary cysts, which arise from a pharyngeal rest in connection with the development of the pituitary gland; the resulting signs are those of pituitary insufficiency, together with those of pressure upon the optic chiasma. (2) Simple serous cysts, which are presumably the remains of soft tumours, which have become completely degenerated. (3) Tumours containing cysts, presumably on the way to the formation of the above. (4) Blood cysts, the rare results of hæmorrhage which has become arrested (5) Cysts which result from softening after embolism and thrombosis.. When occurring in the young, these cysts may lose every trace of their original origin, and form thin-walled cavities, containing colourless fluid, often extending from the ependyma to the pia mater, and involving the whole thickness of the pallium. They are termed "porencephaly." (6) Cystic distension of the ventricles from obstruction, which forms local or general hydrocephaly. These are met with in connection with tumours in any situation and result from adhesive meningitis, particularly syphilitic meningitis. (7) Dermoid cysts. (8) Parasitic cysts, of which the more common is the bladder worm of the tapeworm, *Tœnia solium*, which is called, on account of the thickness of its wall, cysticercus cellulosæ. They are usually multiple, and choose the region of the fourth ventricle as their site of predilection. They may be multiple in the basal meninges, and constitute a "cysticercus meningitis." It is usual for these cysts to shrink and to become calcified and obsolete in from 3 to 6 years. Less commonly, the hydatid of *Tœnia echinococcus* is found. It is usually single, may reach a large size and present the signs of a slowly growing tumour with eosinophilia.

Infectious granulomata.—Tuberculomata are more common in the young; but they may occur at any age. They very in size from that of a millet seed to that of a hen's egg, and are more often found in the posterior fossa of the skull than above the tentorium. When large, coagulation necrosis and caseation occur in the centre, and on section the tumour presents a dry yellowish crumbling or even diffluent centre, with a greyish-red peripheral

growing zone, where are located living tubercle bacilli and actively growing tubercles. The tuberculoma has an important aspect in connection with operation for extirpation. They are often situated favourably for extirpation, yet in every case where this operation has been performed the patient has succumbed to tuberculous meningitis, often after recovery from an apparently completely successful operation. Such a tumour recognised on decompression should be left severely alone.

Syphiloma.—This is not a common intracranial tumour. It grows most commonly from the meninges, and is therefore a surface lesion, though it may burrow deeply in the brain tissue. It is most commonly found above the tentorium. It is occasionally very hard in consistency, and tends in many cases to scar and become obsolete. It is sometimes impossible to distinguish this tumour from a tuberculoma without the aid of the microscope and the serum reaction.

Actinomycomata and tumours from streptothrix infection occur in very rare cases.

Symptoms.—The rates of growth of the different kinds of tumour vary widely. Some cases run their course from onset of symptoms to fatal termination within a few weeks, while in others there is evidence of gradual growth over a period of years. In the latter group it may be only in the final stage that the true nature of the illness becomes apparent, and only in retrospect that earlier symptoms assume their real significance. This perhaps is especially so in the case of those tumours which for months or years have manifested their presence only by generalised epileptiform fits. In yet other cases, an intracranial tumour may remain latent during life, being revealed unexpectedly at post-mortem examination.

Between these two extremes a great variety of symptom-complexes may be presented by an intracranial tumour. Thus, it may first show itself by producing signs of raised intracranial tension alone—that is, by general signs, or by signs of a gradually progressive local lesion alone—that is, by focal signs. Whichever of these two elements is initially lacking will probably appear later. A third manner in which a tumour may first signal its existence is—as has been mentioned—by the occurrence of generalised epileptiform fits in the absence of any other symptoms and signs. In this instance, also, general and focal signs will probably ultimately make their appearance. Again, a sudden onset of symptoms from hæmorrhage into a glioma, or from œdema of surrounding brain, may usher in the clinical course of a tumour within the skull.

The age of the patient is not without influence in determining the symptomatology and clinical course of a tumour. Thus, in childhood the early appearance of greatly raised intracranial tension—that is, of general symptoms, is the rule. This is mainly due to the fact that at this age the tumour is commonly in the fourth ventricle, and is thus favourably placed to produce internal hydrocephalus. In elderly persons, on the other hand, the picture of tumour is apt to be blurred, general signs are late in development, and focal signs are indistinct. Possibly the presence of a background of cerebral arterial degeneration and its associated cerebral change are responsible for this blurring of clinical outline. It may be supposed that the tumour does not write its mark upon a clean slate where there is arterial and cerebral degeneration already present.

General Manifestations.—These symptoms are the result of raising of the intracranial pressure, and accordingly fail when there is no considerable raising. Therefore they tend to be absent in all tumours of the brain stem, in infiltrating tumours of the centrum ovale, and also in advanced age and in the subjects of marked arterial disease. They consist in the following signs: Papillœdema, headache, vomiting, loss of vivacity and mental drowsiness, nasal irritation, giddiness, alteration of pulse-rate, of blood pressure, respiration, and general convulsion.

Papillœdema.—This is by far the most constantly present of all the general manifestations. Papillœdema appears to be a stasis œdema of the nerve-head owing to the increased intracranial pressure forcing the cerebro-spinal fluid into the meningeal sheath which invests the optic nerve, and into the perivascular spaces which accompany the central vessels of the nerve. The nerve sheath becomes distended, and venous stasis occurs. On ophthalmoscopic examination the earliest changes are increased redness of the disk, distension of the veins, loss of distinctness of the nasal margin of the disk, with disappearance of the physiological pit. As the process increases the whole margin of the disk becomes lost. It enlarges in area, and becomes visibly swollen and presents the appearance of a mole-hill as seen from above. The point of emergence of the vessels, at the centre of the disk, becomes buried by white exudation, which occurs also all over the disk, and taking a form determined by the radiating nerve fibrils, gives the disk the appearance of being striated in a radial fashion, like a chrysanthemum. A similar exudate may rupture the membrana limitans interna in little droplets at the macula, and coagulating as it comes in contact with the vitreous humour, produce the characteristic radially arranged macular figure of "macular fan," exactly similar to that seen in renal disease. The venous congestion of the retina leads to multiple hæmorrhages, which infiltrate along the radially arranged nerve fibres, and for this reason are flame-shaped. With the outpouring of much exudation, the disk becomes white. In the course of time the hæmorrhages become white flame-shaped scars, the whole disk contracts, the swelling disappears, and the disk becomes white, flat and atrophic, and distinguished only from that of primary optic atrophy by the scarred remains of the exudate at its edge, producing a fluffy outline like that of torn cotton-wool, along the vessels and at the centre. In the early stages of papillœdema, even though there be considerable swelling of the disk, vision may be little impaired. As the process increases however, in proportion to the degree of the swelling to the amount of the exudate, and to the length of time the papillœdema has lasted in a severe condition, vision becomes impaired, and blindness results. Peripheral constriction of the visual fields, large pupil and dimness of vision, are the signs that, if the papillœdema be not speedily relieved, blindness will certainly result. Perfect vision may be retained for a time, even with a high degree of papillœdema. So important is papillœdema in the diagnosis of tumour of the brain, that it is necessary to bear constantly in mind all other causes which may give rise to it.

Papillœdema may occur in certain general intracranial conditions other than tumour. In meningitis it occurs as a late sign, and rarely before the tenth day, and as so many cases of meningitis do not survive so long, it is chiefly met with in the more chronic forms, such as tuberculous meningitis,

and untreated cases of meningococcal meningitis. Abscess may also cause papillœdema; but it is by no means common in this condition.

Apart from intracranial disease papillœdema occurs in the following conditions: (1) Local conditions of the retina and optic nerves. In connection with tuberculoma of the retina in the neighbourhood of the disk, the most intense papillœdema may be found. Retrobulbar neuritis occurring close behind the disk may cause a similar condition, especially if it be of a syphilitic nature. In these conditions the papillœdema is often unilateral, but in any of them it may be bilateral. (2) Renal disease may give a retinal picture of intense papillœdema, macular figure and hæmorrhages, sometimes quite indistinguishable from that due to tumour. This is often seen in the small white kidney of young subjects, and sometimes in small red kidney, but there is no form of renal disease, even including tuberculous, amyloid and lardaceous kidney, in which papillœdema has not been observed. (3) Anæmic states of every kind sometimes give rise to papillœdema. As regards groups (2) and (3), it is essential to emphasise the facts that papillœdema, headache and vomiting may occur as a symptom-complex, both in renal disease and in anæmic states. (4) Septicæmic conditions, and especially those producing arthritis. Of these infective endocarditis is the most common; but it has occurred with every form of septicæmic arthritis, and even in cases of acute rheumatism. (5) Further, papillœdema has been noted in connection with tumours, and with compressions and fracture-dislocations of the cervical cord, and also with acute myelitis.

The retinal changes in diabetes are always, and those in renal disease often, distinguishable from papillœdema resulting from increased intracranial pressure. In diabetes the change is essentially a hæmorrhagic retinitis from degeneration of vessels, sometimes with waxy-looking exudation in circinate patches; and in renal disease it is often a general œdema of papilla and retina, with hæmorrhages and white patches far away from the disk. The papillœdema resulting from increased intracranial pressure is always bilateral, though it may appear in one eye before the other, unless there be local pressure upon one optic nerve, which always delays or prevents papillœdema appearing in that eye. Otherwise, an earlier commencement upon one side is of no localising value whatever.

Headache.—Although this symptom is a characteristic concomitant of raised intracranial pressure, it cannot be directly attributed to this, since a lumbar puncture which lowers this pressure may lead to increase of headache. It is probable that the pain arises from stimulation of sensory nerves in the walls of the cerebral arteries by changes in tension. The dura mater is probably not the sensitive structure responsible for headache in cases of intracranial tumour. After destruction of the fifth nerve by Gasserectomy, headache never again occurs upon that side. The sensation may vary from a mere feeling of fullness of the head to the most agonising pain. It is more often remittent than continuous, and may be absent for long periods together. It is rarely localised to any definite region, except when the growth actually involves the bone, or when pressure has caused local thinning of the bone, when local pain and tenderness on pressure may occur. Usually it is referred indefinitely to the frontal or to the occipital or to the vertical region. When occipital it may be associated with pain and stiffness of the neck, and head retraction. This is due to a general pressure effect, and does not indicate any

localisation. Headache may be entirely absent, even in the presence of severe papilloedema. It may precede the development of papilloedema, but more often it is later in its appearance.

Vomiting.—Only two-thirds of all cases of intracranial tumour present vomiting as a symptom. It rarely occurs in the absence of the two chief signs of increased intracranial pressure, papilloedema and headache. When the headaches are severe, it may be associated with much nausea, and the attacks are often referred to by the patient as "bilious attacks." Usually a result of increased pressure, it may be directly produced by lesions of the cerebellum, irritation of the vestibular nerve, and by the visual disorientation resulting from diplopia. As a symptom of intracranial tumour it hardly deserves the cardinal importance which has been assigned to it in most descriptions of this disease.

Loss of vivacity and mental drowsiness.—Even when intellectual capacity shows not the slightest impairment, there is from the first onset of symptoms a loss of vivacity, a slight heaviness and an absence of restlessness which is of value in diagnosis. It is almost unheard of for a tumour patient to suffer from insomnia. As the symptoms increase, so do heaviness and drowsiness, though a perfect but slow cerebration may persist until the latest stages of the disease.

Giddiness.—Though this is an inconstant sign, it is often met with, and it may be due to vestibular irritation, when it amounts to an actual vertigo, or it may be a sense of general unsteadiness. It is met with most often in subtentorial tumours, but may be quite a general symptom when very high pressure exists.

Convulsions.—As has been mentioned, generalised epileptiform fits, indistinguishable from those of idiopathic epilepsy, may usher in the clinical course of tumour, and may be present for long periods as the sole indication of tumour. The onset of such fits in an apparently healthy middle-aged individual, never before subject to them, should always give rise to the suspicion of tumour of the brain. When later on in the course of the illness general and focal signs of tumour appear, the convulsions may not increase in frequency, and it is not possible to regard them as a sign of raised intracranial tension. They more probably arise from local circulatory disturbances. Beyond saying that they are most frequently found in tumours of the cerebral hemispheres, no localising value can be attributed to them.

Blood-pressure, pulse-rate and respiration.—There is a slight compensatory increase of the blood-pressure for every raising of the intracranial pressure, so that the cerebral circulation may be kept going. The failure of such compensation is often the cause of the sudden death which occurs in tumour cases. The pulse-rate is in the inverse ratio of the blood pressure, and, therefore, of the intracranial pressure, and the pulse is slower than normal, where pressure is above normal. Respiration tends to be slow, and when the physiological condition of the intracranial contents is much disturbed, it tends to become irregular, grouped, and may show the wax and wane of movements which bears the name of Cheyne-Stokes respiration.

Focal Signs.—These have been fully described in the section upon the localisation of lesions of the brain. In connection with localisation, however, it is important to recognise certain possible sources of fallacy in making a diagnosis. Blindness from papilloedema prevents any localisation by means

of the visual functions. Papillœdema usually causes at one stage great peripheral constriction of the visual fields which might be attributed to a bilateral lesion of the cuneus, and it may cause altitudinal hemianopia, *i.e.* blindness of the upper half of both fields, by sagging of the exudation into the lower part of the retina. Jacksonian epilepsy may occur in long-standing cases without any relation to the position of the tumour.

Paralyses of cranial nerves may be serious pitfalls. They are of value in localisation when occurring early, and in association with alternate hemiplegias, and paralyses of the eighth, ninth, tenth, eleventh and twelfth are always of sure localising value. Paralysis of the sixth cranial nerve, perhaps, should always be disregarded as a localising sign for the following reasons: When the intracranial pressure increases from the presence of a growth, the first effect is that any superfluous cerebro-spinal fluid, of which there is normally very little, is expelled from the skull. Later, with further increasing pressure, since the only escape from the rigid skull is by its only opening, the foramen magnum, the medulla and cerebellum are pushed backwards towards the foramen magnum and come to fill up this aperture as with a cork. In all long-standing cases of increased pressure, the cerebellum will be found on autopsy, and especially when hardened *in situ*, to be deeply marked by the edge of the foramen, part of the cerebellum and medulla actually occupying the spinal canal. Corking up of the foramen magnum in this way offers a marked impediment to the flow of cerebro-spinal fluid, and is a most important factor in the production of hydrocephalus, secondary to tumour. Bearing this in mind the immediately fatal effects which have followed lumbar puncture in long standing cases of high intracranial pressure will be at once understood and for ever avoided. This shifting backwards of the medulla and cerebellum will cause stretching of those cranial nerves attached to the medulla, in proportion as they are directed antero-posteriorly, and take a straight course between their attachments to the dura mater and their origin from the medulla, and of these the sixth nerves will be most affected, and afterwards the third, seventh and fifth in that order. These nerves will not only be stretched, but are subject to the increased pressure also, and they may accordingly cease function simply as the result of the increased pressure. Special mention should be made of tumours of the pituitary body and stalk. In the previous section the localising signs of lesions in the region of the optic chiasma have been enumerated, but since the different varieties of tumour in this locality have their own typical symptom-complexes, the following table may be useful in differentiating them.

Diagnosis.—The differential diagnosis of intracranial tumour has to be made—(1) from other conditions causing papillœdema, (2) from other conditions causing headache, and (3) from other local lesions causing local signs within the brain. Renal disease, conditions of severe anæmia, encephalitis and meningitis may on occasion give rise to a combination of all three of these, very easily confused with the papillœdema, headache and vomiting of cerebral tumour.

Hydrocephalus is only distinguishable from intracranial tumour by the enlargement of the head which takes place in young subjects, but when the skull is rigidly closed, the symptoms are identical with those of a non-localisable tumour.

DIFFERENTIAL DIAGNOSIS OF TUMOURS IN THE PITUITARY REGION (WALSHE)

	Adenoma.			Pituitary Stalk Tumour.	Meningioma.	Glioma of Optic Chiasma.
	Chromophobe.	Chromophile.	Mixed Cel			(rare)
Age Incidence.	From adolescence onwards.			From 10 years to early adult life.	From 30 years onwards.	Usually in childhood.
Fundus Oculi.	Primary optic atrophy.			Papillœdema in children; usually primary optic atrophy in adults.	Primary optic atrophy.	Primary optic atrophy.
Visual Fields.	Bitemporal hemianopia.			Bitemporal hemianopia.	Bitemporal hemianopia.	Bitemporal hemianopia, proceeding to early blindness.
				ccasionally homonymous hemianopia.		
Pressure Symptoms.	Absent, or late.			Early and severe, except in adults.	Absent, or late.	Absent, or late.
Glandular Symptoms.	pitu	Hyperpituit or Hipopituit.		Hypopituitarism.	Nil.	Nil.
Situation.	Sellar.			Suprasellar.	Suprasellar.	Suprasellar.
Radiological.	General enlargement and deepening of sella.			Shadows above and in sella. Sella shallow, and with uneven floor.	Commonly no change.	Enlargement of sella forwards beneath ant. clinoid pro-

Intracranial abscess is not often confused with tumour when it has an obvious cause in the vicinity of the brain, from bone disease, or an embolic cause at a distance, such as ulceration of the lung. It is an acute disease and rarely develops an increasing papillœdema. Accuracy in the early diagnosis of tumour cases depends upon the pertinacity with which every case of headache, every case of "fits" and indeed every case which shows any nervous symptom whatsoever, is systematically examined for signs of organic disease, and importantly upon that skill and practice with the ophthalmoscope which is so easily acquired with patience and a little determination. The presence of a tumour having been determined, the necessity is to localise it.

Above the tentorium tumours may be difficult or impossible to localise. So far as decompression is concerned the least indication, however slight, should determine the position of decompression. The external surface of the head should be carefully examined, and especially after it has been shaved, for now and then important indications of the position of a tumour may be afforded, for tumours may grow from the bone, or when internal may cause local absorption of the bone, and bulging of the skull. X-Ray examination should not be omitted, though it does not often afford important information. Tapping of the lateral ventricles, with analysis of their content as to protein concentration, and the introduction of air into the ventricles, with subsequent radiogram, and especially the injection of a thorium salt into the internal carotid artery in the neck, with immediate radio-instantogram, which shows the cerebral arteries and points out any region evascularised by local pressure, are all methods of value. Ventriculography is dangerous, and should only be performed when immediate decompression is practicable if found to be necessary.

The determination of the nature of a growth may be difficult or impossible, and length of clinical history may be a fallacious guide, since a slow-growing tumour may be long latent, and sudden in its production of symptoms. It may be recalled, however, that in childhood medulloblastoma is the most frequently occurring of all intracranial tumours, and that it has a very characteristic picture: headache, vomiting, papillœdema, bilateral external rectus palsy and unsteadiness of gait. Again, a well-marked picture of a progressive frontal lobe lesion generally indicates the presence of a glioma, and the same may be said of the symptom-complex of a temporo-sphenoidal lobe lesion. But there can rarely be any certainty as to the pathological nature of a tumour, even when it is a secondary carcinoma, since the primary growth may be latent and unsuspected.

It is important to remember that the finding of a positive Wassermann reaction in the serum of a patient presenting signs of intracranial tumour does not necessarily—or probably—indicate that the growth is a gumma. Both syphilis and intracranial tumour are common diseases, and their occasional association is less rare than cerebral gumma.

Course and Prognosis.—An intracranial tumour usually causes increasing symptoms, which progress with exacerbations and remissions, until papillœdema ends in blindness, and until the pathological intracranial condition becomes incompatible with even vegetative existence. At any time death may occur from vascular lesions, acute œdema or sudden raising of pressure. Tumours occasionally become obsolete—thus a tuberculoma may become scarred and calcified, and a glioma may become calcified or cystic; but this result is too rare for consideration within the grounds of practical perspective. The average duration rarely exceeds a year after the diagnosis has become possible.

Treatment.—The natural termination of a case of intracranial tumour is death, and the ideal of treatment must be the successful removal of the growth. Failing this, and it is frequently impossible, all that can be hoped for is the relief of headache and sickness, and delaying of blindness.

In respect of the radical, surgical treatment of tumours, it will be remembered that probably more than half (if we include glioma and secondary carcinoma) are in the brain substance, and can be extirpated only by

mutilating operations, which may leave in their wake grave physical and mental disabilities. The success of such an extirpation cannot, therefore, be adequately expressed in terms of "survival period"—as it is not infrequently assessed—but rather in terms of the kind of existence which is prolonged. This may be purely vegetative, and distressing to the patient and his relatives alike. We may say, then, that the treatment of the gliomas is, and must of necessity always remain, the forlorn hope of surgery. On the other hand, signal successes have been obtained in the case of the meningioma, the auditory nerve tumour, the pituitary adenoma, and a few cystic astrocytomas (particularly of the cerebellum).

It will be seen, therefore, how important it is to be able with some precision to determine the type of tumour present in any given case. When this is not possible, an exploratory operation is often justified. But it would be a mistake to suppose that surgical intervention is a matter of routine in every case in which intracranial tumour is diagnosed. Each case must be considered on its merits.

Failing the possibility of a successful removal, the palliative operation of decompression may be needed to relieve the symptoms caused by raised intracranial tension. This consists in the free removal of bone, and the incising of the dura mater, over the region of the tumour when this is known, or, failing localisation, in the right subtemporal region. For brain-stem tumours, decompression is not only useless, but also dangerous.

Relief of pressure by dehydration.—There are circumstances in which it may be desirable and necessary to reduce the brain volume and the intracranial pressure; for example, to relieve pressure headache, to avert impending coma or death, to render the patient capable of co-operating in his examination and thus facilitating a localising diagnosis, and finally to make surgical procedures more easy. Weed and M'Kibben have shown that the foregoing may be done by administering hypertonic solutions. In the ordinary case, the rectal injection of from 2 to 3 ounces of magnesium sulphate dissolved in 8 ounces of water may be tried. But for a very rapid effect, intravenous injection of from 50 to 75 c.c. of a 50 per cent. solution of dextrose, or of a 15 per cent. solution of sodium chloride, is effective. Pain and vomiting may be relieved with the various analgesics of the coal-tar series. When intracranial pressure becomes so high as to cause agonising pain, pulselessness and impending death, morphine in full doses will always relieve, and it is not dangerous. Convulsions should be combated with administration of bromides.

HYDROCEPHALUS

Definition.—The term "hydrocephalus" denotes a uniform distension of the ventricular system of the brain by the accumulation of cerebro-spinal fluid within it; and this distension is associated, sooner or later, with an expansion of the cranial bones and enlargement of the skull.

Hydrocephalus was formerly divided into acute and chronic, acute being applied to the condition of tuberculous meningitis. But since any marked degree of ventricular distension is unusual in that affection, and enlargement of the head very rarely occurs, this term has fallen out of use. In the majority of cases in which general atrophy of the cerebral tissues

occurs, fluid accumulates both in the ventricles and in the sub-arachnoid space; but such compensatory enlargement is not to be regarded as, in any sense, of the same nature as true hydrocephalus. Such accumulation of fluid is found in cases of cerebral diplegia and general paralysis of the insane in children, and it also occurs in the brains of old people. It is merely the result of wasting and shrinkage of the brain-tissue, and the accumulation of fluid takes place in order to fill up the space which is vacated within the rigid skull.

The enlargement of the head, which is not uncommonly found in rickets, has no connection with hydrocephalus. It is probably the result of malnutrition of cranial bones, which grow irregularly, and, being unduly soft, yield somewhat to the intracranial pressure. In rare cases of moderate degree, ventricular distension has been met with, but the enlargement of the head is never progressive, and the symptoms of hydrocephalus are absent.

According to their clinical aspect, cases of hydrocephalus may be placed in one of three groups—(1) congenital hydrocephalus, in which the enlargement of the head is present at the time of birth; (2) acquired primary hydrocephalus, which may appear at any period of life; and (3) secondary hydrocephalus. Under the name of secondary hydrocephalus may be grouped together all cases in which there is obstruction in the usual path by which the cerebro-spinal fluid leaves the ventricular cavities, or to the venous outflow from the choroid plexuses. But it is by no means clear that such obstruction is the sole or even the important agent in producing the ventricular distension.

Ætiology.—Hereditary influences are of importance in the causation of congenital hydrocephalus. This disease frequently affects several children of the same parents, and it may even appear as a striking family disease, affecting members of several generations of the same stock. Spina bifida, meningocele and hydromyelia are of frequent occurrence in association with this disease, and arrested and irregular development of the brain stem and cerebellum are the rule. Among other bodily deformities not infrequently associated with congenital hydrocephalus, may be mentioned harelip, cleft palate, talipes, rectal and testicular ectopia and imperforate anus. In a few cases definitely syphilitic lesions of the ependyma in the region of the brain stem have been found. The causation of primary hydrocephalus occurring after the time of birth is often obscure. The majority of the cases occur in childhood, yet no period of life seems to be exempt. In children, acute infective diseases, and especially gastro-intestinal infections, may occur as antecedents of hydrocephalus. In adults, syphilis stands in important relation in certain cases, some of which have been examined pathologically.

The causes of secondary hydrocephalus are, first, the sclerosing forms of meningitis, especially posterior basic and epidemic meningitis, very rarely tubercular; secondly, intracranial neoplasms encroaching upon the ventricular system, especially tumours of the brain stem and subtentorial region; thirdly, adhesive phlebitis of the cerebral blood-sinuses.

Pathology.—Hydrocephalus is directly due to an excess of cerebro-spinal fluid present within the ventricular system of the brain. The fluid is normally secreted by the choroid plexuses of the ventricles, which overflow into the subarachnoid space through the foramina of Luschka and Majendie in the roof of the fourth ventricle. It then fills the basal cisterns

and passing forwards between the tentorium cerebelli and the brain-stem flows up over the cerebral hemispheres. It leaves the subarachnoid space through the arachnoid villi, which pierce the walls of the dural venous sinuses and discharge their contents into the venous blood. Some of the fluid passes downwards into the spinal subarachnoid space, but its absorption is probably wholly within the skull by the channels mentioned. Obstruction to the absorption of the cerebrospinal fluid into the blood stream is the essential factor. This obstruction may arise at various points. There may be congenital atresia of the aqueduct of Sylvius which traverses the brain stem and joins the third and fourth ventricles. It may arise from occlusion of the foramina of Luschka and Majendie by adhesions resulting from an old acute lepto-meningitis. It will be apparent from these considerations that congenital hydrocephalus must be due either to atresia of the aqueduct, or to adhesions blocking the exit of the fluid from the ventricular system, these adhesions being the result of some pre-natal inflammatory process. Acquired hydrocephalus may follow an acute lepto-meningitis which has been productive of adhesions at either, or both, of the situations named above. It may also follow some other mode of blocking of the exits from the ventricular system. Such blocking is commonly produced by an intracranial tumour. The distension of the ventricles which necessarily ensues upon defective absorption of cerebro-spinal fluid from any of these causes is naturally maximal in the infant or child in whom the state of the skull vault allows of expansion of the intracranial space and of an enormous degree of stretching of the cerebral walls of the ventricles, especially of the lateral ventricles.

The quantity of fluid which is found in the ventricles after death varies greatly, a usual quantity being from 15 to 20 ounces. In long-standing cases with great cranial enlargement, very large quantities have been met with. The characters of the fluid do not differ greatly from those of normal cerebro-spinal fluid. Its density varies from 1008 to 1010. It is clear, colourless or slightly yellowish, and the reaction is alkaline. It contains a very small quantity of albumin and a comparatively large quantity of alkaline chlorides.

The dilatation of the lateral ventricles is always more extensive than that of the third ventricle, and is usually symmetrical upon the two sides, and it affects the body of the ventricle more than the cornua, so that the central cortex is the most thinned. The foramina of Monro are greatly enlarged and the anterior pillars wasted.

The convolutions are flattened, and the sulci indistinct. The thickness of the cerebral substance is much reduced. In advanced cases, the cerebral hemispheres have the appearance of a thin-walled sac, which collapses entirely when the contained fluid is allowed to escape. In a few cases, the aqueduct has been found closed, as if by antecedent adhesive ependymitis.

Symptoms.—The clinical manifestations of hydrocephalus fall into two groups, which result, respectively, from the effects of the abnormal intracranial pressure, first upon the brain-case, and secondly upon the nervous structures. In the congenital form, the enlargement of the head is the first noticeable feature; and this is true also of some cases of acquired hydrocephalus in young children. In most cases of acquired hydrocephalus, on the other hand, the nervous symptoms are first in evidence—namely, per-

sistent headache, vomiting, mental impairment, convulsions and sometimes papilloedema. The evidence of cranial enlargement may succeed these symptoms, and the older the subject, and consequently the more resistant the cranial walls, the more severe are the nervous symptoms, and the later is the cranial enlargement in appearing. In some cases of congenital hydrocephalus, enlargement of the head takes place during intra-uterine life, and it may be so great as to make delivery impossible without destruction of the head. More frequently, the cranial enlargement, not noted at the time of birth, becomes evident during the first few weeks of life.

Enlargement of the head is the most striking feature of hydrocephalus in children. The increase usually affects all the diameters of the cranial cavity, and is most marked on the vertex and least at the base. Trousseau compared the opening out of the cranial bones, which occurs as the head enlarges, to falling back of the petals of an opening flower. The forehead is large, rounded, and projects forwards; the temporal fossæ are obliterated, and the parietal eminences carried backwards. The vertex is often somewhat flattened, as also may be the occipital region. The direction of the external auditory meatus alters with the increasing size of the head; normally directed obliquely forwards, it comes to look directly inwards, or even obliquely backwards in severe cases. The head is frequently asymmetrical. In young children the sutures may be widely open, and then there is marked bulging along those lines and at the fontanelles. The skull may attain enormous dimensions, and many examples are recorded in which the circumference has been from 60 to 90 cm. The face is characteristically triangular, contrasting markedly with the forehead. Wasting of the facial subcutaneous tissues and retarded development of the maxilla and mandible often render this contrast still more striking. Bulging of the orbital plates of the frontal bone presses down the eyeballs, so that the pupils become more or less covered by the lower lids, and a band of the sclerotic may be visible between the iris and the upper lid. The hydrocephalic child often uses his hands to depress the cheeks, and so draw down the lower lids out of the position in which they impair the line of vision. The hair of the head becomes scanty, the subcutaneous veins of the scalp are often greatly developed and distended, and sometimes a vortex of distended veins radiates from the region of the anterior fontanelle. The general nutrition is poor, and bodily development retarded, in proportion to the severity of the effect of the intracranial pressure upon the nervous system. Auscultation may reveal a cephalic bruit, but this is neither a characteristic nor a constant sign in hydrocephalus, for it is frequently met with in rickety children, and may be present in a normal subject.

The nervous disorders which appear during the course of hydrocephalus are both variable and inconstant, and acute symptoms are of rare occurrence if the disease appears at an age at which the skull is still yielding. On the other hand, if the ventricular distension commences when the growth and ossification of the skull are complete, the nervous symptoms which arise are very severe, and resemble closely the general effects of intracranial growths. In secondary hydrocephalus, the symptoms due to this condition emerge from those of the preceding meningitis or sinus thrombosis, or are blended with those of the coexisting intracranial growth.

In children, the nervous symptoms of hydrocephalus, whether it be congenital or acquired, may be summed up in the following list, the symptoms

being frequent in the order in which they are enumerated; convulsion, mental failure, spastic paralysis of the limbs, headache, optic atrophy, nystagmus, vomiting, papillœdema. There is no constancy in the occurrence of these symptoms. Convulsion may not occur at all, and mental acuity may be unimpaired. Spastic weakness occurs in less than one-half of the cases, whilst optic atrophy is met with still more rarely, and papillœdema is distinctly unusual.

Convulsion.—While it is to be borne in mind that the whole course of hydrocephalus in children may run without the occurrence of convulsion, yet in the majority of cases this symptom is conspicuous. In some of the post-natal cases the symptoms of cerebral disorder are ushered in by convulsion, and it is probable that such convulsions are the immediate expressions of the morbid process, of which the primary hydrocephalus is the final result. The convulsions which recur at intervals throughout the course of the majority of cases of hydrocephalus result from a condition of functional instability of the cerebral cortex, which long-continued increased intracranial pressure brings about. The convulsions are usually general, with loss of consciousness.

All degrees of mental reduction occur, from the least noticeable to complete idiocy. The more severe forms of mental impairment are met with in congenital cases, and especially when cerebral agenesia, porencephaly and teratological defects are associated. The psychical reduction is less prominent the greater the age at which the symptoms commence, and, as a rule, the intelligence is far greater than the severity of symptoms (cranial enlargement, paresis, etc.) might lead one to expect. Cerebration is usually slow and the disposition placid, and periods of somnolence are of common occurrence.

The effect of long-continued ventricular distension in many cases is to cause degeneration of the pyramidal system, and, according to its degree, the latter entails bilateral spastic paralysis with contracture. The first signs of the onset of this event are exaggeration of the deep reflexes, and the change in type of the plantar reflexes from the flexor to the extensor response. The lower extremities are affected earlier and to a greater extent than are the upper, and at one period of the disease a case may present the picture of cerebral paraplegic rigidity comparable with that of Little's disease. The upper extremities are affected later. The paresis of the limbs is almost always symmetrical and equal upon the two sides. Sensibility is generally normal.

Vision is interfered with in a considerable proportion of the cases. The enlargement of the infundibular portion of the third ventricle, by pressure upon the inner borders of the converging optic tracts, may cause bitemporal hemianopia with atrophy of the nasal portions of both optic disks, this condition subsequently progressing to complete blindness and complete optic atrophy. More often the increased intracranial pressure causes atrophy of the optic tracts and secondary atrophy of the optic disks.

In other cases, optic atrophy is the result of papillœdema. In late childhood and in adult life papillœdema is the rule, and optic atrophy seems always to be consecutive to this. Strabismus is commonly present in congenital cases, and it is most frequently convergent. Nystagmus is met with in the subjects of hydrocephalus who are blind from optic atrophy, and it is of

frequent occurrence in long-standing cases in which spastic paresis is well-marked.

Headache is often complained of, and especially during the early days of illness in acquired cases, but this symptom never dominates the clinical picture in children, and is never so severe and persistent as that arising from the presence of an intracranial growth. Cerebral vomiting is of comparatively rare occurrence.

When one considers the profound anatomical alterations which take place in the advanced stages of the disease, the occurrence in some cases of unusual symptoms indicative of interference with the functions of the cerebellum, brain stem and cranial nerves is easily explicable. Unilateral or bilateral ataxy, vertigo, deafness, anosmia and paralysis of cranial nerves, are the most important of such unusual symptoms.

The signs of failure of the nervous system as a whole usher in the fatal result in severe cases. For some days or perhaps weeks before death, bebetude may become profound; spastic paresis gives place to flaccid paralysis with muscular wasting, the deep reflexes disappear, and the sphincter mechanism loses its control and subsequently its tone.

Hydrocephalus which commences in late childhood or in adult life presents an aspect widely different from that just described. At these periods of life, the bones of the skull are firm and resistant, and the sutures resist for a long time before yielding to the increased intracranial pressure. The general symptoms are acute, and the course of the disease is often rapid to a fatal termination. There is usually no enlargement of the head to aid the diagnosis, and the symptoms—headache, vomiting and papilloedema—resemble those of a non-localisable intracranial growth.

The headache is severe and usually paroxysmal, and it may be so intense as to cause sudden death, while, not infrequently, the sufferer loses all control during the paroxysms. Speaking generally, the headache is of much greater severity in adult hydrocephalus than in intracranial growth. Similarly, vomiting is apt to be more severe and persistent than that associated with cerebral growth. In many of the cases, a fatal result occurs before enlargement of the head, and before cerebral degeneration has produced further signs of spastic paresis than an increase of the deep reflexes, foot clonus and the change of the plantar reflexes to the extensor type. General convulsions and attacks of coma are not rare.

Diagnosis.—Where enlargement of the head is manifest the diagnosis of the disease presents no difficulties. The large head of rickets is easily distinguishable from hydrocephalus by its different conformation, by the association of the other signs of rickets, by the absence of nervous symptoms, by its non-progressive nature, and by the results of anti-rachitic treatment. The distinction between the primary and the secondary forms of hydrocephalus in children should present no difficulty, if a correct history of the early symptoms can be obtained. The initial manifestations in the primary form are slight, and cannot be confused with those of meningitis or of sinus thrombosis. Intracranial growths which cause early and marked hydrocephalus are situated in some part of the brain-stem from the third ventricle to the medulla, and growth in such a position must of necessity produce such early pathognomonic localising signs as to leave no excuse for erroneous diagnosis, save imperfect observation.

In adults the absence of cranial enlargement in most of the cases make it impossible to separate the malady with certainty from intracranial growths It must be borne in mind, however, that headache, vomiting and papill-œdema of rapid progress are not necessarily signs of intracranial growth, but may be the symptoms of primary hydrocephalus.

Prognosis.—This depends upon the cause of the hydrocephalus, upon the degree of severity of the symptoms, and upon whether it is progressive or not. In all severe and progressive cases the prognosis is hopeless, and the same is true of hydrocephalus secondary to inoperable neoplasm. In some of the slighter cases, both of the congenital and of the acquired form, the process becomes arrested, and the patient may attain to adult life with the possession of all his faculties. In cases in which the disease becomes stationary, the prognosis as regards mental capacity and the continuance of recurring convulsion has to be considered. If the mental capacity at the time of arrest is fair, it is not likely to deteriorate further, unless epilepsy is established. When mental reduction is marked at the time of arrest, a great degree of improvement cannot be reasonably expected.

Treatment.—While some cases of hydrocephalus cease to progress, and the symptoms disappear permanently under medical treatment, a like result has occurred in cases in which no treatment has been applied.

The importance of syphilis in the ætiology of hydrocephalus suggests the employment of anti-syphilitic treatment.

The results of surgical interference for the relief of pressure and to attempt the re-establishment of a way out for the cerebro-spinal fluid have been, up to the present, so unfavourable, that many writers and authorities consider such measures unjustifiable. It must be borne in mind, however, that in severe and progressive cases one is dealing with a necessarily fatal malady, and a few encouraging results have been published, which appear to justify further investigation. Paracentesis of the ventricle is both useless and dangerous, for when relief follows the operation it is only temporary, and where cerebral tension is very high an immediately fatal result may supervene. Repeated lumbar puncture is advisable in the earlier days; but this is only possible in cases in which the theca is in free communication with the ventricular space.

ENCEPHALITIS

Acute inflammation of the brain occurs under widely different clinical associations. It may occur as a primary disease or as a complication of known infective processes, affecting the system locally, generally, or as an associated event in diseases of the meninges. As a primary condition it is met with in the form of lethargic encephalitis. It is the constant result of trauma to the skull, if this be sufficiently severe. It is found as the result of infection of the brain with pyogenic organisms, either from local sources in the neighbourhood of the brain (septic bone disease), or from pyæmia, and may be then either suppurative (brain abscess) or non-suppurative. Infections by many of the specific fevers may cause it, and especially measles and scarlet fever. Acute encephalitis may occur in rare cases as the sole manifestation of cerebral syphilis. In all forms of meningitis there is some degree of extension of the inflammation into the brain tissue, and this

assumes an important degree in tuberculous meningitis, and sometimes in epidemic meningitis. The symptoms common to all forms of encephalitis are the general symptoms of severe intracranial disease—headache, somnolence, coma, irritability, convulsions, delirium and vomiting; and, in addition, local symptoms of irritation and paralysis, which are determined by the position and extent of the lesions.

1. SUPPURATIVE ENCEPHALITIS

Synonym.—Intracranial abscess.

Ætiology.—Suppuration within the brain substance is never primary, but the result of extension of infection from neighbouring tissues or by the blood stream from foci of infection in distant organs. In rare cases, the focus of original infection is undiscoverable.

The following are the important causal factors:

1. *Trauma.*—In the case of penetrating wounds the missile may be the source of the infection. Lacerated wound with fracture may allow of infection from the surface or from the middle ear, nose or pharynx. In these cases, meningitis often occurs in addition to abscess. Though not traumatic in a strict sense, any local lesion of the brain may become a locus resistentiæ minoris for the settling down of suppurative organisms derived from the blood stream, and in this way abscess has followed upon vascular lesions and the lesions of primary encephalitis.

2. *Extension from infected regions* in the immediate vicinity. The important cause of infection is any form of infective disease in the bones or soft tissues of the skull, calvarium and surrounding regions. Caries of the petrous bone from middle ear disease is the most common cause, while septic conditions of the nasal cavities and their accessory sinuses, or of any of the bones of the skull, suppuration of the scalp, orbital cellulitis and carbuncle of the neck are other causes. The exact manner of advent of the infection into the brain substance may differ in different cases. It may be by a septic thrombosis of a vein communicating between the infected region and the brain, or by extension along lymphatics similarly communicating, or by direct extension, as when the temporal lobe becomes adherent to the tegmen tympani, or it may be trans-meningeal by the direct transference of organisms across the meningeal space, without general meningitis occurring. That this latter mode of infection is a common one is suggested by the facts, that when the primary disease affects the upper surface of the petrous bone, the abscess is in the temporal lobe, and when the posterior aspect of the temporal bone is affected the abscess is in the cerebellum; and, most importantly, in all these cases of abscess from extension, the cerebro-spinal fluid shows the presence of polymorphonuclear leucocytes, thus showing that the meninges have been infected, although no symptoms of meningitis arise.

3. *Pyæmic states.*—Abscess of the brain does not often occur in symptomatic pyæmia. It may occur in infective endocarditis, and then multiple abscesses may be found. Sometimes in this condition multiple small spots of encephalitis, containing many polymorphonuclear cells but not definite abscesses, are met with. Much more commonly, abscess results from a single septic embolus from chronic pulmonary infection, such as bronchiectasis,

empyema and lung abscess. In rare cases metastatic abscess may arise from bone disease, liver abscess and in the course of specific fevers. The micro-organisms responsible for the infection are usually streptococcus, pneumococcus and staphylococcus, and often the infection is mixed. *B. coli* is sometimes found, and in rare cases streptothrix and oidium albicans.

Pathology.—The abscesses which result from local disease of the skull bones and surrounding tissues may be extradural, subdural or encephalic: in the first two cases they are invariably situated in the immediate vicinity of the antecedent seat of infection. The extradural abscess may reach a very considerable size and may burst externally, or into the meninges or into a blood sinus. The subdural abscess is confined in meningeal adhesions between the dura mater and pia mater. The contiguous surface of the brain is generally softened and has often disappeared, the abscess cavity extending deeply into the brain substance. This variety rarely has any capsule on the cerebral side. Encephalic abscess commences generally in the subsulcine white matter of the temporal lobe, and lateral lobe of the cerebellum. In one-half of all cases the abscess is in the temporal lobe, and in one-third in the lateral lobe of the cerebellum. The remainder are divided between the parietal lobe, the pons Varolii and the frontal lobe, in order of diminishing frequency. The size of the abscess varies up to that of a hen's egg. A recently formed abscess is irregular in shape with ill-defined limits, but in about 7 days it shows a definite capsule which may rapidly become of considerable thickness. The interior of the abscess cavity is usually of a greyish-green colour, and the pus is greenish and often fetid. The surrounding brain tissue is always œdematous and often softened. Rupture occurs in about one-sixth of all cases that are not afforded operative interference, and the rupture takes place most commonly into the ventricle and less frequently into the arachnoid space.

Symptoms.—An encephalic abscess has its origin in inflammation, and constitutes, when developed, a foreign body within the skull. Death may result from the effects of continually increasing intracranial pressure and wide interference with cerebral function, or from spread of the infection from the abscess. The symptoms may be grouped in four classes—(1) those of local suppuration; (2) those due to increased intracranial pressure; (3) localising signs dependent upon the position of the abscess; and (4) those of terminal extension of the infective process.

In extradural and subdural cases, the symptoms are generally acute and the course is rapid; the signs of pressure are severe, whilst localising signs are rare and a state of latency is not observed. In the majority of encephalic abscesses, on the contrary, the signs of initial suppuration are slight and are apt to be swamped by the symptoms of the preceding disease, otitis media, empyema, infective endocarditis, etc., and for this reason may be easily overlooked. A latent period in which symptoms are insignificant or completely absent may follow, and last for weeks or months. In the end, the latent period is broken, either by an acute outburst of symptoms, the result of extending infection, or the signs of progressive intracranial tumour arise.

The general symptoms which are likely to appear when a brain abscess is developing or emerging from a latent condition are pyrexia, which may be associated with rigor, headache, vomiting, irritability, vertigo, drowsiness deepening into coma, slowing of the pulse, respiratory and cardiac irregu-

larity, convulsions rarely, and papillœdema as a late sign. In addition, there is a leucocytosis of the polymorphonuclear variety in the blood, and a small number of polymorphonuclear leucocytes in the cerebro-spinal fluid in those cases arising by extension from disease of the cranial bones, but not in metastatic abscesses. The general symptoms vary much in their intensity and in the individual incidence of each of them, and in metastatic abscesses they may be almost absent, the local signs alone giving the indication that a cerebral lesion is present. Headache is rarely absent, and may be intense with spreading abscess. Vomiting is also an almost constant sign. Drowsiness is one of the most valuable of all the indications when any cause for the occurrence of cerebral abscess is present. Slowing of the pulse is also an important indication of a rising intracranial pressure. Papillœdema occurs late, and is often not present in acute abscesses at the time when diagnosis is all-important from a surgical point of view. It rarely occurs until an abscess has been present for a week, and is generally of low grade. With half-latent chronic abscesses, and with metastatic abscesses which attain a large size, it may be intense.

Local signs.—Generally speaking, the more recent and acute the abscess is the less definite are the local signs. In more chronic abscess, and in metastatic abscess, the local signs are usually more distinct. When there is a local cause for the abscess this constitutes an important localising sign, since abscess forms almost always in the immediate vicinity of site of infection. Thus rhinogenic abscesses are situated in the frontal region, and otitic abscesses are almost invariably situated either in the temporal lobe or in the lateral lobe of the cerebellum of the same side as the ear disease.

Metastatic brain abscesses may be situated anywhere, but they are more common in the region of distribution of the Sylvian artery, and in my experience have been more common in the posterior part of this supply—that is, in the parietal and occipital lobes. Metastatic abscess is sometimes preceded by definite indications of the embolism which gives rise to the abscess, such as local convulsion, local transient weakness or loss of consciousness, and such an event may precede the signs of abscess by many weeks. The local signs of lesion in the various regions of the brain are described in the section under that heading. Local diagnosis is often difficult owing to the condition of somnolence preventing the possibility of accurate examination. In these circumstances such slight signs as the absence of the abdominal reflex on one side, the presence of an extensor response in the plantar reflex of one side, or any aphasic signs, are important indications of temporal lesions; and unilateral hypotonia and nystagmus and attitudes, of cerebellar lesions. The initial signs and symptoms of encephalic abscess may lessen and disappear, and the abscess is said to become latent. The latency may be complete, or it may be broken by occasional headaches and transitory symptoms indicative of intracranial mischief. Much more commonly the abscess grows, and death occurs invariably in the absence of surgical interference, either from increasing intracranial pressure or from the rupture of the abscess, either into the ventricle, or on to the surface, with the production of general meningitis.

Diagnosis.—In those cases where there is no local cause for the formation of an intracranial abscess by direct extension, and no distant cause known or discoverable for the formation of a metastatic abscess, diagnosis is difficult,

and the distinction of an abscess from a tumour can hardly be made with certainty. The presence of pyrexia and of a polymorphonuclear leucocytosis in the blood may suggest the diagnosis in some cases. Where, however, the common antecedent causes of abscess exist in the form of ear disease, etc., or suppurative chronic lung disease, the diagnosis is relatively simple. For example, the advent of local or general intracranial signs in a case of chronic bronchiectasis from the first leaves no alternative diagnosis. When ear disease or local septic conditions of the region of the skull are present, local and general intracranial signs are due either to meningitis, abscess, sinus thrombosis, osteomyelitis of the base of the skull, or rarely to acute otitis.

Meningitis can be at once distinguished not only on account of the more irritative and rapidly oncoming symptoms, which differ somewhat from those of abscess, such as head retraction and rigidity of the neck, Kernig's sign, delirium and tremors, but by the lumbar puncture which gives the turbid cerebro-spinal fluid, containing polymorphonuclear cells and organisms in quantity. It must not be lost sight of that an abscess at any stage of its formation may be complicated by the development of general suppurative meningitis. Sinus thrombosis is usually accompanied by much oscillation of temperature, and by repeated rigors and œdema, and tenderness in the region of the emissary veins of the blocked sinus may be present. The diagnosis of the latter condition is not of vital importance, and its consideration should cause no delay in summoning the aid of the surgeon. The presence of any symptoms of intracranial disturbance, where tympanic septic disease exists, calls for immediate surgical interference, and the surgeon, after cleaning out the diseased tympanum, completes the diagnosis by examining the lateral sinus, both the temporal lobes and the lateral cerebellar hemisphere, and proceeds to those measures which the results of his exploration indicate. Acute otitis media may give rise to severe intracranial symptoms like those of meningitis, convulsions even occurring which may subside dramatically after perforation of the tympanic membrane, but it must be remembered that the chronic and not the acute forms of otitis give rise to septic extension to the brain. Osteomyelitis of the base of the skull extends from chronic bone disease in the region of the ear or nose. There is much pain in the base of the skull, and sometimes many cranial nerves are implicated at their foramina of exit. Skiagraphy will indicate the loss of bony structure. The malady is a chronic one, and usually ends in a terminal meningitis.

Prognosis.—Cerebral abscesses with very thick walls and inspissated or even calcified contents have been found post mortem, many years after the presumed time of formation of the abscess. Spontaneous evacuation of an abscess through the diseased ear, or through a sinus in the area of the local disease causing the abscess, has been followed by recovery. It is probable that no abscess becomes permanently quiescent after it has given rise to severe symptoms. The prognosis in cases of cerebral abscess, therefore, is that a fatal result will occur, unless successful surgical interference is possible. If the abscess is reached and drained, recovery often occurs rapidly, but this is never certain, for extensive perifocal softening, meningitis and sinus thrombosis may occur. Moreover, a general suppurative encephalitis may extend, in spite of draining the abscess.

Treatment.—The most rigorous prophylaxis should be employed that all patients suffering from septic nasal and ear diseases, and infective disease of the scalp and cranial bones, shall not pass out of observation until such disease is beyond all doubt cured. The only treatment for developed abscess is exploration and drainage. The liability to the occurrence of septic meningitis may perhaps be lessened by the administration of hexamine. The usual measures for the relief of pain should be employed.

2. LETHARGIC ENCEPHALITIS (see p. 1576)

MENINGITIS

Definition.—The inflammatory processes to which we apply the name of meningitis are infective in origin, and usually have their seat in the lepto-meninges—the pia-arachnoid. A true inflammatory lesion of the dura mater, that is, pachymeningitis, is much less common, and is usually a localised process due to the direct spread of infection from adjacent bone.

Acute leptomeningitis, on the other hand, is usually generalised, and even when it arises from a local focus of infection it spreads rapidly throughout the subarachnoid space, this spread being facilitated by the cerebro-spinal fluid and also by the negligible bactericidal potency of this fluid. Further, the inflammation not only produces its characteristic changes in the pia-arachnoid, but also greatly changes the composition of the cerebro-spinal fluid. These changes may be said to reflect with considerable accuracy the nature and cause of the meningitis, and thus it is that the examination of this fluid has so great a diagnostic value. Acute leptomeningitis may be a primary infection, or may be secondary to some infective lesion elsewhere in the body.

Pachymeningitis may be cranial or spinal, and is usually secondary to either syphilis, tuberculous disease of bone, or middle-ear suppuration. The condition formerly known as "pachymeningitis interna hæmorrhagica" is now regarded as traumatic and not inflammatory in origin, and is described under the heading of chronic subdural hæmatoma (cf. p. 1593).

The fine infiltration of the pia-arachnoid by the cells of secondary carcinoma, of glioma, or sarcoma has been spoken of as a meningitis, but although such an infiltration may give rise to symptoms resembling those of a true meningitis, the term is not strictly accurate, though it is well to bear in mind that this form of new growth does occur and give a picture of meningeal irritation.

Examination of Cerebro-spinal Fluid

The normal cerebro-spinal fluid is clear and colourless. As obtained by lumbar puncture, it is found to be under a pressure of from 60 to 150 mms. of water and to contain from 0 to 5 cells (lymphocytes) per c.cm. Its chemical composition is as follows:

Protein (mainly albumin)	0·01 per cent.	(10 to 20 mgrms. per 100 c.c.)
Glucose	0·05 to 0·08 „	(50 to 80 mgrms. per 100 c.c.)
Chlorides	0·72 to 0·75 „	(725 to 750 mgrms. per 100 c.c.)

The lumbar puncture is made in the first interspinous space above a line joining the highest points of the iliac crests, which is the space between the third and fourth lumbar spines, or it may be made with equal rectitude in the space between the second and third lumbar spines. The needle should be introduced exactly in the middle line and at right angles to the surface, close to the upper spinous process of the interval used. Normally the fluid escapes drop by drop. If it runs rapidly or spurts out, this is an index of the increase of the cerebro-spinal pressure. Such an increase is met with in all meningeal inflammation, congestion and hæmorrhage, and in increased intracranial pressure. But it is also produced by coughing or straining, and its accurate measurement by a manometer is now part of the routine examination of the fluid.

Queckenstedt's phenomenon.—If, with a manometer in attachment to a lumbar puncture needle, the jugular veins be compressed, an immediate rise in cerebro-spinal fluid pressure in the normal person will be noted, the pressure rising as high as 300 or 400 mms. of fluid. It falls as rapidly when compression is released. If there be a block in the spinal subarachnoid space, or in the exits from the ventricular system, there will be no rise (complete block), or a slight rise with a delayed fall (incomplete block). Again, if the removal of a few c.cms. (4 to 8) of cerebro-spinal fluid is followed by a persistent fall in pressure of about 50 per cent., there is probably a block in the spinal subarachnoid space. These two tests afford valuable information in cases of suspected "obstructive" hydrocephalus, or of spinal block from tumour, or other local disease.

Increase of Protein Content.—This is of high importance, and occurs in all conditions of meningitis, and especially when the thecal space is obstructed by tumour, pressure from without or meningeal adhesions. In pathological conditions the protein content may reach 0·8 per cent. or more. A high protein content sometimes associated with xanthochromia, in the absence of cellular elements, is highly characteristic of thecal obstruction and is known as "Froin's syndrome." Lethargic encephalitis does not give any increase of protein.

Xanthochromia is a yellow colour of the cerebro-spinal fluid, and it is met with when the cerebro-spinal space is obstructed by tumours of the cord or meninges, or by external pressure, and in some forms of polyneuritis and meningitis. The yellow colour may result from an extravasation of blood either into the arachnoid or into the central nervous system.

Spontaneous coagulation of the fluid is met with in some cases of meningitis, when there is spinal obstruction, and in some varieties of acute polyneuritis.

Blood may occur from every condition of hæmorrhage, injury and encephalitis, and sometimes in meningitis. Blood that has been long shed into the cerebro-spinal fluid tends to become brownish and later yellowish. Leucocytosis is indicative of meningitis and often occurs in encephalitis, and in the neurotropic virus infections and in mumps. A lymphocytosis is characteristic of tuberculous and syphilitic meningitis, poliomyelitis, lethargic encephalitis, sinus thrombosis and mumps. A polymorphonuclear cytosis occurs in meningococcal meningitis and all the suppurative forms of meningitis. In tuberculous meningitis there is often a mixed cytosis at first, in which the polymorphonuclear cells may form 60 per cent. of the total. In

poliomyelitis, the lymphocytosis disappears after the end of a week. In lethargic encephalitis there is frequently no lymphocytosis.

Pus may be present in quantity in all the septic forms of meningitis, and especially in pneumococcal and epidemic meningitis.

Decrease in Glucose Content.—All conditions of meningitis cause decrease in the glucose.

Alteration of Chloride Content.—Diminution in chlorides is highly characteristic of tuberculous meningitis, and a reduction below 0·65 per cent. is pathognomonic of that condition. Increase in chlorides occurs in uræmia and other conditions of salt retention.

Lange's Colloidal Gold Reaction.—In neurosyphilis and in some cases of disseminated sclerosis, the globulin fraction of the total protein of the cerebro-spinal fluid increases and may almost equal the albumin fraction. The high globulin content gives the fluid a power of precipitating colloids from suspension. The estimation of this power in the case of colloidal gold is the basis of Lange's test. To ten dilutions of cerebro-spinal fluid (from 1 in 10 to 1 in 10,000) constant amounts of colloidal gold are added, and the mixtures allowed to stand for 24 hours. The form of the precipitation curves has a differentiating value. Thus in general paralysis the first six dilutions are precipitated (paretic curve), in tabes dorsalis, the third and fourth dilutions show the maximal precipitation (luetic curve); in meningitis, the sixth to eighth dilutions are precipitated (meningitic curve). In disseminated sclerosis the combination of negative Wassermann reactions in blood and fluid and a paretic curve in the fluid is frequently found.

The nature of the organismal content is determined (1) by the direct examination of films made from the centrifugalised fluid, (2) by cultures from the fluid, and (3) by the inoculation of animals from the fluid.

Name.	Organism.	Cerebro-spinal Fluid
Tuberculous meningitis	Tubercle bacillus.	Clear or turbid. Lymphocytes, either alone or in greater numbers than polymorphs. Tubercle bacilli. Chlorides diminished.
Pneumococcal meningitis	Pneumococcus.	Turbid. Polymorpho-nuclear leucocytes. Pneumococci.
Meningococcal meningitis		Clear or turbid.
Sporadic or posterior-basal.	Still's diplococcus.	Polymorpho-nuclear leucocytes.
Epidemic or "Spotted Fever."	Weichselbaum's diplococcus.	Intracellular diplococci.
Pyogenic meningitis	Staphylococcus. Streptococcus. *B. influenzæ.* Gonococcus. Streptothrix.	Turbid. Polymorpho-nuclear leucocytes. Organisms.
Syphilitic meningitis	*Spirochæta pallida.*	Clear. Lymphocytes only. Wassermann reaction +.
Other forms	*B. typhosus.* *B enteritidis.*	Turbid. Polymorphs.
Rheumatic meningitis	*Diplococcus rheumaticus.*	
Serous meningitis		Clear. Few cells. Sterile.
Traumatic meningitis.		

The Wassermann reaction in the fluid is positive in all conditions of recent syphilitic disease impinging upon the meninges, and always in general paralysis. Though often positive in tabes, it may be found negative. Lumbar puncture is dangerous in cases of long-standing increased intracranial pressure, and if performed in such cases a minimum of fluid should be withdrawn. It may in some cases cause severe headache of long duration. It may be difficult or impossible to perform when there is bone disease of the lumbar vertebræ.

The most useful classification of the varieties of meningitis is according to the nature of the micro-organism producing the inflammation.

1. TUBERCULOUS MENINGITIS

This disease results from the general invasion of the cerebro-spinal lepto-meninges by the tubercle bacillus, and this organism invariably arrives in the meninges by the blood stream from some previously existing focus of tuberculous infection within the system, and most commonly from caseous tracheo-bronchial glands and tuberculous bone disease. Occurring at all ages, it is the form by far the most frequently met with in the second and third years of life. The characteristic features of the cerebro-spinal fluid are, that it is usually under considerable pressure, it is clear or only slightly turbid, has no visible deposit before centrifugalisation, but it often forms a fine flocculent clot. It contains an excess of albumin. The normal sugar is generally absent. There is a pleocytosis with a high proportion of lymphocytes, 70 to 80 per cent. being of this nature, and the rest being polymorphonuclears. Careful examination will almost always reveal the presence of the tubercle bacillus.

Ætiology.—The inheritance of a lowered resistance to the invasion of the tubercle bacillus is an important factor, especially when such a tendency exists in both parents. The sexes are equally affected. Tuberculous meningitis is rare during the first year of life, and especially during the first 6 months of life, when posterior basal meningitis is most common. Its greatest incidence is during the second and third years. It is common throughout childhood and early adult life, after which it becomes increasingly rare. The primary focus from which the organisms are spread to the meninges is most commonly a tuberculous mesenteric or bronchial gland.

Sometimes the source of infection is tuberculous disease of the lungs, of the abdomen, of the ear, of the joints, or of bone. Operations upon the sites of tuberculous disease may directly cause the dissemination of the tubercle bacilli, and especially surgical procedures upon tuberculous intracranial tumours, upon spinal caries, and upon tuberculous disease of bones and joints. The acute specific fevers, and especially measles, are sometimes the exciting causes of the disease. Injury to the head sometimes determines the attack.

Pathology.—In tuberculous meningitis three kinds of lesions of the meninges may be met with—(1) grey tubercles unassociated with inflammatory deposit; (2) tuberculous meningitis characterised by the presence of tuberculous granulations associated with a fibrinous and purulent exudation—the superficial tissue of the nervous system underlying the meninges is in this case always involved; (3) tuberculous tumours of any size up to that

of a pigeon's egg. It is not uncommon to find such a tumour to be the focus of widely spread meningitis. The three kinds of lesions may coexist in the same case.

The flattening of the convolutions and the dry sticky feel of the surface of the brain are highly characteristic. The disease affects the pia-arachnoid and its processes, the small vessels entering the surface of the brain and the superficial tissues of the latter. Occasionally a few tubercles are found upon the inner surface of the dura mater. Generally the convexity of the brain escapes, or is little affected. In the intercrural space, around the optic chiasma, covering the tips of the temporal lobes, along the commencement of the Sylvian fissures and around the brain stem, there is an inflammatory exudation of tough consistency and of a pale yellowish-green colour. Spreading from the edge of this in decreasing numbers, grey tubercles are seen in the pia-arachnoid, particularly along the Sylvian fissures. They may be found wherever the pia-arachnoid extends (the convexity, as a rule, excepted), but except at the base of the brain they are not, as a rule, accompanied by the characteristic tough exudation.

The brain as a whole is soft, and local softening of the walls of the ventricles, of the velum interpositum, and of the fornix is often present. This softening is caused by spreading of the tuberculous process from the pia-arachnoid to the small vessels of the surface of the brain, on the walls of which tubercles develop, sometimes in such numbers that a small entering vessel, when observed under low magnification, after the brain tissue has been removed by careful washing, may resemble a bunch of grapes, each grape being a tuberculous nodule. Thrombosis is a common event in the vessels so involved, and softening follows. Some degree of thrombosis in the superior longitudinal sinus and in the veins of Galen is commonly present. It is probably owing to the softening of the nervous tissues that occlusion of the foramina by which the cerebro-spinal fluid leaves the ventricles does not often take place, and that, therefore, a condition of hydrocephalus does not occur in this form of meningitis. The cranial nerve palsies which are so frequently met with in this disease are the result of implication by adhesions and local interference with the blood supply of the nerves at the base of the brain, by the newly formed adhesive tissue. In the majority of cases the membranes of the spinal cord are affected, and the most common situation of the tubercles is upon the inner surface of the theca, and in the pia covering the lumbar enlargement.

Symptoms.—The onset is usually gradual, with signs of vague and slight illness. In children, general apathy and neglect of amusements and play, headache, loss of appetite, dullness, fretfulness, restlessness at night with grinding of the teeth during sleep, headache, vomiting and pyrexia are common symptoms. In older subjects, lassitude, depression, mental alteration, perversity and hysterical manifestations are common. Constipation is usually present, and the breath has a peculiar fetor. The facial expression is one of illness and frowning discomfort, and there is disinclination to talk. Young children may be speechless for days together. As a rule, in this stage of the disease young children complain of nothing, and delirium is rare; but as age advances, delirium increases in frequency, and headache, usually frontal is increasingly complained of. These slight and vague symptoms may last from a few days to several weeks, and constitute what has been called

the prodromal stage of the malady. An early disappearance of the knee and ankle jerks, and the occurrence of retention or urine are often early signs and should be looked for in suspected cases. In those cases which are said to being acutely, careful inquiry will generally reveal that some symptoms such as the above have preceded the acute onset. The further development of the disease is marked by the appearance of a lethargy, which soon deepens into a stupor, from which it is difficult or impossible to arouse the patient. Vomiting is of frequent occurrence, and headache may be severe. The child lies upon its side in the " cramped " position, resenting any disturbance. The expression becomes vacant, with wide-open eyes and dilated pupils, as if fixed upon some distant object. There is often some retraction of the angles of the mouth, and there is frequently a bright malar flush. In the later stages the limbs are generally extended and rigid. Stiffness of the neck is the rule, and head retraction may occur, but this is never so marked as in posterior basal meningitis. The abdomen is always markedly retracted and a tâche cérébrale is often conspicuous. A single sharp cry, apparently causeless, called the hydrocephalic cry, and which is common in all forms of meningitis and also in other infantile intracranial affections, is sometimes heard.

Ocular phenomena make their appearance towards the end of the first week of the developed disease. All varieties of varying and persistent strabismus and ptosis are met with, paralysis of the external rectus being the most common. Rolling movements and independent movements of the eyeballs may occur. None of these signs is constantly present. The pupils may be contracted at first, and may show varying inequality, but in the later stages they are dilated. Papillœdema is often present towards the end of the second week, if the patient survives so long. It is of moderate intensity, the height of the swelling rarely exceeding two dioptres. Choroidal tubercles sometimes occur.

Convulsions are common in every stage of the disease in children, but rare in adult cases. They may be the first symptom of the onset, but are more often met with in the later stages of the disease. They may be local or general. Repeated rhythmic movements are frequent, and are specially noticeable in connection with the mouth, where sucking and champing movements and grinding of the teeth are common. Rhythmic movements of the limbs may also occur. Coarse tremor upon movement of the limbs is the rule, and spasmodic twitching of the muscles is frequent. In rare cases, movements exactly like those of chorea occur. Kernig's sign is usually present.

The temperature is usually raised one or two degrees, but it presents no characteristic features, some cases being apyrexial throughout. Irregularity of the pulse is the rule, and is of considerable diagnostic importance. Rapid in the early stages, it tends to become unduly slow in the stage of coma, and again rapid as death nears. Cheyne-Stokes breathing and grouped breathing are common. Constipation is usually a marked and persistent feature.

Course.—The course of tuberculous meningitis is progressive to an invariably fatal termination in from a few days to 3 weeks after the appearance of definite symptoms, and no case of recovery is known to me in which the diagnosis has been unquestionably proved by the recovery of the tubercle bacillus from the cerebro-spinal fluid.

Diagnosis.—The early symptoms of the disease may give rise to difficulty in diagnosis, but the latter is relatively simple when the disease is advanced. The diseases liable to be confused with tuberculous meningitis at its commencement are gastro-intestinal catarrh, the exanthemata—especially enteric fever—and pneumonia. It must be borne in mind that in children convulsion, strabismus, head retraction and stiffness of the neck, with pyrexia, may be symptomatic of many maladies apart from meningitis, especially of apical pneumonia. In enteric fever the temperature is higher and the headache more severe, and irritability and resentment of interference are not present; the decubitus is usually dorsal. Widal's test is of importance in this connection. When distinctive signs of intracranial disease have appeared the diagnosis has to be made from other forms of meningitis, sinus thrombosis, tumour, abscess and middle-ear disease. Careful examination of the retina and of the tympanic membranes is then necessary. In all cases the diagnosis must be made certain by the examination of the cerebro-spinal fluid, which will be found to contain lymphocytes in excess and tubercle bacilli. These organisms are sometimes difficult to isolate from the fluid, but their presence can be readily demonstrated by injecting the fluid into the subcutaneous tissue of guinea-pigs, when the characteristic lesion of tubercle results. It must be remembered that in some cases the polymorphonuclear leucocytes may be in excess, but these cases are at once distinguished from other forms of meningitis by the presence of numerous lymphocytes, by the absence of the meningococcus and of the other germs producing suppuration, and by the presence of the tubercle bacillus. Pirquet's skin reaction is often absent in tuberculous meningitis.

Treatment.—From the unvarying fatal issue of the malady, treatment can only be directed towards the relief of symptoms. Temporary improvement and relief of headache may be brought about by lumbar puncture, which may for this purpose be repeated several times. Bromides, chloral, aspirin and other analgesic drugs may be used to relieve the headache, check the convulsion and diminish the restlessness. Hexamine in large doses, inunction of mercury and administration of tuberculin have been largely used, but without any success. General treatment must be that which will secure such comfort as is possible for the patient. Where swallowing is difficult nasal feeding should be adopted.

2. PNEUMOCOCCAL MENINGITIS

Pneumococcal infection of the meninges most commonly follows upon a similar infection elsewhere in the body, empyema and pneumococcal otitis being the commonest lesions, while pneumonia, abdominal infection, abscess and joint infection are less common. In one-third of the cases, however, the meningeal infection is primary. The characteristics of the cerebro-spinal fluid are that it is purulent and sometimes so thick that it will not flow through the needle. It is greenish-yellow in colour, contains a large amount of albumin, and multitudinous polymorphonuclear cells, among which the characteristic pneumococcus is found. In fulminant rapidly fatal cases the fluid may be turbid from the presence of pneumococci alone, no reaction in the form of pleocytosis being present.

Ætiology.—The disease may occur at any age. It is sometimes a terminal

event of a pneumococcal infection elsewhere, and passes almost unnoticed, or is discovered only at the autopsy. Meningitis which follows operations upon the nose and disease of the nasal bones is usually of the pneumococcal variety.

Pathology.—The surface of the brain and spinal cord is highly characteristic. Usually the whole surface of the vertex and of the base is covered with a thick, tenacious, greenish-yellow pus, which is contained in the meshes of the arachnoid, and between this and the dura. The ventricles often contain pus. A similar exudation is found upon the spinal cord, more especially upon the dorsal aspect, and in the cervical and lumbo-sacral regions. The major affection of the vertex of the brain is the peculiarity of this disease, and only in the rarest cases is the base alone affected. The exudation is characterised by the greater amount of fibrin than in other forms of meningitis.

Symptoms.—The symptoms are those which are common to all forms of meningitis. Some of the cases are indistinguishable symptomatically from cases of tuberculous meningitis. Others run a very rapid course and present few features other than headache, vomiting and pyrexia, with rapidly oncoming and quickly fatal coma. In others again, the meningeal symptoms are concealed in the terminal asthenia of a previously existing pneumococcal infection elsewhere, such as empyema, purulent pericarditis or peritonitis.

Diagnosis.—This rests upon the presence of signs of meningitis or the existence of coma alone, together with a cerebro-spinal fluid which is purulent from the presence of polymorphonuclear leucocytes, containing the pneumococcus.

No case of recovery from this form of meningitis has hitherto been recorded. Lumbar puncture and intrathecal injections of anti-pneumococcal serum may be performed, but on account of the thick nature of the exudate, little relief must be expected from the former, while the latter cannot possibly avail except in primary cases.

3. MENINGOCOCCAL MENINGITIS (see p. 36)

4. PYOGENIC MENINGITIS

Apart from meningococcal and pneumococcal infections, suppurative meningitis may result from the invasion of the meninges by staphylococci, streptococci, gonococci, *B. influenzæ*, *B. anthracis* and streptothrix.

Staphylococcal and streptococcal infections are by far the most common. They may result in young children from septic conditions of the umbilicus and from infections of the skin. Usually they are due to extension of an infection of adjacent structures to the meninges, and follow disease of cranial and spinal bones, especially caries of the middle ear, erysipelas and other infections of the scalp, wounds of the meninges, especially bullet wounds, rupture of intracranial abscess, and they may occur in the course of a general septicæmia.

Pathology.—The pathology of these conditions does not materially differ from that of pneumococcal meningitis. In all cases the exudation

is purulent, and in the meningitis due to *B. anthracis* it is of a red colour, due to concomitant blood effusion. The cerebro-spinal fluid contains large numbers of polymorphonuclear leucocytes, together with the micro-organism responsible for each variety. Suppurative meningitis resulting from bone disease and from wounds of the meninges may be localised by the formation of meningeal adhesions, and an intrameningeal abscess may result. Such an abscess situated upon the upper surface of the temporal bone is not an uncommon result of caries of the middle ear.

The clinical aspect is that common to all forms of acute meningitis, high pyrexia, rigors and delirium being conspicuous. The course is rapid to an almost invariably fatal termination. In the localised form where drainage can be ensured and extension of the infection prevented, recovery should take place. Several cases of recovery from gonococcal meningitis have been reported. Influenzal meningitis is invariably fatal.

Diagnosis.—This depends upon the presence of the clinical signs of meningitis and of a cerebro-spinal fluid containing polymorphonuclear leucocytes in large quantities, and upon the recognition in this fluid of the several micro-organisms responsible, by microscopic and cultivation methods. The recognition of *B. influenzæ* requires that cultures should be made upon some blood medium, for otherwise the organism may be easily overlooked and the fluid reported as sterile. Further, the presence of some well-known cause for suppurative meningitis, such as ear disease, staphylococcal infection, etc., suggests the diagnosis.

Acute otitis media may give rise to symptoms closely resembling those of meningitis, such as headache, pyrexia, vomiting, head retraction and delirium. In such cases examination of the ear, which should be made a routine in all cases where meningitis is suspected, will reveal tympanic distension, the relief of which is followed by a speedy disappearance of the symptoms. In this connection it must be borne in mind that meningitis and intracranial abscess never follow directly upon acute otitis, but they are the sequelæ of chronic otitis, which has resulted in caries of the temporal bone. When evidences of caries of the middle ear are present in a case presenting cerebral symptoms, distinction has to be made between meningitis and abscess of the brain or cerebellum. Here the presence of localising symptoms, either temporal or cerebellar, and the presence of papillœdema and any tendency to a temporary abatement of the symptoms point to the existence of an abscess, and further lumbar puncture will in all but the rarest cases settle the point. In cases of abscess in which cells and organisms are found in the cerebro-spinal fluid, these exist in small numbers only, as compared with the copious cells and organisms present in the fluid of suppurative meningitis.

Treatment.—In cases of meningitis secondary to temporal caries, the source of infection should be at once cleared out by surgical procedure. Repeated lumbar puncture may relieve symptoms, and injection of an anti-serum to the organism present may be tried. Vaccines may also be used.

The *treatment* and *prognosis* of all the foregoing forms of meningitis, except tuberculous meningitis, have undergone a great change since the introduction of sulphanilamide and its derivations. The mode of employment of these drugs is dealt with on p. 49 (cerebro-spinal fever).

5. BENIGN ASEPTIC MENINGITIS

Synonyms.—Epidemic Serous Meningitis; Benign Lymphocytic Meningitis.

Ætiology.—This is unknown. No organisms have been found in the cerebro-spinal fluid. The malady so named appears of wide distribution.

Pathology.—Since recovery is the rule, nothing much is known of this, but lymphocytic infiltration of the lepto-meninges has been found in one fatal case.

Symptoms.—Children are mostly affected, but no age appears exempt. The onset is abrupt, with headache, sickness and fever. The typical signs of meningeal irritation are present, neck and spine rigidity, Kernig's sign, irritability and restlessness and sometimes delirium. Somnolence is unusual. In young children convulsions may occur. The fever mounts to 102 or 103 and fluctuates. It may disappear in 2 or 3 days, or persist for 3 weeks. Lumbar puncture yields a cerebro-spinal fluid under pressure, usually clear but sometimes opalescent. The cell count ranges from 50 to 1500 per c.mm. After the first two or three days these cells are almost wholly lymphocytes. The sugar and chloride contents remain at normal height, thus differing from the findings in other forms of acute lepto-meningitis, and resembling the findings in acute poliomyelitis.

Diagnosis.—This depends upon the cerebro-spinal fluid findings and upon the benign course of the illness. For a few days differentiation from poliomyelitis may be impossible.

Prognosis.—Recovery is the rule.

Treatment.—Repeated lumbar puncture reduces the intracranial tension. Beyond this, only general nursing care is needed.

6. SYPHILITIC MENINGITIS

Miningitis due to infection by the *Spirochæta pallida* is one of the characteristic lesions met with in practically all cases of syphilitic disease of the central nervous system, and plays its part in the production of the symptom complexes of these maladies, from acute cerebral syphilis and acute myelitis to general paralysis and locomotor ataxy. It may occur at any period after infection, but one-half of the cases occur during the first four years. In a few cases the symptoms have been noticed coincidently with the syphilitic roseola.

Pathology.—The morbid process consists essentially in an infiltration of the meninges with lymphocytes and plasma cells, spreading from the perivascular lymphatics where the spirochætes multiply freely, and it may lead to scarring and opacity of the membranes, with consequent strangling of the nerves and vessels and occlusion of the arachnoid space, or to massive gummatous formation in the mininges. It is essentially a chronic form of meningitis though it may result in the production of acute symptoms. A marked feature is that the meningeal changes may be found actively progressive in one spot, and equally regressive in another. The disease may be local or diffuse, and it may attack the dura (pachymeningitis) and involve the overlying bone, or it may spread from the pia-arachnoid into the sublying nervous tissue (meningo-encephalitis).

The cerebro-spinal fluid is characteristic. It is usually under increased

pressure, is clear and colourless, and contains lymphocytes and no other cell forms. The number of the lymphocytes present is in direct proportion to the activity of the meningeal syphilis. The spirochæte has rarely been found in the fluid, yet inoculation of apes with the fluid has proved successful.

Symptoms.—Apart from those conditions of nervous syphilis in which meningitis is associated with arterial disease, the formation of massive gummata and neuronic degeneration, syphilitic meningitis may be described as giving rise clinically to the following conditions:

1. *Headache.*

2. *Hydrocephalus.*—In those acute cases of cerebral syphilis characterised by rapidly oncoming headache, vomiting and papilloedema, mental reduction and somnolence without localising symptoms, and which respond readily to treatment, it seems certain that ventricular distension, consequent upon adhesive meningitis and ependymitis, is responsible. A more slowly oncoming ventricular occlusion may give rise to symptoms which cannot be distinguished from those caused by a non-localisable intracranial tumour. Syphilitic meningeal occlusion may give rise to typical hydrocephalus, and a considerable proportion of the cases of infantile hydrocephalus are of this nature and are due to congenital syphilis. A few cases are recorded in which chronic hydrocephalus of this nature has occurred in adult life.

3. *Infantile syphilitic meningitis.*—This is a chronic malady which commences insidiously during the first few months of life, with signs of general nervous deterioration. The appearance of the brain is very characteristic. The membrane over the vertex is opaque and thickened and adherent to the cortex. The gyri are shrunken, the sulci wide and the surface of the brain has in parts the appearance of wash-leather. The child does not get on, and takes an ever-decreasing notice of its surroundings. Power of movement lessens, the limbs become rigid and the clinical aspect comes to resemble exactly that of a severe cerebral diplegia. Convulsions are of frequent occurrence. The diagnosis is not difficult, for the signs of meningitis are obvious and those of congenital syphilis may be present. There is an excess of lymphocytes in the cerebro-spinal fluid, both in which and in the blood there is a positive Wassermann reaction. The prognosis in any case where the symptoms have become marked is most unfavourable.

4. *Adult syphilitic meningitis,* with a symptom-complex closely resembling that of tuberculous meningitis, has been reported on many occasions. In some of the cases the onset coincided with the appearance of the syphilitic roseola. The diagnosis depends upon the presence of signs of active syphilis, upon the cerebro-spinal lymphocytosis and upon the existence of a positive Wassermann reaction. The prognosis under appropriate treatment is good.

5. *Paralysis of cranial nerves.*—This common and often isolated symptom of nervous syphilis may result from sclerosing basal meningitis or from the presence of a gumma in the course of the nerve. Several of the nerves may be involved together in one patch of meningitis. Any of the cranial nerves may be affected from the olfactory to the hypoglossal, but the third or oculomotor nerve is by far the most frequently attacked.

Treatment.—The treatment of the above conditions is that appropriate for nervous syphilis in general (p. 1636). The combined administration of mercury by inunction and of arsenic compounds by intravenous injection

gives the best results. Iodide of potassium is not nearly so useful as when massive gummata are present, and, moreover, it seems to increase the scarring process. Its use should be avoided until the patient has been under the influence of mercury for some time.

7. OTHER FORMS OF MENINGITIS

Meningitis due to the typhoid bacillus is a rare malady. It may occur as a primary disease, but is usually a complication in the course of enteric fever. It is to be remembered that while many cases of enteric fever present cerebral symptoms, in very few can meningitis be proved to exist. The meningeal exudation, generally serous, is sometimes purulent. The cerebro-spinal fluid contains lymphocytes, and Eberth's bacillus is present. The symptoms resemble those of acute meningitis in general. The diagnosis depends upon the presence of enteric fever, of Widal's reaction and the discovery of Eberth's bacillus in the cerebro-spinal fluid. The malady is generally fatal, but a considerable number of recoveries have occurred, especially in children. In rare cases symptoms of meningitis occur in the course of rheumatic infection, and Poynton and Paine have brought forward evidence that such symptoms are the result of infection of the meninges with the *Diplococcus rheumaticus*. The term " serous meningitis " is applied to those cases of meningitis in which the cerebro-spinal fluid is clear and sterile. In such cases recovery is the rule, and the symptoms are not rarely rapidly relieved by lumbar puncture. The term " meningism " is used for a group of cases which present symptoms of meningitis and in which no pathological change can be found either in the cerebro-spinal fluid, or, if death occur, in the meninges or cerebral tissue. It is met with in children in association with acute febrile diseases, and is presumably due to the toxin present. Recovery is usually rapid and complete.

VIRUS DISEASES OF THE NERVOUS SYSTEM

Certain viruses have a selective affinity for the nervous system and are therefore spoken of as " neurotropic." They act upon the nerve cell, and to a less degree upon glia cells, but not upon the white matter. They are capable of multiplication and of exerting their pathogenic action only within the nerve cell, where their life and activity are short-lived. Thus, the infections to which they give rise are known as self-limited.

The essential lesion resulting from their presence is an acute necrosis of the nerve cell, leading to the death and destruction or to the damage of the cell. A secondary glial and vascular reaction ensues as a result of which lymphocytes pass into the cerebro-spinal fluid from the perivascular spaces in the affected regions of the nervous system.

Such virus infections are primary infections of the nerve cell and not invasions of the central nervous system secondary to general infection. The portal of entry in all cases, except that of rabies, is probably the nasopharynx by the mechanism of " droplet infection." The virus is carried thence via the olfactory filaments into the olfactory bulbs and tracts. Gaining direct access

to the brain in this way it seems certain that the virus is thereupon transported within the system through axis cylinders. This at least appears to be the mechanism in the most closely studied of the virus infections of the nervous system, acute poliomyelitis.

The so-called post-infective encephalitis that may follow the acute exanthemata is not a true virus infection of the nervous system, since the lesion is a demyelination and not an attack upon the nerve cell. This form of encephalitis, therefore, is probably to be regarded as an intoxication of the nervous system associated with a systemic virus infection.

F. M. R. WALSHE.

ACUTE ANTERIOR POLIOMYELITIS

Synonyms.—Infantile Paralysis; Heine-Medin Disease.

Definition.—An infection of the nervous system by a neurotropic virus which acts primarily upon the nerve cell, the interstitial tissues of the nervous system and the leptomeninges being secondarily involved. Contrary to what was formerly believed, there is no initial phase of general systemic infection; from the outset, poliomyelitis is a disease of the nerve cell. The virus is an obligatory intracellular parasite, and has a special affinity for the ventral horn cells of the spinal cord, within which it multiplies during its brief period of activity.

Ætiology.—A constant feature of the disease is its incidence in young children. They appear to be immune during the first year of life, susceptibility being greatest in the second, third and fourth years, and thereafter declining. Cases during adolescence and early adult life are not uncommon, but the disease is rare after middle life. It is possible that a very large proportion of the community has at some time been infected by poliomyelitis, only a very small proportion (less than 1 per cent.) having developed symptoms of infection. From 50 to 80 per cent. of the adult population possess serum containing protective antibodies, and this fact is taken as presumptive (though not certain) evidence of previous infection. That such clinically latent infection is possible may be seen from the occurrence of the many "abortive" cases of poliomyelitis in all epidemic outbreaks. The disease is much more prevalent during the hotter months of the summer, usually the months of August and September in the Northern hemisphere, and the months of March and April in the Southern. It is spread by human carriage by infected persons in the initial stage of their illness, and probably also by healthy carriers. The nasopharyngeal secretions are infective during the first ten days of the illness, and spread probably takes place by what is known as "droplet infection." It has been said that case-to-case infection does not occur, but the long-continued case-incidence in certain small, enclosed communities strongly suggests that, however difficult it may be to trace, such infection does in fact occur, and must be allowed for in dealing with outbreaks of the disease. There is some evidence that milk may also act as a channel of conveyance of the virus.

THE PATH OF INFECTION.—It is exceptional for the virus to be found in the blood or cerebro-spinal fluid, and it is not by either of these channels that it reaches the central nervous system. The portal of entry into the body is

the nasopharynx, whence the virus enters the free ends of the olfactory nerve filaments, and travels by the axis cylinders directly into the olfactory bulb, and thence into the brain. The subsequent passage of the virus to the ventral nerve cells is believed to be entirely axonal.

It is believed that *all* the symptoms of the declared disease, from the first onset to the appearance of paralysis, are due to the effects of the virus acting upon nerve cells in its passage from the site of entry into the brain, until it reaches its site of election in the ventral horn cells of the lumbar region of the cord.

Pathology.—The virus of poliomyelitis is an obligatory intracellular parasite, and its action takes place entirely within the nerve cell. The changes seen in the nervous system vary with the virulence of the infection. In very severe infections the nerve cells undergo acute necrosis. If the experimentally infected animal be destroyed at this initial stage no lesions other than these cell changes are found, and the rapidly ensuing cellular exudation and meningeal infiltration seen in fatal human cases are not present. But the necrosis of nerve cells in the surviving patient is naturally shortly followed by phagocytic processes, and amœboid (microglial) cells and polymorphonuclear leucocytes rapidly invade the affected areas and clear away the dead nerve cells. It is essential to bear in mind, however, that these processes are secondary and not, as used to be thought, the primary and essential lesion of poliomyelitis. In less severe infections, less acute forms of nerve cell changes are seen, and with these the cellular exudation is almost wholly of amœboid microglia cells. These phagocytic cells fill the perivascular spaces in the affected parts of the cord. Together with leucocytes, these cells finally overflow into the cerebro-spinal fluid. They appear here even before the development of paralysis; and it is this early indication of meningeal infiltration that led to the view formerly held that a meningitis preceded the involvement of the nervous system. In the affected regions of the grey matter of the ventral horns, some cells always remain unaffected by the virus.

Lesions in the viscera have been described: namely, hyperplasia of the lymphoid tissue and splenic enlargement—but these are not constant, and their presence at the final stage of the malady is of uncertain significance. They are no longer held to indicate the occurrence of systemic infection in poliomyelitis.

Cerebro-spinal fluid.—The fluid is clear, colourless, or faintly yellow, and under high pressure, and the titre of chlorides and sugar is normal. The protein content is increased. There is usually a pleocytosis from a moderate to a very large number of cells, which disappears rapidly with convalescence and is usually gone in a fortnight. It is usually described as polymorpho-nuclear at first and rapidly becoming lymphocytic, but in our experience this is certainly not the rule. We have seen the fluid normal throughout in indubitable cases; we have seen a pure lymphocytosis throughout and from the preparalytic stage; and we have seen high polymorph pleocytosis, both early and late, and also with a relapse on the tenth day. The nature and number of the cells seem not to afford any prognostic indications.

Blood.—In the early stages of the malady, there is a constant and very marked polymorpho-nuclear pleocytosis, which may reach as high as 30,000, with lymphocytic leucopenia. This leucocytosis disappears when the fever abates.

Symptoms.—It has been the practice to divide the clinical course of poliomyelitis into an initial stage of general infection; a second stage of meningeal involvement; and a final stage of paralysis from invasion of the nervous tissues. Cases in which recovery ensued after a brief febrile illness and without paralytic manifestations were spoken of as "abortive," it being supposed that the infection had died out before the virus had invaded the spinal cord. This classification, based as it was upon an erroneous pathology, may now be abandoned in favour of a division into preparalytic and paralytic stages; it being understood that in both stages, and therefore also in abortive cases, the virus has in fact invaded the nervous system before any symptoms whatever have appeared, and that even the symptoms of the preparalytic stage are almost certainly the expression of the action of the virus upon the nervous system. In short, there is no clinical stage of poliomyelitis in which the virus has not already gained access to nerve cells, and begun to exert its pathogenic effects. The failure of serum therapy in the past is probably to be explained by this fact.

The preparalytic stage.—This may last from 1 to 4 or 5 days. It is almost invariably febrile, the temperature rising to 103 or 104 degrees. The pyrexia lasts for from 1 to 3 days and then declines, sometimes finally, sometimes recurring for a day or two as paralysis develops.

To those who have studied the disease in the course of a large epidemic there can be no doubt that the clinical picture of the opening phase is pathognomonic, and clearly to be distinguished from that of other febrile illnesses of childhood. Draper has given a very vivid account of this stage, from which the following statement is taken. The child is commonly flushed and miserable, and may be drowsy, but it presents a typical appearance of mingled apprehension and restlessness, and may be very irritable. In severe infections the child breathes rapidly, appears pre-occupied and in a state of tenseness. An ataxic tremor and involuntary muscular jerkings may be present. Extreme fearfulness, and confused and alarming dreams are common. The child is hypersensitive to even the lightest touch and resents being moved. Vomiting, probably of central origin, may also be present. Headache, pain in the neck and back, stiffness of the spine and pain in the back on active or passive flexion, diminution of tendon jerks, and some diffuse weakness all appear in sequence, and finally paralysis suddenly appears in one or more groups of muscles. On the hypothesis that the sequence of symptoms in poliomyelitis from the opening of the clinical picture until the appearance of paralysis accurately represents the passage of the virus through the nervous system from olfactory bulb to ventral horn cell, Faber has drawn up the following table of symptoms.

Progress of Virus.	*Characteristic Symptoms.*
Olfactory bulb to hypothalamus and brain stem.	Fever, drowsiness, alternating with restlessness, sweating, general hyperæsthesia, apprehension, fear, irritability, heightened sensibility to pain, headache and vomiting.
Posterior columns of cord. Posterior root ganglia.	Localised pains and tenderness, disturbances of pain sensibility, pain on flexion of spine, Kernig's sign, transiently increased tendon jerks. Temperature may fall now.

Progress of Virus.	*Characteristic Symptoms.*
Anterior horn cells.	Twitchings, tremor, unsteady movements. Flaccid paralysis, loss of tendon jerks.
No further spread: Infection dies out.	Diminution of extent of paralysis, disappearance of pain and tenderness.

It would probably be premature to say that every stage in this progress of the virus has been finally and conclusively proved, but it is of course quite reasonable to take the view that all the initial symptoms of poliomyelitis are capable of being produced by an infection wholly confined to the nervous system; in other words, the assumption that there is an initial stage of general infection is superfluous, and without supporting evidence.

The paralytic stage.—It was formerly the practice to differentiate a number of types of poliomyelitis according to the localisation of the paralytic symptoms. Thus there were cerebral, cerebellar, brain-stem, spinal and neuritic types. As Weston Hurst has pointed out, it is impossible to produce in the experimental monkey, no matter what the site of inoculation of the virus, any but a spinal type of paralysis, and it is extremely doubtful if in the human disease there are any other than brain-stem and spinal cases. The remaining cases are probably due to some other cause than the virus of poliomyelitis, and they will not be considered here.

1. Spinal Form.—In young children, the paralysis is often not apparent until the second or third day of the illness. In older children and in adults, the paralysis is usually present within 24 hours of the onset. The paralysis is always of the flaccid variety, with loss of the deep reflexes in the region of the paralysis, and subsequent atrophy of the muscles if it is lasting; it develops very rapidly in most of the cases, and seems to have its full limit of distribution at the moment of its appearance, which facts correspond exactly with the experimental pathology. In some cases, however, the paralysis spreads rapidly from its original site, either in ascending or, more rarely, in descending fashion. The ascending cases are very liable to be terminated with fatal bulbar involvement. In rare cases, relapse occurs, and the paralysis, after remaining stationary for several days, may spread suddenly to other regions. This event, which is due to a recrudescence of the infection, has also been observed in experimental poliomyelitis. It is often stated that relapsing cases are usually fatal, but in a very considerable experience of such cases we have never seen a fatal issue, which on theoretical grounds should be highly improbable, on account of the rapid development of immunity after infection.

The paralysis is generally much more widely spread at the onset than it is destined to be permanently. At first all four limbs may be completely helpless, and later there may be complete recovery in all but one limb. The widely spread temporary paralysis is due to a recoverable affection of the nerve cells, whereas the permanent palsy is the result of an actual destruction of the cells by a necrotic lesion. The paralysis may affect any muscles of the body, but those of the legs are by far the most commonly involved, while those supplied by the nuclei of the brain stem are never permanently paralysed. The trunk muscles may be affected alone, giving rise to spinal deformity, usually of a scoliotic or kypho-scoliotic type. Thus, poliomyelitis

comes to be one of the very common causes of spinal curvature in the young. The narrowing down of the initial paralysis begins to show itself after the end of the first week, and any muscle which will recover useful power will have done so before the end of the third month. The paralysed muscles undergo atrophy, which is more rapid and complete in those cases in which there will be no subsequent recovery; they give the reaction of degeneration. They are flaccid from the first, and in the course of time tend to develop a variable degree of contracture, and yet it is common to see a limb which remains permanently flail-like. Any muscle which shows a response to faradism 3 weeks after the onset will completely recover. When a limb is paralysed, there is usually a considerable degree of vasomotor paralysis, and there may be subsequent retardation of growth. Considerable deformities of the body and limbs may arise as the result of the loss of support, which results from the paralysis, from the action of unopposed muscles, and from the contractures. Such deformity may involve actual dislocation of joints, as in the shoulder joint, where the deltoid is paralysed and the pectorals escape.

The local lesion of the spinal cord is by no means confined to the grey matter, and may involve the contiguous white matter of the lateral column sufficiently to give rise to signs of lesion of the pyramidal tract, and in rare cases of lesion of other neighbouring tracts, such as the spino-thalamic tract with a result in a Brown-Séquard's syndrome of pyramidal deficiency upon the same side and loss of pain and temperature sense on the opposite side below the lesion. Paralysis of the cervical sympathetic is not rare when the lower part of the cervical enlargement is involved, with the usual signs of a small pupil and low-lying lid on the affected side. It is, however, generally a transient event.

Disturbances of sensibility of an objective kind are rare, and are almost always transient, and amount to blunting of pain and temperature sensibility, from involvement of the spino-thalamic tracts which are continuous to the ventral horns. Subjective disturbances are common, and consist of severe local pains in the limbs, back and neck. Tenderness of the muscles, and pain on moving the joints are sometimes very prominent, and may persist for many weeks. The dominance of the clinical picture by persistent pains in the periphery constitutes the so-called "neuritic" form of poliomyelitis. Sphincter paralysis is quite common in the early stages in cases in which the lumbo-sacral enlargement is affected, but it is always rapidly transient.

The reflexes, both superficial and deep, are at first lost in the affected region, and indeed are generally absent throughout the body in the early stages of a severe case, from the general effect of the virus upon the nerve elements. In the later stages they return, or remain permanently absent, according as the muscles recover or not. Any sign of a returning reflex, either deep or superficial, in the early days of the illness is a most useful prognostic indication that the muscles concerned with the reflex will entirely recover.

2. The Brain-stem Form.—In this type, the incidence of the lesions is upon the grey matter of the brain stem from the medulla to the region of the red nucleus. The general symptoms of the onset are as in the spinal form. In place of the paralysis of trunk and limbs there is bulbar, facial, trigeminal or ocular paralysis, according to the situation of the lesions. An extensive lesion of the medulla itself proves very rapidly fatal. Lesions of

the upper brain stem are more commonly survived, and the resulting clinical pictures are, in order of frequency of occurrence, facial paralysis, spastic tremulousness from involvement of the upper part of the brain stem, and lastly ocular paralysis with nystagmus.

Course.—Most commonly within a few days of the onset of the paralysis a very considerable remission occurs, and the paralysis becomes much narrowed down in its limits; thus, with an initial paralysis of all four limbs and trunk, the limbs recovered rapidly, leaving a permanent partial paralysis of the trunk, and in a case where both legs were paralysed, the one recovered power within the first week, leaving the other permanently crippled. Sometimes, however, there is no rapid improvement or narrowing of the region of paralysis whatever.

The paralysis remaining after the rapid improvement is final, and admits of such improvement only as may occur from the recovery of a few cells which have escaped destruction upon the confines of the inflammatory lesions, and such recovery is very slow and never reaches more than a slight degree. A certain slow improvement in those paralysed muscles which retain some voluntary power is often observable, and is referable to hypertrophy of function in those elements which remain and to the acquisition of the aptitude which necessity produces. On the other hand, children afflicted with this disease during the period of active growth will often show what seems to be a progressive diminution of power in the weak muscles, and which is, in reality, a relative failure of these muscles under the strain of the increasing weight and length of the body and limbs.

Death is uncommon at any stage in the spinal form of poliomyelitis except during epidemics, when severe general symptoms are followed by widely spread paralysis, involving all the respiratory muscles, and in these cases it takes place on the first day of appearance of the paralysis. Weakness of the respiratory muscles and especially total intercostal palsy is not infrequently an indirect cause of death, even at long periods after the onset, if bronchitis or broncho-pneumonia occur.

Diagnosis.—During the stage of general pyrexial symptoms and before the paralytic manifestations appear, a definite diagnosis can hardly be made; but it may be suggested by the time of year, by the prevalence of an epidemic, and by the combination of a polymorpho-nuclear leucocytosis in the blood with a lymphocytosis in the cerebro-spinal fluid. When the paralysis first sets in, the diagnosis has to be made from acute rheumatism, in which the painful joints may cause an appearance of severe paralysis. In the same way, syphilitic pseudo-paralysis (acute syphilitic epiphysitis) may be diagnosed from poliomyelitis. From acute polyneuritis and Landry's paralysis, both of which maladies may have a pyrexial onset with similar general symptoms, poliomyelitis can generally be distinguished by the sudden onset of the paralysis and by the absence of any spreading tendency, and probably by the lymphocytosis in the cerebro-spinal fluid, and later on by the permanent atrophic paralysis. In the rare spreading types of poliomyelitis, the latter two points alone serve to make the diagnosis.

From almost all of the local lesions of the spinal cord, membranes and roots, whether these are of rapid onset, as for example hæmatomyelia and acute myelitis, or of slow onset, such as tumour, inflammation and pressure, poliomyelitis is at once distinguished by the absence of the conspicuous

sensory loss and sphincter trouble which accompany the former diseases. In the final stage of permanent muscular paralysis and atrophy, deformities and contractures, poliomyelitis presents little difficulty of diagnosis, but it should be borne in mind how frequently deformities of the trunk and especially lateral curvature of the spine have their origin in slight attacks of this malady where the lesions are confined to the dorsal region.

Poliomyelitis may simulate meningitis so closely as to be hardly distinguishable. The skin in the former malady may be suggestively flushed and pink. A sterile cerebro-spinal fluid with no micro-organisms and with a mixed lymphocytic and degenerating polymorph pleocytosis and with the chlorides and sugar content normal can hardly be from any other case than one of poliomyelitis.

Prognosis.—It is rare for complete recovery to occur in any case of spinal poliomyelitis in which paralysis has once set in. Though recovery may be nearly complete, yet there seems always to be some region in which permanent muscular atrophy persists, and in cases which otherwise clear up, this is frequently in the spinal muscles, giving rise to a lateral curvature. From this condition of nearly complete recovery to one in which there is not the slightest recovery from the initial paralysis, there is every gradation. The prognosis is not influenced by the severity or otherwise of the general symptoms, for the paralysis may be slight where the general symptoms are severe, and vice versa. Incomplete paralysis or the presence of reflex action, either superficial or deep, in any region at the end of the first week after the paralysis has set in, is a sure indication that useful recovery will occur in that region. Those regions which remain completely paralysed for several weeks after the onset are certain to remain permanently disabled. The prognosis as to the eventual usefulness of disabled limbs, or as to eventual power of walking, depends upon a consideration of the muscles which are permanently paralysed, as to whether they are essential muscles or not, and whether they can be assisted or supplanted by any mechanical apparatus which is light enough for the weak limbs to carry.

Second attacks of poliomyelitis are exceedingly rare, but two such cases have been recorded by Eshner and by Sanz. The occurrence of progressive muscular atrophy in subjects who have in early life been afflicted with poliomyelitis is not very rare, and it is usual for the progressive atrophy to commence in the region originally affected by the poliomyelitis. Potts has recorded a series of 28 such cases, and several others are to be found among the records of the National Hospital.

Treatment.—In the acute stage, the patient should be kept at rest upon a soft bed and fed upon a diet suitable to the febrile condition. Since the malady is an infectious, specific fever, and since the virus is known to exist upon the nasal, buccal and respiratory mucous membranes, and is presumably spread therefrom, bed and utensil isolation is necessary, with sterilisation of any contamination from the mucous membranes and mild daily disinfection of the mouth and nose. Salicylates, especially in the form of aspirin, will relieve the pain and fever, and seem to be decidedly beneficial. If pain be very severe there is no contra-indication to the use of morphine. If the respiratory muscles are seriously involved, belladonna or atropine is of great service both in stimulating the respiratory mechanism and in checking accumulation of bronchial secretions.

In cases in which the respiratory musculature is involved and in which a fatal issue may for this reason ensue, apparatus has been devised to effect an artificial respiration in the hope that the paralysis may recede and the respiratory musculature resume its function. It is particularly during epidemic outbreaks that such cases are seen, the paralysis progressively ascending from the lower limbs, or spreading by "jumps" at short intervals. There are two main types of apparatus, the Drinker respirator and its derivatives which consists of a closed compartment in which the patient lies recumbent, his head protruding through a rubber collar. A motor then produces alternating air pressures which passively move the chest. Another type, the Bragg-Paull respirator, consists of a rubber apparatus strapped round the chest which, again by the use of a motor, by alternate inflation and emptying, moves the chest. There may be a few cases in which a really good result can be achieved, namely, a useful measure of general muscular recovery ensues and the patient can take up a more or less active life. More numerous, however, are those in which although sufficient active thoracic movement to sustain life returns, the patient remains bedridden for life. Cases are on record also in which survival depends upon permanent retention in a Drinker respirator. It is probable, therefore, that such machines will find their greatest field of usefulness in other maladies than poliomyelitis, such, for example, as carbon monoxide poisoning and other essentially temporary causes of respiratory weakness. A modification of the Drinker machine is now provided in most hospitals throughout the country.

It has recently been claimed by Contat in Switzerland that heavy dosage with potassium chlorate during the pre-paralytic stage of the illness averts the development of paralysis. It is known that the virus of poliomyelitis is highly sensitive to oxidising agents. The patient is given nasal instillations of 2 per cent. solution of the substance, 5 drops four times daily. By mouth the dose ranges from 5 grains in the 24 hours in an infant to a total daily dosage of from 60 to 80 grains in an adult. This total is spread over frequent small doses during the 24-hour period. The administration is begun as early as possible and continued during the febrile period (2 to 3 days), and progressively diminished to cease on the fifth or sixth day. It is said that no albumin, red cells or casts are found in the urine during this medication. Contat also employed potassium chlorate as a prophylactic in contacts.

Serum therapy.—Since Netter first initiated this method of treatment some twenty-five years ago, the administration of the serum of individuals who had recovered from a known attack of poliomyelitis ("convalescent serum") has been a widely used method of treatment. Convalescent serum has been experimentally found to contain protective antibodies, and it has been thought that it may prevent the development of paralysis if administered during the preparalytic stage, and may limit the extent and severity of paralysis if given early in the paralytic stage. Recent re-assessment of the clinical evidence strongly suggests that these beliefs are illusory, and that serum therapy is unavailing at any stage of the malady. This result is indeed what the experimental evidence should have led us to expect. For Flexner found that the administration of convalescent serum to an inoculated monkey protected only if it were given at the same times as the dose of virus, or within 12 hours and *before* the appearance of symptoms. Administered after this moment, it was uniformly ineffective. But it is only after the

appearance of symptoms that it can be given in the human subject. Again, the theory adopted to rationalize serum therapy was that poliomyelitis was a general infection, with later involvement of the nervous system. Serum administered in the preparalytic stage was thought to prevent invasion of the nervous system. We know now that the nervous system has already been invaded before any symptoms whatever develop, and that this supposed prevention is from the nature of things quite impossible. Recent controlled observations in New York, in which 50 per cent. of the patients in an extensive epidemic were given serum and the remaining cases denied it, have indicated that serum therapy has no influence upon the course of the individual case.

Kleinschmidt, in his analysis of the 1938 epidemic in Cologne, adds further confirmation to this judgment.

Rest and posture.—It is all-important to secure as complete physiological rest as is possible for the weak or paralysed muscles for some time after the onset. Even in the slightest cases, the patient should be kept in bed for at least 3 weeks, during which time attempts at volitional movements should be discouraged. The posture of the paralysed region should be such as to secure the relaxation of the paralysed muscles; for if they are kept stretched by the action of opponent muscles which are not paralysed, recovery is greatly hindered. Appropriate postures can be secured by pillows, sandbags, splints and other devices. After a few weeks have elapsed, massage and passive movements should be regularly employed and re-educational exercises commenced, where there is sufficient power. Electrical treatment in any form is of very doubtful value. Re-education should be assisted by every appropriate mechanical device, but it must be carefully borne in mind that every mechanical apparatus which overweights the weak limb places a millstone around the neck of recovery. The lightest possible shoes should be worn, and if splints are indicated the excellent and almost weightless, moulded, celluloid splints should be employed, to the absolute exclusion of all heavier varieties. In the re-education of the legs for walking, a walking-machine on wheels is a necessity. Contractures and deformities, which hinder useful action, should be dealt with by passive movements, splinting, tenotomies and other surgical procedures.

There have recently been recorded several cases of acute bulbar poliomyelitis in children upon whom tonsillectomy and adenoidectomy had been performed during the course of a local outbreak of poliomyelitis. It appears that this operation opens a port of entry to the virus. The onset of the disease is at an interval of 10 to 20 days after operation, and the issue is commonly fatal. The performance of these operative procedures upon children is therefore strongly contra-indicated during outbreaks of poliomyelitis.

LETHARGIC ENCEPHALITIS

Synonym.—Epidemic Encephalitis.

Definition.—An acute febrile disease, occurring sporadically and epidemically, due to the infection of the nervous system, presumably from the nasal passages and by a purely axonic route, by a virus, which can be inoculated into the nervous system of monkeys, reproducing the disease. The

clinical aspect is that of a lasting, as opposed to an evanescent, infection, producing chiefly inflammatory reaction, and principally incident upon the upper parts of the nervous system, the cerebrum, basal ganglia and brain stem. Though very definite, it is remarkably polymorphic, and it is sometimes mono-symptomatic, and its type has changed greatly during the passage of an epidemic. The absence of evidence forthcoming of case-to-case infection has necessitated the assumption that infection is transferred by carriers, or by those in the pre-symptomatic stage of infection only.

History.—When we read of the influenza epidemic which swept over Europe in 1580 and which was accompanied by a malady so peculiar as to gain the title of "schlafkrankheit," and afterwards of the epidemic described by Sydenham in 1675 as "febris comatosa," the "sleeping sickness" of Tübingen in 1712 and Dubini's epidemic of the fatal "electrical chorea" in Northern Italy in 1846, we cannot but agree with von Economo's conclusion that these epidemics were epidemics of lethargic encephalitis. The subsequent epidemics of Mauthner's "Nona" in Piedmont in 1891, and also Pfuhl-Leichtenstern's "hæmorrhagic encephalitis" in 1905 have been proved identical with lethargic encephalitis, both clinically and pathologically. The malady became pandemic from 1917, reaching a maximum in 1920, since when it has gradually declined and it is now comparatively rare, if indeed any true cases occur. We have, however, seen a good many end-results of cases which had their commencement from 1910 onwards, showing that in England this malady was increasingly present, though unrecognised.

Ætiology.—During the period of its incidence, the disease occurred both sporadically and epidemically, with no centre of spread. It was more prevalent in the cold season of the year. No age is exempt from the malady, and cases have occurred in the seventh decade of life, but it is rare in young children and seems to be most incident in the first half of adult life. Infection presumably takes place, as in poliomyelitis, from human vectors alone, and by droplet infection. When once the virus has gained access to the nervous system by a peripheral axonic route, it is "virus en cage," to use Economo's term. It is imprisoned within the nervous system and cannot get out, but it may there survive for very long periods, giving rise to second and third attacks after apparent recovery, or to exacerbations of symptoms after long intervals of remission, or to insidious and progressive severe abrogation of nervous function long years in train of slight trivial and evanescent symptoms which marked the epoch of infection. Whether the infection thus pent up in the nervous system does on occasion manage to escape from the peripheral nerve terminals, as it does regularly into the saliva in the case of rabies and often into the skin in the case of herpes, and so get free, has not been determined.

The height of the epidemic incidence of lethargic encephalitis has many times coincided with a severe epidemic of influenza, but no further connection between the two conditions is known. Claimed at one time as an aberrant form of poliomyelitis infection, von Economo's disease has proved quite distinct, both in its age incidence, seasonal prevalence, morbid anatomy and symptomatology. Economo first succeeded in transferring the disease to the monkey by intracerebral inoculation in 1916, and Loewe and Straus first proved that the infective agent was filtrable.

Pathology.—The pressure and quantity of the cerebro-spinal fluid are

always increased, and in a few of the cases blood or the products of hæmorrhage are present. In a third of our cases the cell count has been normal. In the rest there has been a moderate lymphocytic pleocytosis, with little or no protein increase, the titre of the sugar tending to a high normal and that of the chlorides being normal. No prognostic indications can be derived from the nature of the fluid. The vessels of the brain are markedly congested and full of blood, and the colour shows a characteristic change from the normal throughout the whole of the grey matter, varying from a rosy flush to a deep salmon-pink, giving rise to the term "the rose-coloured brain." When hardened in formalin, this colour becomes a heavy purple grey. Both subdural and deeply seated hæmorrhages are occasionally found. Economo describes the anatomical picture as one of unvarying constancy. It is that of an œdematous and congested brain, with all the grey matter conspicuously reddened in contrast to the white matter, which is of normal colour. There is a non-purulent and, properly speaking, a non-hæmorrhagic inflammation of the whole grey matter exclusively, the white matter being uninvolved. There is most conspicuous perivascular lymphocytic cuffing remarkable for the absence of any polymorphs, with an intense cellular infiltration of the grey matter with elements of the microglia, while the neuroglia is unaltered and demyelination does not occur. Accompanying and succeeding these inflammatory changes is a certain measure of neuronophagia, with primary loss of the ganglion cells.

Symptoms.—In the acute forms of the malady the onset is often ushered in by general symptoms, such as shivering, malaise, headache, and fever and bodily pains, a characteristic thickly coated white tongue and constipation, and sometimes vomiting and persistent hiccough. This train of symptoms usually appears in the story as an attack of "influenza." The pyrexia does not usually last longer than a week. Countless such attacks of "influenza," distinguishable only by the occurrence of transient diplopia, or of slight somnolence, and often even without any such distinguishing features, have been completely recovered from at the time, but have been followed, after long intervals, by the slow onset of the Parkinsonism of lethargic encephalitis. Again, the epoch of infection may apparently give rise to no symptoms at all, and long afterwards an insidious onset of Parkinsonism ensues, as has happened nowadays in many of the examples of Parkinsonism in childhood.

So many and varied may be the clinical aspects of this disease that it is useful to consider the separation of clinical types which Economo has laid down:

A. Acute Types.

(1) The somnolent and ophthalmoplegic type.
(2) The hyperkinetic type. Spontaneous involuntary movements, sleeplessness, great mental unrest, delirium and mania are here characteristic.
(3) The amyostatic and hyperkinetic type. In this type Parkinsonian tremor and rigidity, salivation and the greasy face are conspicuous.
(4) The cerebellar type. The symptomatology is that of the cerebellum, and recovery usually occurs.
(5) The bulbar type.
(6) The ophthalmoplegic type.

(7) The neuritic type, which simulates acute fibrositis.
(8) The mono-symptomatic type :
  (*a*) Characterised by persistent trismus.
  (*b*) Characterised by persistent hiccough.

B. Chronic Types.
(1) The progressive Parkinsonian type.
(2) The mental type.

A combination of all the types is very common.

THE NERVOUS SIGNS.—*Mental symptoms.*—An increasing lethargy, which often becomes very deep, is present in many of the cases. In this condition the patient will lie for days without stirring a muscle, taking no heed of his surroundings and passing the dejecta under him unheeding. Yet when roused by command and vigorous bodily stirring, he will wake up and hold a very intelligent conversation, lapsing back at once when he is left alone, even though his mouth be half full of unswallowed food. In this condition, flexibilitas cerea may often be demonstrated in the limbs. The lethargy may last for three weeks or longer even in patients who completely recover. It passes away gradually. Unrousable coma is invariably a sign of impending dissolution. Subsequent memory of events during the early days of the lethargy may be remarkably retained. Insomnia may be a troublesome early symptom, and even when the patients are markedly lethargic they will complain that they cannot sleep. Lethargy, however, may be completely absent and the early mental state be that of vivacious excitement and talkativeness. Irritability and restlessness may be present. In some cases the first nervous sign may be delirium or mental aberration, which may rapidly develop into acute and violent mania ; such cases are rapidly fatal. In cases which recover after severe symptoms, considerable mental reduction and self-obvious mental change may persist, but we have not seen any case in which insanity has resulted. Indeed, it has been said that no sufferer from this disease ever regains his original mentality, and it is a common experience to find personality very seriously changed in the way of mental reduction. Complete incapacity for any sustained work, entire change of character, anti-social tendencies, moral perversion and depressed neurasthenic states are not uncommon sequels of the disease. (See also page 1833.)

Convulsions are very rare, but they may undoubtedly occur as in other forms of encephalitis. Indeed, the initial clinical picture may be dominated by convulsion, and closely resemble " status epilepticus " from other causes.

Ophthalmoplegia and other paralyses in the region of the cranial nerves are most often nuclear in type, but peripheral paralysis of any cranial nerve may be met with, most commonly unilateral paralysis of the facial nerve. The pupils may show every abnormality which a lesion of the nervous system can produce. Inequality, unroundness, eccentricity and loss of light reflex and ciliary paralysis may occur. The loss of light reflex may be unilateral. The external ophthalmoplegia, being nuclear in origin, involves both eyes in terms of their conjugate movements, and the upward and downward movements are as a rule more severely impaired than are the lateral movements. Bilateral ptosis is very usual, and is a most important and valuable early indication of the disease. The common error is to consider it part of the sleepy state. The nuclear ophthalmoplegia is often irregular, giving

rise to strabismus and diplopia. Either in addition to the above or existing alone, there may be peripheral paralysis of any of the oculo-motor nerve trunks. The degree of the ophthalmoplegia varies in different cases from slight diplopia with hardly noticeable strabismus to complete paralysis of both eyes. It may be rapidly transient or permanently severe. In severe cases which survive there is always some improvement in the degree of paralysis in the course of time.

Vision.—The diplopia and loss of accommodation cause much defect of vision, but many of the patients complain of a loss of vision in each eye, which is too great for any such explanation, the cause of which is not yet explicable. Papilloedema has been reported in a few cases, in one of which at least meningeal hæmorrhage had occurred. It is transient and never reaches a high degree.

Oculogyric crises.—This term is applied to recurring attacks of tonic conjugate deviation of the eyes, most commonly upwards, sometimes upwards and to one side, less commonly downwards, or downwards and to one side, We have observed one case of a child in which the oculogyric spasm always proceeded to a torsion spasm of neck, trunk and limbs so severe as to roll the patient out of bed on to the ground with each access. The spasm is met with in the chronic stage of the malady, and there is always some degree of Parkinsonism. The attacks may last from a few seconds to 4 hours or more, and may occur frequently or at intervals of several days, and as the eyes are commonly fixed in an upward direction, they are peculiarly incapacitating. They have not been reported in any other disease than lethargic encephalitis, and may constitute, with some slight facial Parkinsonism, the sole sequels of this malady. We have not found any treatment which influences the frequency or severity of the attacks.

Bilateral nuclear facial paralysis and bulbar paralysis are not uncommon. Paralysis of any individual cranial nerve may occur, and also of any individual spinal root. Such paralyses always completely recover in the course of time.

Symptoms indicative of lesion of the basal ganglia are among the most common features of the disease, and they are often the most persistent. These consist of weakness of movement, rigidity with slowness of movement, and spontaneous involuntary movements. The weakness, rigidity and slowness of movement give rise to a peculiar immobility of facial and bodily expression and movement. The face is mask-like, the neck stiff and the head moved little and slowly, the trunk bent forward and stiff, the arms held away from the trunk, the whole appearance of the patient closely resembling that of paralysis agitans. Rapid fluttering of the eyelids when gently closed is characteristic of this condition. The spontaneous involuntary movements may be of a rhythmic tremulous nature, as in paralysis agitans, or there may be slow rhythmic, choreiform, athetoid, myoclonic, irregular or highly complicated movements: these may be met with at any stage of the malady, but most commonly appear some little time after the acute stage has passed away. Fibrillation and fascicular twitching of the muscles is very common in the acute stage. In cases where bulbar symptoms, either of a spastic or flaccid kind, are present, hypersalivation of the nature of a true sialorrhœa is often a most troublesome, though transient, symptom.

In addition to the above common symptoms and signs, other indications of involvement of the cerebral hemispheres may occur. Bilateral spasticity

with signs of involvement of the pyramidal systems, increased jerks, lost abdominal reflexes and extensor plantar responses are common. Hemiplegia, aphasia and hemianopia may occur, presumably as the result of local subcortical hæmorrhages. Meningeal symptoms may be very marked in the early stages, such as suboccipital headache, painful stiffness of the neck, head retraction, vomiting and Kernig's sign. Indeed, we have seen rapidly fatal cases in which the clinical picture throughout was hardly distinguishable from that of acute meningitis, but none of these cases showed any leucocytosis in the cerebro-spinal fluid. A major incidence of the lesions upon the cerebellum gives rise to the picture of acute cerebellar ataxy following a lethargic onset, and the end-result may be a condition closely resembling a usual type of disseminate sclerosis. Such cases make a good recovery in the course of time.

Peripheral pains are sometimes very severe and are usually quite local. They may be the first signs of the illness, and several of our patients had been treated for trigeminal neuralgia, brachial neuritis or sciatica before any other sign of the malady appeared. These pains may persist for months after recovery. They are obviously due to the lesion around the nerve roots which has been already referred to.

Spinal symptoms.—Since the lesions have been found in the spinal cord, it is only to be expected that focal spinal lesions should be met with in rare cases. These are usually acute atrophic paralyses similar to those of poliomyelitis. Those that we have seen have completely recovered. It has been argued, however, that this atrophic palsy is due to a lesion of the spinal roots. More severe lesions may apparently give rise to a condition resembling acute transverse myelitis.

Sphincters.—The incontinence which is almost constantly present, even when the lethargy is far from deep, is the result of the lethargy. Transient conscious dysuria is however not infrequent in the early stages of the disease. The deep reflexes may be lost in severe cases during the acute stages, and they are usually absent in premortal conditions. Otherwise they tend to be exaggerated, especially if involvement of the pyramidal system be present. The condition of the abdominal and plantar reflexes depends upon the presence or absence of lesions affecting the pyramidal tracts. In the former case, the abdominal reflexes will be absent and the plantar reflexes of the extensor type.

Attention must be drawn to a group of cases in which the initial manifestations of the disease are so slight as not even to interfere with the daily work or to call for medical attention, and yet in the course of months, or it may be even years, the most serious and completely incapacitating paralysis appears. A patient of ours noticed that he saw double, and did not feel very well for a few weeks. He recovered, but, two years later, had to give up work, by reason of a slowly oncoming Parkinsonism, which became extreme. A similar result in the slow and late development of grievous symptoms may follow any attack of lethargic encephalitis and make the prognosis in this malady very difficult.

Sequelæ.—The disabilities which this malady may leave in its wake seem endless and ever increasing as clinical experience widens. The mental, paralytic and Parkinsonian end-results have already been referred to, but special mention must be made of involuntary spontaneous movements,

recurring rhythmic movements, spasms and altered respiratory rhythm. Ceaseless rhythmic pulsatile movements may occur in any muscle, movements like those of convulsive tic may incapacitate the patients. Hideous recurring spasms may appear, sometimes local, sometimes general. Torticollis may occur. An unduly rapid respiratory rhythm may be established. (See also p. 1705.)

Course.—The course of the disease is extremely variable. It may be a slight transient illness lasting but a few days, and leaving no sequelæ after a few weeks; or a most malignant disease, fatal in a few days. In others, symptoms indicative of fresh lesions may occur repeatedly weeks and even months after the onset.

Diagnosis.—A diagnosis of lethargic encephalitis is even at this date (1941) not rarely made, but must be received with the very greatest reserve. Under this title most neurologists have encountered a great variety of nervous disease, including intracranial tumour, cerebral abscess, subdural hæmatoma, tuberculous meningitis, and the like. In typical cases the diagnosis presents no difficulty, the rousable lethargy, incontinence, ophthalmoplegia and negative, lymphocytic, or blood-containing cerebro-spinal fluid being so characteristic as to preclude possibility of error. The less usual forms of the malady, and especially those with very gradual onset and slight symptoms, often present great difficulty and require much care and full knowledge of the possible symptomatology of the disease for their recognition. There is no specific laboratory test for the malady, and the diagnosis must be based upon clinical grounds. Where meningeal symptoms are prominent, distinction has to be made from other forms of meningitis and from poliomyelitis. Here, the cerebro-spinal fluid is of the highest importance, as no polymorpho-nuclear leucocytes occur in lethargic encephalitis. In cases commencing with peripheral pains, excitement, maniacal symptoms or convulsions, careful look-out should be kept for the advent of ptosis, ophthalmoplegia, or lethargy, the appearance of which, following such symptoms, should at once suggest the diagnosis. It must be borne in mind that the clinical picture of the disease may be dominated by a hemiplegic condition, and that an apoplexy may occur during the acute stage of the disease. Slight cases of the disease are frequently unrecognised, or are indeed unrecognisable in the early stages, but here the diagnosis can often be made with certainty from the end-results; the peculiar ophthalmoplegia, the spontaneous involuntary movements, and the paralysis agitans-like syndrome being almost pathognomonic of the malady.

Prognosis.—A rapid onset and quick development of severe symptoms, marked pyrexia, delirium and maniacal excitement are bad prognostic signs and indicate a rapidly fatal issue. After the third week of the disease, the probabilities are all in favour of survival. The prognosis, however, as to how much permanent damage to the nervous system will eventually remain is hardly possible, since slow improvement may go on for months and even years. Of the acute cases occurring at the height of an epidemic, 40 per cent. are quickly fatal, 30 per cent. are reduced to chronic invalidism, and 30 per cent. recover completely (Economo). The spontaneous movements, even when very marked, may clear up in from 3 months to a year. The weakness, rigidity and tremors, which form the paralysis agitans-like picture in many of the cases, persist indefinitely.

Treatment.—Nothing being known of the infectivity and mode of spread of the disease, isolation and disinfection are not usually employed. Each case must in England be immediately notified to the public health authorities. No treatment is known which has any specific influence upon the disease. Intravenous injection of collosol iodine solution (150 c.c. for a dose), repeated on the second and fourth days, has been advocated, and is certainly without harmful effects. Intravenous sodium salicylate, in 15-grain doses in normal saline daily, certainly seems to clear up the symptoms in some cases and may do permanent good. It remains therefore to use those measures which will help to keep the patient alive and those which relieve symptoms. Relief of the constipation is most important and is often followed by striking improvement in the symptoms. After the acute stage, treatment is concerned with combating the physical and mental listlessness and depression, removing the rigidity with massage, passive movements and exercise, and withal brightening the days of a convalescence which is often long, tedious and hard to bear.

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Revised by F. M. R. WALSHE.

HERPES ZOSTER

Synonym.—Zoster; Shingles.

Definition.—An acute infection of the posterior root ganglion, probably by a neurotropic virus, leading to severe pain in the distribution of the corresponding posterior root, and to the appearance of a crop of vesicles in the cutaneous distribution of the root.

Ætiology.—The virus of zoster stands in some as yet undetermined relation to that of chicken-pox, and the appearance of the latter malady in a susceptible subject some 14 days after contact with a case of zoster has been too frequently recorded to be of the nature of coincidence.

The disease is seen at all ages, but according to Head is perhaps most common in adolescents. In elderly patients it is frequently a more serious as well as a more painful affection than in young persons. It may arise without discoverable cause and with a febrile reaction and considerable malaise. It may also occur apparently "symptomatically" during the course of arsenical medication, or during such illnesses as pneumonia, tabes dorsalis and tuberculosis.

Pathology.—The essential lesion is an acute inflammation of the dorsal root ganglion of the same histological character as the lesion of acute anterior poliomyelitis. There are degenerative nerve cell changes, with accompanying microglial reaction and perivascular infiltration with round cells. Later, degenerative changes occur in the fibres of the dorsal roots and of the peripheral sensory nerves. The Gasserian ganglion and the thoracic and upper two or three lumbar ganglia are most often affected. There is an increased protein and lymphocyte count in the cerebro-spinal fluid.

Symptoms.—There may be an onset with fever which persists for 2, 3 or even 4 days. There is from the first pain at the place at which later

the herpetic eruption is to appear. This occurs on the third or fourth day of the illness. At first the rash is a patchy erythema, upon which appear small vesicles filled with clear fluid. From the fifth to the tenth day the vesicles dry up and shrink progressively until a scab is formed. This finally drops off, sometimes leaving considerable scarring. These scars may be anæsthetic to touch, pinprick and temperature sense. The pain before and during the evolution of the cutaneous lesion may be intense. It is of a burning and itching quality, and in frail and elderly persons it may persist as a most intractable post-herpetic neuralgia for months or even years.

Zoster of the ophthalmic division of the fifth nerve is most commonly found in elderly persons. Corneal vesicles may form and burst, giving rise to ulcers, which may spread and end in residual scarring (nebulæ), which impairs vision.

Herpes of the geniculate ganglion occasionally occurs. The vesicles are found in the pinna, and there is pain in this region, over the mastoid, and sometimes in the fauces (see p. 1512).

Localised paralysis may accompany herpes. Thus, in ophthalmic herpes there is occasionally third-nerve palsy, with ptosis and squint. In geniculate herpes, facial palsy and loss of taste over the anterior two-thirds of the tongue is the rule. In herpes of the lower thoracic ganglia there may be paralysis of the oblique abdominal muscles on the affected side. The marked local bulging of the abdominal wall which ensues resembles at first sight the presence of an abdominal tumour. These paralyses do not invariably clear up, though the facial palsy of geniculate herpes does so more frequently than the paralysis of the abdominal muscles.

Treatment.—The course of the cutaneous lesions is not influenced by treatment, which is directed to keeping the vesicles dry and free from infection. For this purpose a dusting-powder of starch or zinc oxide, or a collodion dressing may be used.

During the acute stage, pain may be relieved by aspirin or phenacetin, but the post-herpetic neuralgia of some elderly and debilitated patients may prove intractable, and so severe as to render life scarcely tolerable. A neurosis may be grafted on this pain and render the situation extremely difficult for the doctor. Various local remedies have been recommended, including rays of all kinds, local heat, electrical currents, analgesic applications, and so on. But none can be relied upon to afford material relief, though the neurotic patient may obtain some comfort from any of them that commands his faith. It may be necessary to keep the patient under some such mixture as the following: tinct. gelsemi min. 10, phenazone grs. 10, phenobarbitone sol. gr. ½, sod. bromid. grs. 10. Aq. chlorof. ad fl. oz. 1 t. d. s.

A warning may be sounded against prolonged bromide medication for elderly subjects. It sometimes renders them confused and feeble, and these debilitating effects may take some weeks to pass off even after bromide is withdrawn from administration. For such patients, small and carefully adjusted doses of phenobarbitone are probably better.

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RABIES

Synonyms.—Hydrophobia ; Lyssa.

Definition.—This is an infective disease due to a filtrable virus which is located in the salivary glands and central nervous system. It is transmitted to man and most warm-blooded animals through infective saliva of canines or blood-lapping bats. There is a long and variable incubation period, and a short pyrexial illness of sudden onset characterised by fever, nervous exaltation and violent muscular spasms involving the œsophagus and respiratory system. Once symptoms have supervened, the patient invariably succumbs.

Ætiology.—The disease is generally transmitted either by the licking of a freshly abraded surface of skin or the bite of an infected dog. In Eastern Europe and the Orient, wolves not uncommonly transmit the disease and, owing to extensive laceration of the tissues, a greater proportion of people bitten by them develop the disease than with either dogs or jackals. It has been estimated that wolf bites entail a mortality of 80 per cent. In Trinidad, in 1925 an epidemic of paralytic rabies in man was attributed to the bites of vampire bats, cattle being the original source of infection.

The virus of rabies.—This is now known to belong to the class of neurotropic viruses that have a special affinity for attacking the grey matter of the nervous system. To this class belong also the viruses of acute anterior poliomyelitis and of Borna disease.

Pasteur, in 1881, discovered that rabies could be transferred in series from animal to animal by subdural inoculation of emulsions of central nervous tissue derived from an infected dog. In rabbits, after some twenty passages, the virus became modified : firstly, the incubation period of ordinary street virus which varied from 8 to 60 days was reduced to 7 days ; and, secondly, it lost its capacity to reproduce the disease on subcutaneous inoculation. Such a virus is known as fixed virus or virus fixé. Street virus, on the other hand, is transmitted from the local wound via the peripheral nerves to the central nervous system, and if the sciatic nerve be inoculated the lumbar cord becomes infectious several days before the virus can be demonstrated in the brain (di Vestea and Zagari). This accounts for the fact that cases bitten about the face, head and neck have such a short incubation period. The salivary virus is filtrable through coarse Chamberland and Berkefeld filters —not so, emulsions of infective brain tissue. The virus is destroyed at 50° C. and is attenuated by drying—a fact made use of in the preparation of antirabic vaccine by the Pasteur method.

Pathology.—Excess of cerebro-spinal fluid, petechial hæmorrhages of the piarachnoid and injection of its vessels may be found at autopsy. Histological examination reveals cellular infiltration of the perivascular lymph spaces as well as Negri bodies within the cytoplasm of the nerve cells and their processes. These bodies were described by Negri in 1903. They are globular or ovoid structures, of variable diameter (0·5–25·0 microns), and are especially common in the Purkinje cells of the cerebellum and the hippocampus. Though demonstrable in the brain of 97 per cent. of dogs infected with street virus, they never appear in the salivary glands—a fact which supports the view that they are not parasitic protozoa, as Negri suggested, but rather some kind of cell inclusion or degenerative structure.

Symptoms.—The period intervening between the bite and the clinical

manifestations varies from 1 to 2 months as a rule, the limits being 11 days to over a year. Face, head and neck bites have a shorter incubation period than those on the upper extremity, and arm bites a shorter incubation than those implicating the leg. The onset is generally sudden, but prodromal symptoms are sometimes noted for a day or two before a hydrophobic syndrome appears. For convenience, three stages are described.

1. *The invasion stage.*—This includes prodromal features such as pain in the scar, fever, headache, rapid pulse, anxiety, restlessless, insomnia, irregular and sighing respirations, and phases of rushed speaking.

2. *The stage of excitation.*—This supervenes in 24 to 48 hours. There is intense restlessness, mental excitement, hyperæsthesia and hydrophobia which consists of a sudden spasmodic spasm of the muscles of the mouth, pharynx and larynx and, to a greater or lesser degree, the whole respiratory musculature. A typical attack may be induced by offering the patient water. As the glass approaches the mouth, the head retracts in a series of spasmodic jerks associated with gasping respirations, while any water reaching the mouth is immediately ejected. The shoulders are elevated, the chest expanded, and the sterno-mastoid and platysma muscles contracted. Later, the synaptic resistance in the reflex arcs becomes so lowered that a variety of sensory stimuli such as a sudden sound, cold air, strong light, a strange smell, and even the suggestion of water may suffice to induce the attack. The voice is altered. Frothy saliva collects in the throat and mouth and is flung off the lips during the attacks which may be characterised by intense fury or the most profound terror. Later, opisthotonus and general respiratory spasm are superadded. In the interval the mind is clear, the patient remaining quietly at rest in bed. Examination of the central nervous system reveals, as a rule, nothing more than increased deep reflexes. Glycosuria is not uncommon, and vomiting, exhaustion and emaciation characterise the final stage of the illness. Death during the paroxysm may occur from dilatation of the right heart, though sometimes near the end the spasms ameliorate or cease altogether.

3. *Stage of paralysis.*—If the patient survives long enough, paralysis of various types, including Landry's ascending paralysis, paraplegia and hemiplegia, may supervene. The patient lies helpless and exhausted, and generally dies in coma. In man this stage is rarely seen in canine-transmitted rabies, but paralytic rabies is commonly encountered in the bat-transmitted variety in Trinidad.

In the Trinidad outbreak all the cases were of this variety, and all proved fatal. The onset is acute, with fever and headache. Numbness and burning sensations in one or both legs, paresis of the legs and retention of urine follow. After 2 or 3 days the paraplegia becomes more complete, and the plantar and tendon reflexes disappear. One limb is commonly affected before the other. In a few days the paralysis begins to ascend, involving the muscles of respiration, of articulation and deglutition. There is dyspnœa, restlessness and death. The sufferer remains conscious, but may be delirious. Sensory changes are of variable intensity. A final brief coma precedes the fatal issue. During this time the temperature swings round 103° F., and there is profuse sweating. Hydrophobic symptoms are exceptional, and when present slight. The cerebrospinal fluid yields an increased globulin content, but is otherwise normal. The duration of the illness is from 4 to 8 days.

Rabies in the dog.—These animals never show the hydrophobic syndrome

observed in man. The earliest manifestation appears to be a change in temperament, followed by irritation and exacerbations of vicious fury in which the animal runs amok, biting wildly anything in its path. Later, swallowing becomes difficult, the bark is altered, the jaw drops and general paralysis ensues. Death invariably follows some 2 to 5 days after the first symptoms appear. In dumb rabies the stage of excitation is absent.

Diagnosis.—As a rule, little difficulty is experienced in diagnosis, but occasionally tetanus, the cerebral type of typhus fever, bulbar paralysis from any cause, and datura and other poisonings encountered in Oriental countries may need differentiation. Lyssophobia or hysteroid counterfeiting of the disease generally manifests itself within the first 10 days, and is unaccompanied by fever or other serious features.

Prognosis.—By no means all patients bitten by rabid animals die, but once clinical manifestations appear the disease invariably ends fatally. Estimates varying from 5 to 33 per cent. have been made of the death-rate in untreated patients, but of those receiving early anti-rabic inoculations in Pasteur institutes, not more than 1 per cent. die. The mortality varies with the site of the bite, the interposition of clothing, the number of tooth-marks, the extent of tissue laceration and the rapidity with which efficient local treatment has been instituted. Head, face and neck bites are particularly dangerous, as well as bites from wolves and jackals.

Treatment.—This is entirely preventive, and in England the muzzling order and the strict quarantine of all imported dogs has led to the eradication of rabies. In endemic areas canine bites should be promptly treated, and the suspected dog chained up, muzzled, and kept under observation. Should the animal be alive at the end of 10 days it is proof that the bitten person has not been infected. This rule, universally followed in Pasteur institutes, is based (1) on the knowledge that the infected dog never survives longer than 6 days from the onset of its illness, and (2) that the saliva of a rabid dog is never infective for more than 4 days before the onset of symptoms. In suspicious cases, especially the head, face and neck bites, treatment should be commenced without delay and discontinued if the dog survives.

The virus of rabies differs from that of yellow fever in not passing through the intact skin, and where there is a history of being licked by an animal suspected of rabies prophylactic inoculation need not be advised unless fresh skin abrasions were present at the time.

Local treatment.—If seen within 30 minutes, bleeding should be encouraged by the application of a ligature just tight enough to obstruct the venous return and the parts bathed with permanganate solution. Subsequently, each tooth-mark should be probed separately and cauterised or treated with pure phenol. For 3 days the wound should not be sutured; this particularly applies in the case of face bites.

Anti-rabic vaccination.—Owing to the long incubation period, it is feasible to attempt immunising the patient either by the inoculation of attenuated, living, fixed virus, as in the Pasteur and Högyes methods, or by the injection of carbolised or etherised vaccines in which the fixed virus has been killed. The Pasteur treatment consists of a series of 18 injections of emulsions made from the spinal cord of rabbits which had been dried for periods of from 14 to 3 days. Semple introduced carbolised vaccine; the most potent preparation consists of a 5 per cent. carbolised suspension of sheep brain

infected with Paris virus. In mild cases the course consists of 2 c.c. injected subcutaneously each day for 7 days; in average cases of 5 c.c. for 14 days; and in severe cases, such as head, neck and face bites, in wolf bites, or in children bitten on the bare skin, 10 c.c. are injected daily for 14 days. Itchy swellings may appear at the site of the inoculations about the eleventh day, but other complications following inoculation are fortunately rare. Paralytic accidents, however, have been recorded with all methods; they include a mild facial neuritis, dorso-lumbar myelitis and an ascending paralysis of Landry's type which is fatal in about 30 per cent. of cases.

Treatment of the paroxysm.—No specific treatment is known. Measures directed to alleviate the suffering of the patient should be instituted. These include chloroform inhalations and morphine, hyoscine, chloral and atropine in large doses. Curare and tetrado-toxin have both been employed for the relief of spasms.

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CEREBRAL VASCULAR LESIONS

ANEURYSM

Pathology.—Miliary aneurysms, which are small seed-like dilatations of the finer arteries in the substance of the brain, are not uncommonly present in cerebral arterial degeneration. They are usually multiple. The extensive researches of A. G. Ellis in 1909 and of Pick in 1910 have proved conclusively that miliary aneurysms are of little practical importance apart from the associated arterial degeneration.

True aneurysms of the larger cerebral arteries are not uncommon and have in the past been the subject of a very extensive literature. In a recent analysis of over a thousand cases McDonald and Korb have ascertained the following facts:

(i) The arteries involved in order of frequency are the middle cerebral, basilar, anterior communicating, internal carotid, vertebral, anterior cerebral, posterior communicating and posterior cerebral.

(ii) Aneurysms occur at all ages; about 11 per cent. were below 20 years, 35 per cent. from 20 to 40 years and 54 per cent. above 40 years of age.

(iii) The sex incidence is approximately equal.

(iv) 63 per cent. of the vessels examined showed pathological changes, the remainder being described as normal. The predominant lesion was atheroma, and less common in order of frequency were mycotic aneurysm and syphilitic changes, only 5 per cent. showing changes of the last-named order. At all ages pathological changes in the affected arteries predominated, mycotic aneurysms being most common in young persons, atheromatous changes in older subjects.

These aneurysms may give rise to no symptoms during life, being merely post-mortem findings, they may rupture, or they may be of sufficient size to evoke tumour symptoms. Of these possibilities, rupture appears to be the most common, the artery most frequently affected in this way being the anterior communicating.

The aneurysms found on normal arteries are usually regarded as due to developmental defects in the wall, commonly seen at junctions on the circle of Willis. They may be multiple, and from their shape are spoken of as "berry" aneurysms. They may rupture freely, leading to a rapidly fatal issue, or they may leak recurrently. The wall may contain calcified material which shows as a ring shadow in the radiogram. Mycotic aneurysms arise from septic infection of the arterial wall, usually in association with septic endocarditis.

Symptoms.—Clinically, cerebral aneurysms fall into two main groups: (1) Those which rupture during life with the extravasation of blood, in greater or less amount, into the suburachnoid space, and sometimes also into the cerebral substance and into the ventricles. These form the so-called *apoplectic* group. (2) Those which produce symptoms in virtue of the pressure they exert on neighbouring structures, thus giving rise to paralytic symptoms. These form the *paralytic* group. It has to be added that this second group may ultimately rupture. There are also cerebral aneurysms that during life are clinically latent, being merely necropsy findings.

The clinical picture of subarachnoid hæmorrhage, following upon the rupture of cerebral aneurysms is now widely recognised, but that of the paralytic group is only now being clinically differentiated. Recent studies by G. Jefferson has clarified their clinical picture considerably, and in most cases their presence should be diagnosed.

1. SUBARACHNOID HÆMORRHAGE

Synonym.—Spontaneous Subarachnoid Hæmorrhage.

We have seen that bleeding into the subarachnoid space may be an accompaniment of head injuries in which the meninges are torn. It may also follow primary intraventricular hæmorrhage, but the usual cause of uncomplicated, or as it is sometimes called, spontaneous subarachnoid hæmorrhage is rupture of a cerebral aneurysm on the circle of Willis or on one of its component arteries. The situations in which such aneurysms are commonly found have been already enumerated. What has been called here the "berry" aneurysm may rupture suddenly and freely with the production of fatal apoplexy, or there may be recurrent leaking of blood in small amounts from such an aneurysm, leading to a syndrome of meningeal irritation.

1. *The apoplectic syndrome.*—The subject may have been subject to frequent headaches, or the episode may be quite unheralded until a sudden intense headache, rapidly followed by sudden lapse into unconsciousness, signals the free rupture of the aneurysm. It may be thought that an ordinary cerebral hæmorrhage has occurred when the comatose patient is first seen, but careful examination will generally reveal the absence of signs of a gross lesion in one cerebral hemisphere (cf. p. 1527) when this has occurred, whereas in uncomplicated subarachnoid hæmorrhage no signs of hemiplegia are present. On the other hand, a bilateral Babinski plantar response will be obtained and there will be marked neck rigidity. At first both pupils may be small and sluggish, but in fatal cases the pupils ultimately dilate. Lumbar puncture produces a fluid that resembles pure blood.

Recovery from hæmorrhage of this severity is by no means unknown.

In fatal cases death commonly ensues within 24 to 36 hours, or at some time during the first fortnight from fresh bleeding. If this period be safely passed the prognosis as to recovery is good. Some patients enjoy years of normal health after such an episode, while others are subject to recurrences of greater or less severity.

2. *The meningitic syndrome.*—In this case, the hæmorrhage is less abundant and therefore consciousness may not be lost. There is violent headache, restlessness, delirium, rigidity of neck and spine, Kernig's sign, bilateral extensor plantar responses, and sometimes diplopia and squint. Within a few hours, or somewhat later, ophthalmoscopic examination may reveal the presence of flame-shaped hæmorrhages in the nerve fibre layer of the retina, or massive hæmorrhage in the subhyaloid space. The last-named are characteristic of subarachnoid hæmorrhage. Both forms of hæmorrhage arise from the passage forwards of the extravasated blood into the subarachnoid space surrounding the optic nerves. A low grade papillœdema is occasionally also observed.

In non-fatal cases of both types, the temperature may remain raised for 7 or 8 days, and the urine for the first 48 hours only may contain abundant albumin and some sugar. The addition of these features to the clinical picture may, if the possibility of their occurrence is overlooked, lead to an erroneous diagnosis of urœmia or diabetes.

In small leaking hæmorrhages the cerebro-spinal fluid is more or less heavily bloodstained, and may for two or more weeks be discoloured, yellow or brownish according to the amount of blood originally present. As with all other conditions of high and rising intracranial pressure, sudden and unexpected death is a common event in undrained cases. Subarachnoid hæmorrhage does not always reach the general subarachnoid space freely. When effused upon the vertex, it may spread out and clot at its edges and from without, while the bleeding is still going on at its centre. Thus, a pancake-like hæmatoma accumulates upon the surface of the brain, thin and clotted at its edges, which prevents further spread, and still liquid and ever accumulating at its centre. Not infrequently the pressure of the growing liquid centre bursts into the hemisphere causing the addition of a sudden hemiplegia to the syndrome, and this has been named by Froin the " meningo-cerebral hæmorrhage." Draining of the cerebro-spinal fluid gives no relief when this pancake hæmatoma is present.

3. *The lumbago-sciatica syndrome.*—This rare condition, first described by Professor Arthur Hall, commences with pain and stiffness in the lumbar region, followed by pains in the legs, and sometimes the leg jerks are absent. For a week or more there may be no indication that the cause is intracranial, but thereafter in undrained cases the symptoms spread upwards to the arms and neck, and head retraction, headache and vomiting are added. Pyrexia is the rule. The diagnosis depends upon the characteristic cerebro-spinal fluid of subarachnoid hæmorrhage. The explanation of this syndrome is not easy. It may be that deposit of fibrin upon the roots of the lower theca is the cause of the quite local meningeal irritation. All the reported cases that have been treated with regular drainage by lumbar puncture have made good recovery.

4. *The recurring coma syndrome.*—The description of a typical case will best illustrate this condition. A man of 28, during a period of four years,

on four occasions, and at long intervals without any prodromal symptoms, fell unconscious in the street, and on each occasion he was taken to the nearest hospital where, on account of the persistent coma, lumbar puncture was done, with the discovery of blood in fair quantity in the cerebro-spinal fluid. On each occasion, the coma disappeared somewhat suddenly after 24 hours, and the patient insisted on leaving hospital and returning to work within a week, as he felt quite well. This patient came under my observation for the prevention of further attacks. The only abnormality found was a yellow cerebro-spinal fluid resulting from long antecedent hæmorrhage. The presence of leaking aneurysm has been pathologically proved in several similar cases.

Differential Diagnosis.—The recognition of subarachnoid hæmorrhage is an easy matter in those cases in which the train of symptoms calls at once for the examination of the cerebro-spinal fluid and blood is found in that fluid. The distinction of the apoplectic forms from other varieties of cerebral hæmorrhage can only be made: (1) by the age of the patient, practically all hæmorrhagic apoplexy being in the first half of life the result of ruptured aneurysm; and (2) by preceding symptoms, such as headache, diplopia, ophthalmoplegia and migrainous phenomena. In those cases in which blood does not escape into the cerebro-spinal fluid, as in very many of the subdural hæmorrhages, the diagnosis is both difficult and uncertain. The insidious onset of irregular headaches with periods of mental confusion and drowsiness alternating with period of recovery, especially if following a fall or slight blow on the head, should, during the second half of life, always suggest the possibility of subdural hæmorrhage. Adie has suggested that all cases of migraine with transient ophthalmoplegia are due to aneurysms. It seems certain that many of the numerous cases of sudden death occurring in ophthalmoplegic migraine have been the result of terminal hæmorrhage due to the presence of aneurysm. On the other hand, the majority of the cases of migraine with ophthalmoplegia make perfect recovery.

Prognosis.—When the aneurysm ruptures frankly and widely and the bleeding can be free, the outlook is hopeless, and death occurs in from a few minutes to a few hours; nor does drainage avert the consequences of so large an opening into a main arterial trunk. If, as so commonly happens, there is a slower leakage which perhaps is intermittent, the outlook will depend: (1) upon the cessation of the bleeding and the healing of the leak by clotting; and (2) upon the possibility of the free escape of the effused blood into the subarachnoid space and its removal by repeated lumbar drainage. In many of the cases of subarachnoid hæmorrhage, the bleeding ceases and the pressure and the dangerous results therefrom can be well relieved by lumbar drainage, repeated whenever the symptoms demand it, and healing of the aneurysm, by clotting and calcification, occurs with complete recovery. In other cases there may be repeated attacks of leaking at intervals of weeks, months or even years, and again many of such patients make good recovery in the end. When the bleeding is wholly or mainly subdural and when a subarachnoid hæmorrhage clots at its edges upon the surface of the brain, drainage and the relief of symptoms is impossible, and the prognosis is serious in the extreme but for the possibility that the site of the bleeding may be located and the clot turned out and the hæmorrhage arrested by surgical procedures.

Treatment.—In the case of subarachnoid hæmorrhage the patient must be kept absolutely at rest, with the administration of sedatives. An immediate injection of morphia is indicated when the patient is not comatose and has the usual intense headache. It also may be necessary on the recovery of consciousness on account of headache and restlessness to take this step. It is doubtful whether repeated lumbar puncture is advisable, as it may lead to recurrence of hæmorrhage, but if there be signs of raised or of rising intracranial tension (and progressive slowing of the pulse is generally a reliable indication of this), then lumbar puncture may be expedient. When recovery sets in, the patient should still be kept in bed for at least 3 or 4 weeks. During the first fortnight recurrent hæmorrhage is more likely to occur than later during the course of convalescence.

2. UNRUPTURED ANEURYSM OF THE INTERNAL CAROTID ARTERY

Synonym.—The Paralytic Syndrome.

The aneurysms of this group, like the berry aneurysm, mostly occur at the bifurcation of an artery. In this case, on the internal carotid artery where the ophthalmic artery arises, or at the junction of the anterior cerebral and anterior communicating arteries. There seems no doubt that they are more often seen in women than in men, mostly in middle life.

Symptoms.—The onset may be sudden, in which event diagnosis is relatively easy; or the symptoms may develop so gradually as to make a diagnosis of intracranial new growth probable. The arrangement of the circle of Willis and its components is such that the visual pathway (optic nerves, chiasma and tracts) are very commonly affected by the development of an aneurysm in this situation. Similarly, when there is a carotid aneurysm the proximity of the carotid artery to the cavernous sinus commonly leads to ocular palsies.

ANATOMICAL CONSIDERATIONS.—The arrangement of the circle of Willis and its relations to the visual pathway (optic nerves, chiasma and tracts) are such that aneurysms in this situation usually exert pressure upon some part of this pathway and thus give rise to visual defects. Further, the proximity of the internal carotid artery to the cavernous sinus may lead in similar manner to ocular palsies and to disturbances in the field of the trigeminal nerve. The optic tracts pass forward above the posterior communicating arteries, the chiasma lies within the arterial circle, and the optic nerves pass forward below the anterior cerebral and anterior communicating arteries. In other words, the visual pathway in its passage forward passes through the circle Willis from behind and above, and leaves it anteriorly on its under side.

It will be seen, therefore, that there are supra-clinoid and sub-clinoid aneurysms of the carotid trunk. The latter arise in the cavernous sinus, do not commonly interfere with the visual pathway, but may compress the third nerve and the ophthalmic division of the trigeminal nerve. The supra-clinoid aneurysm arise from the carotid where the ophthalmic artery goes off or at the final fiburcation of the main trunk. In these circumstances the visual pathway is generally affected.

Symptoms.—The symptoms may evolve slowly, as though a new growth were in question, or may develop with dramatic suddenness. There may be

paralysis—partial or complete—of the third, fourth and sixth nerves with squint and ptosis, severe pain, and some sensory loss round the eye in the field of the first division of the trigeminal nerve. There may be slight proptosis of the eye, and rarely only some papillœdema. The visual field defects vary from case to case. There may be monocular blindness when the optic nerve alone is compressed, or monocular blindness with a temporal hemianopia in the eye on the side away from the lesion. Other recorded defects are bitemporal and homonymous hemianopia. Pain is a prominent symptom. Symptoms of pituitary dysfunction are usually not found. X-ray examination may reveal a ring calcification of the aneurysm, while angiography may show the shadow of the aneurysm.

Treatment.—Ligature of the carotid artery appears to be the only method of treatment of an unruptured aneurysm of this type.

CHRONIC SUBDURAL HÆMATOMA

Subdural hæmatoma stands in no ætiological relationship to subarachnoid hæmorrhage, but is invariably traumatic in origin, the hæmorrhage occurring from cerebral veins as these traverse the subdural space. Yet it is convenient to consider it at this juncture.

Ætiology.—The condition under consideration was formerly known as pachymeningitis hæmorrhagica, the name expressing the belief that an inflammatory process was in question. It was further supposed that the lesion was in some unexplained way peculiar to chronic alcoholic subjects and to sufferers from general paralysis.

W. Trotter was the first to point out that in reality the lesion was traumatic in origin, and that the frequent absence of a history of injury was what might be expected in the individuals specified above, who are both more than normally liable to falls and head injuries of a minor order and less than normally capable of recalling these injuries. In fact, subdural hæmatoma is found at all ages and is invariably traumatic. Falls on forehead or occiput, not at the time apparently productive of serious injury, may yet lead to a tearing of the cortical veins as these pass from the surface of the brain to enter the dural sinuses. The tear is commonly in the subdural space on one or both sides of the vertex (superior longitudinal surface). When after the shock of the fall the blood pressure rises again to normal and on subsequent occasions when there is a transient rise in this pressure blood leaks from the torn veins and collects in an ovoid mass on each side of the vertex.

Rarely such a subdural collection may be found at the base of the brain. The periphery of the blood clots thus formed tend to organise so that a fine capsule is built up round the hæmatoma. This may remain solid or its centre may liquefy with the formation of a cyst containing a thin brownish fluid. In time the dura over this cyst and the cyst walls become thickened and stained, and it is clear from the condition sometimes found at necropsy that a subdural hæmatoma may be compatible with many years of survival and may during life give rise to no clearly recognizable symptoms. Such hæmatomas may reach a large size, and a 10-ounce mass over each hemisphere has been observed.

Symptoms and Diagnosis.—The difficulty which still frequently sur-

rounds the diagnosis of subdural hæmatoma depends in large measure upon a general unawareness that it is a not uncommon lesion, and from a survival of the old and now obsolete notion that its occurrence is largely confined to sufferers from the two affections named above. It must be emphasised again, therefore, that subdural hæmatoma may follow an apparently trivial head injury in persons at all age periods; that essentially its symptomatology is that of a space-occupying lesion, with a feature characteristic of hæmatoma: namely, a remarkable fluctuation in the course and severity of the symptoms; that owing to the bilateral nature of the lesion the signs are apt to be difficult of localising interpretation; and finally that in the presence of such a somewhat blurred picture of raised intracranial tension a history of head injury some days, weeks, or even months before the onset of symptoms should always give rise to the suspicion that a hæmatoma, and not a new growth, may be present.

There is almost invariably a clinically latent period in the development of a subdural hæmatoma. This may vary from a matter of days to one of weeks. On the whole, it may be said that in young persons, the latent period is apt to be shorter and the symptoms more severe and of more rapid evolution than is commonly the case in elderly subjects. In young subjects, too, there is usually no difficulty in obtaining a history of head injury, either a fall upon the head or a blow sustained at sport or in some other way. The initial symptom is usually headache, fluctuating in intensity, apt to be most severe on awaking in the morning or on physical exertion. With the passage of days or weeks this becomes more severe and soon other symptoms are added to it. The patient has days on which he is drowsy. He may pass rapidly into stupor or even coma, emerging again to become almost normal. Transient accesses of diplopia with squint may be noted. Examination during a period of maximal symptoms may reveal a papillœdema, sometimes severe in rapidly developing cases. The plantar responses may, on one or both sides, be of the extensor type. There may be an inequality of tendon jerks on the two sides, the abdominal reflexes may be diminished on one or both sides. They may even be absent. Periods of mental confusion may also occur.

This fluctuation in the severity of the symptoms, the fugitive character of the physical signs and the generally downhill tendency of the illness, despite the fluctuations are amongst the features which are characteristic of subdural hæmatoma and help to differentiate it from that of intracranial new growth. When the syndrome develops rapidly, it is more common to meet a marked slowing of the pulse than in new growth.

In most instances there is no trace of blood in the cerebro-spinal fluid.

In all cases there is a great liability to a rapid development of coma with a fatal issue. Yet, the occasional finding at necropsy of what is clearly a subdural hæmatoma of very long standing, unsuspected during life, shows that from time to time the sequence of events briefly reviewed above fails to develop. Though it has to be confessed that even in such cases it is highly probable that careful clinical examination and an awareness on the part of the examiner of the symptom-complex of hæmatoma might have made diagnosis possible during life.

Diagnosis and Treatment.—The features which should make clinical diagnosis possible have been described, but in certain doubtful cases certainty

can be obtained only by an exploratory operation. This may consist in bilateral trephine holes and tapping of the subdural space, or in the turning down of osteoplastic flaps and the evacuation of the cyst when found. It is clear that treatment is essentially surgical.

EMBOLISM

The majority of embolisms of the cerebral arteries occur in valvular heart disease, 89 per cent. (Saveliew). Embolism may also occur from detached portions of clot from an aneurysm, from thrombi in connection with atheroma or syphilis of the aorta, and from detached clots which may form in the region of the pulmonary veins and left heart where there is no cardiac valvular disease. This latter condition is not an infrequent cause of puerperal apoplexy. It occurs in suppurative and gangrenous conditions of the lungs, and is an essential factor in the production of "pulmogenic" cerebral abscess. Embolism is rather more frequent in women on account of the greater incidence of mitral stenosis in that sex, and from the puerperal cases.

The embolus comes from the left heart and may be a vegetation from a quite recent endocarditis, but is more commonly a detached vegetation from a chronic and especially from a septic endocarditis. Very frequently it is a detached portion of clot which has formed in the left auricle in mitral stenosis. The middle cerebral arteries are the usual sites of lodgment of the emboli, and the left middle cerebral is rather more frequently affected than is the right. Embolism of the other cerebral vessels may occur, but is extremely rare.

The pathological events which may follow the plugging of a cerebral vessel with an embolus are varied and are highly important. In the first place, secondary thrombosis may proceed from the embolus throughout the whole distal distribution of the vessel, and lead to complete softening of its area of supply, and the clinical aspect will be that of severe and unchanging damage to the brain. The softened area may shrink or may undergo cyst formation, or it may be completely absorbed, giving rise to a porencephalus. Secondly, the embolus in the absence of secondary thrombosis may become adherent to one spot of the vessel wall at the site of its lodgment, and retracting from the vessel wall elsewhere, the blood channel becomes reopened, and the clinical results of the embolus, at first very severe, may disappear with unexpected and dramatic rapidity, and complete recovery ensue. Thirdly, the embolus may contract at the site of its primary lodgment, and become detached and shifted on by the blood stream to find a second resting-place in a much smaller artery. This event is manifest clinically by rapid clearing up of the physical signs in many regions, with persistence or even deepening of the involvement of one particular region. For example, a severe and complete hemiplegia clears up suddenly on the third or fourth day, leaving a brachial monoplegia only. Fourthly, an embolus may be impacted at the termination of the internal carotid artery, giving rise to severe hemiplegia with blindness of the opposite eye from blocking of the ophthalmic artery—*carotid hemiplegia*. Owing to the re-establishment of the circulation by the circle of Willis the hemiplegia is likely to recover rapidly, while

the eye remains permanently blind owing to secondary thrombosis extending through the ophthalmic artery. When an embolus is finally lodged and completely occludes the artery, the condition, both pathologically, clinically and from the point of view of treatment, is one of thrombosis, the cause of the embolism being taken into consideration. As with thrombosis, the immediate result of permanent occlusion is a condition of infarct and acute œdema in the region from which the blood supply is cut off. The acute œdema causes local pressure and increased general intracranial pressure, and is a common cause of the transient coma which often supervenes a few hours after the stroke, in both embolic and thrombotic apoplexy.

Stroke from embolism is the most suddenly occurring of all apoplexies, and the ictus is not preceded by any prodromal cerebral symptoms. Consciousness is apt to be lost at once if the whole middle cerebral artery be occluded, especially if the lesion be upon the left side. Or it may be retained throughout if the embolus lodge in a small vessel only.

Diagnosis.—This rests upon the occurrence of sudden apoplexy without prodromal symptoms in the presence of an obvious cause for embolism such as cardiac valvular disease, aortitis, pulmonary thrombosis or the puerperal state. The diagnosis can be a matter of probability only in those conditions where either embolism or thrombosis is likely, such as enfeebled cardiac states and the puerperal state.

Prognosis.—The prognosis in cerebral embolism depends upon the size of the vessel which is plugged, as deduced from the severity of the initial symptoms and their extent, and upon the immediate pathological changes which occur in the obstructed vessel as above described; and according to the nature of these changes it may be the most severe and least recoverable, or, on the other hand, the least severe and most recoverable of all forms of apoplexy. The prognosis of the condition causing the embolism is often the more important.

Treatment.—The treatment is that of cerebral thrombosis (see p. 1606) together with that of the condition giving rise to the embolus.

ARTERIAL THROMBOSIS AND HÆMORRHAGE

Cerebral thrombosis and cerebral hæmorrhage seem hitherto to have been described in text-books of medicine as quite separate conditions, almost antagonistic and mutually incompatible, between which it was highly essential and even possible to make a differential diagnosis for the purpose of applying a very dissimilar line of treatment in the respective conditions, each line of treatment being the worst possible for the other condition. It cannot, however, be too forcibly pointed out that primary arterial thrombosis and primary arterial hæmorrhage depend in every case upon degeneration of the arterial wall, and that every condition of degeneration of the arterial wall may cause either thrombosis or hæmorrhage indifferently. It is a usual experience to find in patients who have had severe strokes that thrombosis was the cause of the earlier, and hæmorrhage of the final apoplexy. Even in that condition, which has always been held to be the most important antecedent of cerebral hæmorrhage—renal disease with

high arterial tension—Janeway has recently found that thrombosis and not hæmorrhage was the cause of apoplexy in many of his cases.

On account, therefore, of the identity of the underlying pathological condition in every case, and the clinical association of thrombosis and hæmorrhage of the cerebral arteries, and the difficulty of distinguishing them clinically, the two conditions are here described together.

Ætiology and Pathology.—The arterial degeneration which may result in cerebral thrombosis and hæmorrhage is due to the following causes: (1) Syphilis, which is the commonest cause of thrombosis in the first half of adult life, and which is less commonly the cause of hæmorrhage. It may affect both the large and the small arteries, even to the smallest. All the coats of the artery are affected, and in the case of the finest vessels there is conspicuous lymphocyte accumulation or "cuffing" round the vessel. In the neighbourhood of the affected vessels there is always syphilitic cerebritis in the form of lymphocyte exudation and œdema, and meningitis, if the lesion come to the surface. This is the most recoverable of all thrombotic lesions of the brain. (2) Atheroma, which is the common cause both of thrombosis and of hæmorrhage in the second half of adult life, and which is by far the commonest cause of hæmorrhage. It must be especially borne in mind that cerebral atheroma may be local in the cerebral vessels, and unassociated with general atheroma of the systemic vessels. (3) Arterial hypertrophy, with secondary focal degeneration of the media, with or without its commonly associated renal disease, which is of the nature of "small white kidney" in children and younger adults, and of the various types of "granular kidney" in older subjects. (4) Abnormal conditions of the blood, especially when associated with feeble cardiac action and low blood pressure, as in the puerperal state, and in septicæmic conditions, and at the time of the menopause. Hæmorrhage into the brain may also complicate polycythæmia and acute leukæmia. (5) In association with new-growths of the brain, both thrombosis and hæmorrhage are common events, especially when the neoplasm is soft and rapidly growing. The vascular lesion may occur quite early in the course of the new-growth, and apoplexy may be the first sign of its presence. (6) Inflammatory conditions of any nature may cause thrombosis and hæmorrhage. The vascular lesions are usually small, but they may be extensive, and may cause death. (7) Traumatic lesions, such as the passage of a bullet through the brain, or a blow upon the head, or concussion from high explosives, may cause extensive thrombosis or hæmorrhage.

While cerebral hæmorrhage results often enough from the direct rupture of a true aneurysm, or of one of those irregular local thinnings of the vessel wall which is called a "false aneurysm," and may take place from an artery the wall of which is softened by disease though there be neither thinning nor bulging of the vessel wall, yet it is probable that cerebral hæmorrhage is very often the direct consequence of thrombosis, and especially of thrombosis which has occurred some time previously. The sequence of events is as follows: An area of thrombosis occurs within the brain, and the usual softening and necrosis follow. On the confines of this area, the necrosis spreads to come in contact with the wall of a living and unthrombosed artery, perhaps of considerable size. The arterial wall of this vessel was nourished by the capillaries of the necrosed area, and with its nutrient supply now

cut off there is local degeneration of the wall of the living artery. Moreover, the shrinking of the necrosed area of brain causes loss of support to the degenerate wall of the vessel, which ruptures as the result, under the influence of any sudden increase of blood-pressure. It is for this reason that one commonly finds in patients who have had multiple attacks of apoplexy, that the final and fatal attack is one of hæmorrhage, and that the preceding attacks have been attacks of thrombosis. These spots of thrombosis, which cause hæmorrhage, need not be of large size, and they may be so small as hardly to cause symptoms on their occurrence. Marie first called attention to these small spots of thrombosis as *plaques jaunes*, small yellowish-brown spots, softened and sometimes cystic, and pointed out their importance as a cause of cerebral hæmorrhage. In a similar way the thrombosis of syphilitic arterial disease may cause subsequent hæmorrhage.

Syphilitic cerebral thrombosis is not usually a pure pathological process, for the vascular disease is often accompanied by acute syphilitic encephalitis, with much lymphocyte extravasation in the vicinity of the diseased vessels, and acute local œdema, which increase the evascularisation when thrombosis occurs. The symptoms of cerebral loss of function are not all due to the thrombosis, but are in part owing to the recoverable acute inflammatory condition, and it is for this reason that syphilitic apoplexy often shows much more recovery than do other forms of apoplexy.

Thrombosis is a more common cause of apoplexy than is hæmorrhage, but it is much more frequently survived, while hæmorrhage is frequently fatal, within from a few hours to a few days of its onset. It follows therefore, that in the autopsy room of a general hospital, hæmorrhage is seen much more often than is thrombosis, while in infirmaries, where the survived cases of apoplexy collect, thrombosis is almost invariably the lesion found to be primarily responsible for the apoplexy.

Thrombosis tends to occur when an habitually high blood pressure is temporarily lowered and the circulation less active, and is always strongly suggested when apoplexy occurs during sleep and conditions of quiet, and after exhaustion, exposure to cold, severe purgation, and in debilitated states generally. It is preceded by slowing of the circulation in the area affected, and this may be productive of prodromal symptoms. Or there may be slight local thromboses preceding the main thrombosis, also giving rise to prodromal symptoms. Thrombosis may thus have an ingravescent onset, especially when clotting occurs in distal branches of an artery and extends towards the main vessel; but, on the other hand, it may have an absolutely sudden onset when the clotting occurs primarily in a large artery. The immediate effect of the thrombosis is a condition of infarct with œdema, extending widely in the vicinity, and it is this œdema which causes the loss of consciousness so commonly seen a few hours after the apoplexy has occurred. The œdema tends to pass off in a few days, and the area bereft of circulation by the thrombosis tends to become narrowed by collateral circulation from surrounding regions, and any recovery of function within the affected region must be by collateral circulation from elsewhere. The affected area at an early stage is bright red in colour, and soon becomes soft and shrunken (red softening). Later, the blood pigments degenerate with the production of bilirubin and are partly absorbed, producing a yellow-coloured lesion (yellow softening). Finally, much of the thrombosed tissue becomes necrotic and is

absorbed, leaving one or several cystic cavities. These cavities are never so sharply defined as those resulting from embolism, because of the more complete necrosis occurring with the later lesion. Still, a severe arterial thrombosis occurring at an early age may result in a porencephaly. Cavities found in cases of apoplexy after years have elapsed, are too often attributed to hæmorrhage. In reality they are nearly all due to thrombosis or embolism. The cerebro-spinal fluid in thrombosis is never found to contain blood, but some little time after the apoplexy it is often coloured yellow or yellowish-brown from escape of changed blood pigments, when the lesion has reached the surface of the convexity or the surface of the ventricle.

Hæmorrhage, which is usually described as an apoplexy of sudden onset, may be so when the escape is from a large vessel. When the bleeding commences from a smaller vessel, the symptoms are not sudden in their onset, but gather rapidly. Such a hæmorrhage is much like an avalanche. Commencing from a small vessel the hæmorrhage tears a small cavity, and in so doing opens up fresh bleeding points, and with increasing destruction more and more bleeding occurs from every piece of torn tissue, until the hæmorrhage reaches such a size as to burst commonly into the ventricle and much more rarely on to the surface. Indeed, it is difficult to conceive how a hæmorrhage into such a soft and vascular tissue as is the brain should ever stop. As a matter of fact, it very rarely does so, but causes death in the first attack of hæmorrhagic apoplexy, within from a few hours to a few days after the onset, from widespread tearing up of the nervous system and bursting into the ventricle. One of the most important clinical distinctions between apoplexy due to thrombosis and apoplexy due to hæmorrhage is that the former is often survived, and that the latter is almost invariably fatal within a short time of the onset.

Hæmorrhage may occur anywhere within the nervous system, but its common seat of commencement is in the centrum semiovale, and the vessel which bursts is one of the perforating arteries, of which the lenticulo-striate which carries the name of the "artery of hæmorrhage" is the most common. Such bleedings are often called "capsular hæmorrhages." It must be pointed out that this term capsular refers to the region outside the corpus striatum or external capsule, and not to the compact internal capsule as it converges to the crus cerebri. The cerebro-spinal fluid in cases of hæmorrhage contains blood within a very short time of the onset, and lumbar puncture often withdraws what is practically pure blood in large quantities. I have found blood present in large quantities very often within an hour of the onset.

Both thrombosis and hæmorrhage may occur in any part of the brain, while massive embolism is rare, except in the middle cerebral artery. The semioval centre, the calcarine region and the pons are the common sites of both hæmorrhage and thrombosis in that order of frequency. Hæmorrhage is rare except in these regions, while thrombosis is not uncommonly met with elsewhere.

Symptoms.—The nature of the symptoms in apoplexy will depend upon the site of the vascular lesion; and as the semioval centre or region of the middle cerebral artery is the commonest site for all the vascular lesions, hemiplegia is the common result; and this is associated with aphasia, if the lesion

is in the left hemisphere, and involves or isolates the cortex. When the calcarine artery is the site of the lesion, hemianopia results; and this is apt to be accompanied by word-blindness, if the lesion be on the left side. Pontine apoplexy involves the appearance of double hemiplegia, bilateral ataxy and bilateral loss of sensibility, with signs of involvement of cranial nerve nuclei and cranial nerves. Cerebellar apoplexies and thrombosis of the posterior inferior cerebellar artery produce acute ataxy with forced movements and vomiting.

Prodromal symptoms in the form of transient weakness of one or both limbs of one side, transient aphasia and giddiness occur in thrombosis only. An ingravescent onset occurs in thrombosis only and when the clotting occurs in the periphery of arterial distribution first and spreads towards the main trunk. When commencing in the parietal region, tingling and numbness of an extremity first occur, followed by a spread of these symptoms over half of the body, and subsequent weakness deepening into hemiplegia. When commencing in the left temporal region gradually oncoming aphasia is first noticed, and when commencing in the ascending frontal convolution a peculiar sensation of heaviness in the limbs gradually increases until hemiplegia is obvious.

The onset in embolism is always instantaneous; it may be sudden in thrombosis, and in hæmorrhage from a large vessel. In hæmorrhage it is always rapid. Consciousness is lost or not, according to the severity of the initial lesion and the site it occupies, and to the magnitude of the processes which follow the initial lesion, namely, the œdema of embolism and thrombosis and tearing of the brain tissue in hæmorrhage. In hæmorrhage, consciousness is lost soon, and the rapid development of severe symptoms which progressively deepen, is a most important early indication that this is the nature of the lesion.

In calcarine thrombosis the initial symptoms may be so slight as to pass unnoticed by the patient, whose first indication of defect may be, that he runs into objects on his blind side.

Convulsion sometimes occurs at the onset, and this nearly always indicates thrombosis, rarely embolism, and never hæmorrhage. There may be some local spasm in the region of the cranial nerves in pontine hæmorrhage, but this is not convulsion.

Conjugate deviation of the eyes is a common feature of all apoplexy. When the lesion is irritative at its onset, and not too destructive, and always when convulsion occurs at the onset, there may be active conjugate deviation, the eyes being turned away from the side of the lesion and towards the paralysed or convulsed side in hemiplegic cases, or the blind side when hemianopia is present. But this active conjugate deviation lasts but a short while and is followed by a paralytic conjugate deviation in the opposite direction, both eyes being directed away from the paralysed side and towards the side of the lesion. This variety of conjugate deviation may last for a considerable time, but usually disappears with the onset of deep coma.

The pupils are often unequal; they may be contracted, or dilated widely, and may be insensitive to light. In severe apoplexy, when as the result of the cerebral shock or when hæmorrhage or œdema have so raised the pressure as to greatly reduce the physiological activity of all the intracranial elements with the production of deep coma, the pupils are widely dilated and insensi-

tive. In pontine lesions, the pupils are often contracted to pin-point size, and this condition is of important localising significance.

In proportion to the severity of the general intracranial disturbance, respiration tends to be hurried, noisy and stertorous, and with increasing pressure to become irregular, grouped or of the Cheyne-Stokes type. The blood pressure tends to be raised and the pulse full in all conditions of apoplexy, provided the heart will respond to the requirement of an increased blood pressure in the face of an increased intracranial pressure.

Swallowing is often impossible, and the sphincters may be relaxed or retention may occur.

In the usual variety of apoplexy where the lesion is in the area of the middle cerebral artery and the local sign of the lesion is hemiplegia, it will be obvious that when the general intracranial pressure becomes severe and the coma becomes deep, the hemiplegia becomes less apparent, or masked by the universal condition of paralysis consequent upon the general intracranial condition. The physician often sees the patient for the first time when there is considerable coma, and he must determine upon which side the lesion is situated, and endeavour to have some perspective as to prognosis by determining the severity of the lesion.

The following points will serve to determine the side of the lesion when these signs are present: (1) The paralytic conjugate deviation is towards the side of the lesion. (2) The corneal reflex, when any is present, is diminished or lost on the hemiplegic side. (3) Painful stimulation will elicit less response or no response upon the hemiplegic side (hemianæsthesia). (4) The patient may respond by blinking to a feint made with the observer's hands towards the patient's eyes upon the sound side, and not on the hemiplegic side (hemianopia). (5) The limbs on the hemiplegic side when raised and allowed to fall passively, do so in a more lifeless, inert and flaccid fashion than upon the sound side. (6) And when there is any difference between the knee-jerks, abdominal reflexes and plantar reflexes, the former tend to be diminished and lost on the hemiplegic side while the plantar reflex will be of the extensor type on the hemiplegic side. It must be remembered in this connection, that a severe lesion of one cerebral hemisphere abrogates for a time at least most of the functions of the whole hemisphere, and that the hemianæsthesia and hemianopia, here referred to, do not necessarily indicate that the destructive lesion involves the visual and sensory paths. And further, that the condition of coma due to increased intracranial pressure of itself causes such signs as bilateral loss of abdominal reflexes and knee-jerks, and bilateral extensor responses in the plantar reflex.

The severity of the lesion may be judged—(1) From the depth of the coma; (2) from the degree to which the patient responds to any form of stimulation and from the general signs of nervous depression present—for example, a condition of complete bilateral flaccidity with complete loss of all reflex action and of all response to stimulation indicates a most severe lesion; and (3) from signs of failure of respiration as shown by irregular, grouped or Cheyne-Stokes breathing. It is further important to arrive at a determination if possible as to whether the condition present is stationary, deepening or showing signs of amelioration.

Vomiting is not an uncommon occurrence in the early hours of apoplexy and before coma becomes deep. Hyperpyrexia is often seen in fatal cases

before the end. It is especially common and may reach a high degree in pontine apoplexy. It may be preceded by initial depression of temperature. It is of fatal prognostic import.

HEMIPLEGIA is the commonest sequel of vascular lesions of the brain. The signs which serve to indicate its presence in the comatose subject have already been enumerated.

After cerebral thrombosis it may happen that the initial hemiplegia is completely recovered from, but unless this recovery begins early and progresses rapidly it is not likely to be complete.

The essential feature of hemiplegia is the loss of voluntary movements, but as this loss begins to pass off, certain new features make their appearance. These are muscular hypertonus, increased tendon jerks, and associated movements.

The restoration of movements follows a certain order. Deviation of the tongue and facial asymmetry clear up early; next, the leg begins to recover; and finally—and often very incompletely—the arm. The return of movements in the limbs is selective. In both upper and lower limbs, movement at the proximal joints recovers soonest and most completely. In the leg, extension and plantar flexion recover more completely than flexion and dorsiflexion. As a result, the patient can often stand when he cannot lift the foot and leg to step properly, and has instead to circumduct the limb when walking. In the arm, flexion movements recover soonest and best, while the fine skilled movements of the hand and fingers are frequently lost for ever.

The development of hypertonus, or spasticity, is as selective as the return of movements. In the leg, the extensor group becomes spastic; in the arm, the flexor group. Thus, the arm tends to take up a position of adduction, with flexion at elbow, wrist and digits. The leg is always spastic in extension, and does not go into flexion contracture, as may happen in spastic paraplegia from spinal cord lesions. The degree of hypertonus varies, and is greatest when the loss of movement is greatest.

The tendon jerks are exaggerated, and there is clonus (knee and ankle) in the affected limbs. The Babinski plantar response persists, but the abdominal reflexes, which are initially lost on the affected side, sometimes return after a period of months.

The forced immobility of shoulder and distal joints in the arm may lead to the formation of adhesions.

The so-called associated movements are involuntary changes of attitude of the paralysed limbs which accompany forceful voluntary movements, or such involuntary movements as, yawning.

CEREBELLAR APOPLEXY.—This is usually the result of thrombosis of the posterior inferior cerebellar artery, which is a branch of the vertebral artery, and the clinical picture is very unlike that of cerebral apoplexy. The patient is seized with a sudden intense vertigo which carries him to the ground, as in Ménière's disease. Incessant vomiting and forced movements follow, the forced movements rotating the patient, so that he comes to rest prone, with that side of the face corresponding with the side of the cerebellar lesion in contact with the pillow. There is intense ataxy, usually bilateral at first, and later becoming confined to the limbs and trunk on the side of the lesion. The patient is unable to lift his head, or to maintain the sitting or standing

position. When placed in such a position he positively dives to the ground when released. Nystagmus with the long slow movement to the side of the lesion, and a short fast movement in the opposite direction is conspicuous, and the skew deviation of the eyes is sometimes seen. There is much general hypotonia of limbs and trunk which soon becomes limited to the side of the lesion. Head retraction, pain and stiffness of the neck and opisthotonos may occur. When the patient's condition recovers sufficiently to allow of examination, all the signs of a unilateral cerebellar lesion will be found. Consciousness is not often lost. Since the posterior inferior cerebellar artery also supplies the lateral region of the medulla, signs indicative of disturbance of this region are usually present, and these may dominate the clinical picture rather than the cerebellar signs. Chief amongst them are analgesia and thermanæsthesia of the face and head, due to implication of the as yet uncrossed quinto-thalamic path, and of the limbs and body upon the opposite side, due to involvement of that part of the spinothalamic tract which has crossed below this level. Between these two areas of sensory loss there is often a gap where sensibility is normal, corresponding with that part of the spinothalamic tract which is crossing obliquely at this level, and therefore is too near the middle line to be affected. Paralysis of the motor vagus is often found from involvement of the nucleus ambiguus, and, from the extension of the lesion or of consecutive œdema towards and across the middle line, sometimes causes severe dysphagia and dysarthria, and one of the great dangers of this form of apoplexy is extension of the thrombosis to that part of the medulla which contains the respiratory and other vital centres. When, however, such extension does not take place, and if the destruction of the lateral lobe is not too extensive, the most remarkable recovery may take place.

Diagnosis.—*The nature of the lesion.*—Embolism should be diagnosed in all cases where there is an obvious cardiac valvular lesion, particularly mitral stenosis, septic endocarditis, aortic disease and aneurysm. It is true that syphilitic cerebral thrombosis may occur with syphilitic aortitis, but the combination is rare, for syphilitic aortitis usually occurs at a much later age than does syphilitic cerebral thrombosis.

Further conditions of cardiac feebleness and corresponding feebleness of circulation must obviously predispose to thrombosis if arterial disease be present. Mistakes in diagnosis will, however, not often occur, and they are not of moment to the patient, for embolism, when once the embolus is lodged, is for all purposes of treatment and prognosis the same condition as is thrombosis. Thrombosis should be diagnosed in all primary apoplexies in young syphilitic subjects, for syphilitic hæmorrhage usually occurs at some time considerably subsequent to a syphilitic thrombosis. In this connection the serum reaction and the cytology and reactions of the cerebro-spinal fluid are all-important in the diagnosis.

Thrombosis should be diagnosed, notwithstanding the presence of high arterial tension or renal disease, in all cases of apoplexy without organic cardiac valvular disease, when the onset occurs during sleep or under circumstances of quiet, depletion or exhaustion, and in all cases where prodromal symptoms are marked, or where the onset of the apoplexy is gradual, and in apoplexies occurring in advanced age, for then hæmorrhage is almost unknown. All slight apoplexies and nearly all those that survive the first 10 days after the ictus, are due to thrombosis.

Puerperal apoplexy and that occurring at the time of the menopause in women are mostly due to thrombosis.

The cerebro-spinal fluid affords important indications, since hæmorrhage into the brain in most of the cases soon bursts on to the surface or into the ventricle. If blood is absent from this fluid a few hours after the ictus, thrombosis or embolism is highly probable and hæmorrhage is very unlikely. Any infarct condition coming to the surface may in the course of time cause the fluid to be blood-tinged or yellow. It is important to bear in mind that the infarct conditions of embolism and thrombosis are followed by packing of the infarcted region with polymorphs, and that these may escape from the surface in such numbers as to load the cerebro-spinal fluid with such a high polymorph pleocytosis as to suggest the presence of suppurative meningitis. Hæmorrhage is a likely cause of apoplexy occurring during exertion, especially if it occurs at a moment of severe physical strain, or at the height of passion. It is always a probable lesion in cases where a previous thrombotic apoplexy has occurred, the final event, where multiple strokes have succeeded one another, being almost invariably hæmorrhage. An apoplexy with rapid onset and with symptoms rapidly deepening, with a quick onset of deep coma, and the development of pyrexia and signs of respiratory failure, is usually due to hæmorrhage. The certain test that an apoplexy is due to hæmorrhage is the presence of blood in quantity in the cerebro-spinal space as proved by lumbar puncture. In cases of small white kidney in the young and of granular kidney before the age of 50 years, where the blood tension is very high, and where there is severe retinitis, hæmorrhage is the most likely cause of stroke.

The position and extent of the lesion.—The position of the lesion may be judged by the nature of the initial signs, whether visual, sensory, motor or aphasic, cerebellar or pontine, and later by the permanent symptoms resulting from the lesion. It must be carefully borne in mind in this connection, that a severe lesion of a cerebral hemisphere may entirely abrogate the functions of that hemisphere, initially by a process of shock and afterwards by the occurrence of œdema in the vicinity of the lesion, which may spread widely.

The extent of the lesion may be gathered by the severity or otherwise of the early symptoms and their rate of increase, and by early or immediate loss of consciousness, and by the completeness of the paralysis resulting. The more severe the extent of the lesion the sooner do grave signs of general cerebral failure appear.

Differential Diagnosis.—The diagnosis of coma due to a cerebral vascular lesion is usually made without difficulty from the history, and from the presence of unequivocal signs of local lesion of the brain. In a patient without history, and when the coma has become so deep as to remove the unilaterality of physical signs, from the severity of the general intracranial pressure, the diagnosis may be difficult from other causes of coma such as uræmia and diabetes, poisoning by opium, alcohol and its derivatives and illuminating gas, and in cases of difficulty search is to be made for the usually obvious signs of these conditions. Uræmia may present especial difficulties, for it is often associated with cerebral vascular lesion, and transient hemiplegic attacks may occur in this condition. This is true also of the crises of essential hypertension, which are described in more detail on page 1608. Absolutely

sudden death which is so often recorded in death certificates as due to apoplexy, is usually associated with a stoppage of the heart following the obliteration of one of its coronary arteries. Apoplexy never causes sudden death. There is one recorded case of death from cerebral hæmorrhage in 5 minutes, but it is rare in any apoplexy for death to occur in under 2 hours. Other conditions causing hemiplegia with coma must be taken into consideration. Epilepsy and especially hemi-epilepsy may be followed by marked unilateral paralysis (Todd's paralysis), which may last for a considerable time. Here the history of recurring attacks and the complete recovery will easily prevent confusion.

Cerebral malaria and sunstroke may closely resemble apoplexy, and should always come to mind when rapid coma follows the development of cerebral symptoms in circumstances where these causes are likely.

The congestive attacks of general paralysis of the insane are peculiarly difficult to diagnose from apoplexy. Perhaps they are due to suddenly occurring acute cerebral local œdema. They are liable to mistaken diagnosis, of course, only when occurring as the initial manifestation of the disease, These attacks take the form of rapidly occurring attacks of hemiplegia, aphasia, hemianopia, hemianæsthesia or of some combination of these conditions, usually associated with initial convulsions and followed by coma. The diagnosis of a syphilitic thrombosis is made with reason on the positive serum reactions, and cerebro-spinal fluid examination. If energetically treated it recovers with marvellous rapidity and completeness, to slowly develop the characteristic signs of general paralysis. It is the too rapid recovery in a case of apparent syphilitic thrombosis which should suggest the possibility of the stroke being a congestive attack in general paralysis of the insane. In all cases of coma without history, especially when there are signs of local cerebral involvement, a very careful examination of the head should be made for traces of recent injury, and if signs of injury be found, the skull and meninges should be opened, and the nature of the lesion sought out and dealt with surgically.

Prognosis.—A majority of the cases of apoplexy from syphilitic thrombosis make a fair recovery, which obviously depends upon how much permanent thrombosis occurs in the lesion of acute syphilitic encephalitis which is responsible for this condition, and upon the early application of appropriate treatment for syphilis. In some of these cases even, no recovery occurs.

In embolism the course and prognosis depend upon the extent of the vascular supply cut off when the embolus comes finally to rest; and upon the amount of collateral circulation afforded, and upon the cardiac condition.

In thrombosis due to atheroma the apoplexy may be rapidly fatal from extension of the thrombosis and secondary œdema, which raise the intracranial pressure beyond the limits of survival. In cases which survive, considerable recovery may occur in proportion to the extent of the lesion, but in these subjects an apoplexy is usually the beginning of the end, since the underlying pathological causes, arterial disease and failing cardiac action, still exist and are not amenable to any radical treatment. It is astonishing, however, how many of the cases of apoplexy due to atheromatous thrombosis survive for years without any recurrence of the thrombosis or occurrence of hæmorrhage. In cases of hæmorrhage, the immediate prognosis

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is the gravest possible, the great majority of the cases surviving but a few hours.

Treatment.—When arterial disease is known to be present, the only measure which can in any way tend to safeguard the patient from apoplexy is moderation in all things: in diet, alcohol, mental and physical exercises, and above all moderation in all measures tending to lower the blood pressure, for hæmorrhage is due not so much to the immediate high blood pressure as it is to an antecedent period of low blood pressure in a high tension subject, which has allowed of thrombosis and which, when the tension is high, at some subsequent period causes rupture of a vessel in the thrombosed area. It is highly probable that no treatment influences the course and fatal issue of apoplexy due to hæmorrhage. Thrombosis and embolism, however, allow some scope for treatment, which should be the same in the two conditions; and as I have argued above that medical treatment in cases of hæmorrhage is useless and cannot avert the fatal result, I advise one line of treatment to be taken in all cases of apoplexy.

From the onset of symptoms in every case, a careful stimulant line of treatment must be adopted, and all depletive measures that may be calculated to lower the blood pressure and diminish the force of the cardiac action should be scrupulously avoided. It has been pointed out in the preceding passages how much the local and general symptoms of apoplexy are the result of cerebral ischæmia produced by the raised intracranial pressure, either from hæmorrhage or from œdema, and how nature attempts to combat this ischæmia by a reflex raising of the blood pressure, to keep the cerebral circulation going, and that how when the intracranial pressure exceeds that of the mean intracranial venous pressure, death must at once result from stoppage of the cerebral circulation. As Thomas truly emphasises, "How can the lowering of arterial blood pressure possibly help such conditions?" Absolute rest is, in the first place, essential when prodromal symptoms appear, and at the onset of an attack diffusible stimulants in the form of alcohol and liquid food; the heart's action may be improved by strychnine, while restlessness may be combated with bromides. If the patient is conscious, he should make as little effort as possible. His head and shoulders should be raised, special care being taken that the neck is not bent, and that nothing shall interfere with the return of blood from the head. If there is unconsciousness with stertor, the head and shoulders should be turned upon one side, so that the tongue should not fall back and impede respiration. If there be much cyanosis from impeded respiration, as is often seen in plethoric subjects, it is advisable to withdraw blood by venesection, for such relief of embarrassment acts as a stimulant to the circulation. Purgation should be avoided, and the bowel relieved at intervals by enemata. Stimulating food in a liquid form should be administered with stimulants at regular intervals; and if there is any difficulty in swallowing, the food should be administered with the nasal tube. The bladder should be carefully watched from the first, lest retention should occur, and the catheter passed when necessary. Lumbar puncture should, when necessary, be performed for diagnostic purposes, and it frequently gives relief from symptoms due to the high intracranial pressure. I have many times seen consciousness return within a few minutes of lumbar puncture, when much fluid can be withdrawn. It is advisable to withdraw all the fluid which will run out at a rate above the normal. Bed-sores and

hypostatic bronchitis must be avoided by the usual measures. In the cases that survive the first few days, passive movements should be used daily to all the joints of the affected side in hemiplegic cases, for this will obviate the painful rest adhesions which form in the joints of the paralysed limbs, and especially in the shoulder joint, and subsequently cause so much pain and misery to the patient. With the return of the power of voluntary movement, active exercises take the most important place in treatment. The final state of hand-and-finger movements depends not alone on the severity of the damage done to the brain, but in part upon the thought given to devising active exercises for it and the assiduity with which the patient can be persuaded to employ them. To avoid fatigue it is best to ordain a given daily period of some minutes to systematic exercise. A rubber sponge of appropriate size, fixed in the palm by a strip of webbing passing round the hand, will limit the passive flexion of the fingers, and will provide a resilient resistance against which the patient may move his paretic digits. Massage is an adjuvant, but never a substitute, for active exercises in the patient who can undertake them. Electrical stimulation of the muscles is absolutely contra-indicated. It has no other effect than to aggravate the spasticity that is so serious a hindrance to free movement. A hemiplegic patient after apoplexy, should be got upon his legs and encouraged to make attempts to walk as early as ever the returning power allows any possibility of the attempt.

HYPERTENSIVE ENCEPHALOPATHY

In the preceding section on the differential diagnosis of apoplexy, mention was made of the sudden and transient cerebral symptoms associated with essential hypertension, and some further reference to them is necessary. It is known that the subjects of this variety of hypertension may ultimately succumb to cerebral hæmorrhage, but it should also be borne in mind that they are subject from time to time to what are known as "hypertensive crises." The patient is the possessor of a persistently high blood pressure. The attack is precipitated by a further rise in this, and develops with intense headache, sickness and sometimes drowsiness or even semi-coma. Examination will reveal the presence of hypertensive retinitis in most cases, but in a proportion there is a definite papillœdema with retinal hæmorrhages and exudate. Accompanying these symptoms there may be hemiparesis, hemianopia, focal or generalised fits, or other indications of local cerebral lesion. The crisis is brief, lasting from a few hours to several days, and usually ends in recovery, but recurrence is likely, and finally many subjects develop cerebral atheroma and succumb to cerebral hæmorrhage. Intervals of several months may intervene between succeeding crises.

The presence of papillœdema is taken to indicate that cerebral œdema is complicating the situation. The transient nature of the crisis, and particularly the rapid appearance and disappearance of such symptoms as hemiparesis, exclude the possibility of arterial thrombosis or other material lesion of the kind, and spasm of the arteries has been invoked to account for the symptoms. There is of course no conclusive evidence that this occurs. Yet while the cerebral arteries are not under the same measure of

vasomotor control as arteries elsewhere in the body, it is known that some such control exists, and it may be that in arterial hypertension more intense spasm is possible than in healthy arteries. At least, it may be said that no hypothesis better founded or more in harmony with the facts of clinical observation has been formulated.

Differential Diagnosis.—As has been indicated, the transitory character of the symptoms exclude gross vascular lesions such as thrombosis, and the same may be said of intracranial tumour and lead encephalopathy. Yet it may be admitted that while it is present the hypertensive crisis shows many points of resemblance to the last two named conditions, especially when papillœdema is found. Plumbism in children and young persons not uncommonly develops with headache, vomiting, convulsions and focal signs, and the development of an intense papillœdema, sometimes also with high blood pressure and albuminuria, and search for other indications of lead poisoning and careful history-taking are necessary to exclude this condition. In intracranial tumour, the systolic blood pressure is rarely above normal limits, the history is longer and the condition progressive. Uræmia can usually be excluded, since in essential hypertension the blood urea is within normal limits, and the only abnormality in the urine may be a trace of albumin.

Treatment.—Venesection is indicated as the first step, and when there is papillœdema or other signs of cerebral œdema (convulsions, high cerebrospinal fluid pressure) lumbar puncture and the withdrawal of cerebrospinal fluid, and also the intravenous or intramuscular administration of hypertonic solutions are necessary. As a measure of urgency from 50 to 70 c.cm. of a 50 per cent. solution of dextrose may be given intravenously. For less urgent cases and as a measure that can be repeated for the relief of headache, six ounces of a 20 per cent. solution of magnesium sulphate may be given per rectum at 6 hourly or less frequent intervals. The convulsions may be treated by rectal administration of paraldehyde (240 to 360 minims in water), or by the hypodermic injection of 3 grains of soluble phenobarbitone in solution.

The subsequent management of the case is that of the underlying essential hypertension.

SINUS THROMBOSIS

Thrombosis of the cerebral sinuses may occur rarely as a primary condition, or it may be secondary to infective processes spreading to the sinuses from contiguous infected regions.

Ætiology.—Primary thrombosis is a rare condition. It is said to affect the superior longitudinal sinus most commonly. It is more common in the first year of life than at any other period, when it may follow diarrhœa, bronchitis or the conditions of exhaustion met with in tuberculous disease, and in congenital syphilis, and it may follow acute diseases such as measles diphtheria, etc. It may also occur at any age, up to advanced old age, in the terminal stages of cancer, phthisis and other chronic diseases.

The essential cause of secondary thrombosis is the advent of micro-organisms to the sinuses. The infection is often a mixed one, but the common organisms present are streptococcus, pneumococcus and *Bacillus*

coli. The sinus may become infected as a part of a general pyæmia, or infection may spread directly through its wall from a focus of local disease, most commonly from an extradural abscess. In most cases, however, the sinus becomes infected from a local spreading septic thrombosis of the veins which open into the sinus, from an infected spot at a distance. Thrombosis of sinuses may also occur from injury, as by bullet wounds and fractures of the skull, and may also result from surgical procedures in the region of the sinuses.

Pathology.—The affected sinus is bulged and distended, and feels to the touch, as if it were injected with a solid mass. In the infective forms, the clot may very quickly break down into pus, and general pyæmia result. When the superior longitudinal sinus is thrombosed, there is marked congestion of the convolutions of the convexity of the brain, often with cord-like clot-distended veins. There is bloody serum in the sub-arachnoid space contaminating the cerebro-spinal fluid withdrawn by lumbar puncture. Later, there is extensive bilateral softening of the cerebral hemispheres, most marked in the paracentral and surrounding convolutions. The cavernous and lateral sinuses do not drain the brain directly, and blocking of one of them does not cause so much cerebral disturbance, on account of the presence of alternative paths for the blood. Thrombosis of the cavernous sinus, however, may extend to the ophthalmic veins and cause blindness with an anæmic and infarcted condition of the retina. The nerves which lie in its outer wall, namely, the third, the fourth, the ophthalmic division of the fifth and the sixth nerves, may be paralysed.

Symptoms.—The clinical aspect of this condition is made up of three groups of symptoms—(1) the general signs of some bodily condition likely to be associated with thrombosis, such as marasmus, pyæmia, local cranial injury or septic disease of cranial bones and neighbouring tissues; (2) general signs of intracranial disturbance, which will depend upon how much the cerebral circulation is upset by the blocking, and which will be severe in cases where the superior longitudinal or the straight sinus is affected, and perhaps altogether absent where the cavernous sinus or the lateral sinus is affected; and (3) local signs of blocking of an individual sinus.

The general signs depend upon congestion, œdema, meningeal exudation and increased intracranial pressure. Headache, drowsiness, deepening into coma, and vomiting are common, while delirium and convulsions may occur. Papilloedema is not infrequent, while head retraction and rigidity of the neck, trismus, strabismus, inequality of the pupils, nystagmus, and irregularity of pulse and respiration may occur. In infective thrombosis, high pyrexia and rigors are the rule.

Local Signs.—*Superior longitudinal sinus.*—The general signs are severe and convulsion is common, and bilateral hemiparesis or paralysis is likely to develop. There may be cyanosis and œdema of the forehead. The angular parietal and temporal veins may be distended, and in rare cases thrombosed.

Lateral sinus.—The clot may extend into the jugular vein and cause pain and stiffness on that side of the neck, and occasionally the thrombosed jugular vein may be felt beneath the anterior border of the sterno-mastoid as a tender solid cord. There may be tenderness and swelling over the region of the mastoid emissary vein.

Cavernous sinus.—There is œdema of the orbit, with proptosis and œdema of the conjunctiva, forehead and face. Amblyopia or blindness is the rule. Ophthalmoscopic examination reveals swelling of the disk with multiple hæmorrhages. Paralysis of the ocular muscles and anæsthesia of the eye on the same side may also occur.

Diagnosis.—If local signs, which give conclusive external evidence of sinus thrombosis, are absent, it may be very difficult to distinguish this condition from meningitis, abscess, encephalitis or other intracranial lesions. The septic forms of meningitis should be distinguished by the polymorphonuclear leucocytosis in the cerebro-spinal fluid. It must be remembered, that in the primary forms of sinus thrombosis in children, a copious lymphocytosis is met with, which may cause confusion with tuberculous meningitis. Abscess and sinus thrombosis often exist together.

Prognosis.—This disease is, as a rule, rapidly fatal from ever-increasing intracranial pressure; but some subjects, both in the non-infective and in the infective forms, survive. This is especially the case when the thrombosis is confined to one cavernous sinus. Cases of infective thrombosis of the lateral sinus following middle-ear disease have often been saved by timely surgical interference with ligature of the jugular vein and of the lateral sinus on either side of the thrombosed area, and with incision and turning out of the clot.

Treatment.—Beyond vigorous prophylactic measures against the causes of this condition and the palliative treatment of symptoms, surgical measures in cases of local infective origin alone are of avail. Further, in dealing with injuries of the skull in the region of the superior longitudinal sinus, trephining and exploration should be undertaken with a clear understanding of possible thrombosis of the sinus, and its appalling results.

APHASIA AND OTHER DEFECTS OF SPEECH

APHASIA

General Considerations.—The function of speech, which is the highest and most recently evolved human function has as its anatomical substratum a region of the cerebral convolutions situated in the left hemisphere and having its centre a little behind the middle of the first and second temporal convolutions. It is limited above by the posterior limb of the Sylvian fissure, occupies probably the tip and the whole external convexity of the left temporal lobe, and spreads backwards into the supramarginal and angular gyri, while it extends forwards over all the convolutions of the insula and possibly to the posterior ends of the second and third frontal gyri of the left side.

This "speech region of the brain" comprises not only the cortex but also the subcortical white matter which carries the paths of communication between the speech region and other parts of the brain. Posteriorly it receives an important white tract from the visual region of the cortex. An interruption of this tract results in the condition known as "pure word-blindness," or inability to appreciate written speech. Upon its deep aspect

the speech region of the convolutions receives the temporal projection of fibres conveying the auditory impressions, and destruction of this system by a lesion undercutting the convolutions in the centre of the temporal lobe produces "word-deafness," or inability to appreciate spoken language. In this same region another set of afferents impinges upon the speech area which convey the muscular sense impressions and other sensory impressions which are produced in the movements of articulation and which are the only guidance which the "deaf mute" has in the knowledge of correct execution in his articulation.

A lesion deep in the temporal lobe which interrupts both the foregoing paths, isolates the speech region from any appreciation of correct execution, with the result that spoken language becomes unshapen and degenerates into a voluble jargon, "jargon aphasia."

In the anterior half of the speech area a tract of white fibres gathers by degrees, and passing forward constitutes the bulk of the "temporal isthmus," which joins the temporal lappet to the insula, and runs beneath the insula to the region beneath the first and second frontal convolutions, from whence it is connected with the pyramidal path of the left side, and by way of the corpus callosum with the pyramidal path of the right side. This is the executive outgoing path for speech movements and a complete lesion of this path, as by a limited subcortical lesion underlying the posterior end of the left third pre-frontal gyrus and anterior part of the insula, will result in complete inability to exteriorise either spoken or written speech—"pure aphasia" and "pure agraphia."

In the speech area of the brain thus limited, little or nothing is known of any localisation of function. It is generally held that there is a gradual passing over from receptive function (appreciation of spoken and written language) in the posterior regions, to executive function (exteriorisation of spoken and written language) in the anterior regions.

Inasmuch as the phenomena of "word-blindness" and "word-deafness," as well as executive "aphasia" and "agraphia" result from lesion of the speech area, these seem to result from lesion of the tracts concerned and not from interference with the function of the cortex. These phenomena are of common occurrence in connection with lesions of the speech region and led to the formulation of localised areas of the cerebral cortex with specific functions in regard to speech. Thus, Broca's centre in the cortex of the posterior part of the left third prefrontal convolution was the motor centre for spoken language, while Exner's centre in a similar position in the second left prefrontal gyrus was the motor centre for written language. The "auditory word-centre" in which auditory memories of words were stored was in the cortex of the first and second temporal gyri, and the "visual word-centre" in which visual memories for words were impressed was in the cortex of the angular gyrus. These various centres were connected together by to-and-fro paths which could be separately affected by a lesion, and the attempt was made to explain the multitudinous and varied phenomena which occur in lesions of the speech region by damage to one or other of these hypothetical word-centres or to their connecting paths. The result was highly unsatisfactory, for the cases generally refused to correspond with the theories clinically, and practically never corresponded pathologically. Dejerine, by his discovery that a subcortical lesion in the right place could produce "pure

aphasia and agraphia " at the front end of the speech area and " pure word-blindness " at the posterior end, the cortex being intact, went far to make untenable the theories of narrow localisation of function within the speech centre. Subsequently the work of Pierre Marie, Head and others has placed modern conceptions of speech function upon a less artificial basis.

The speech function seems to be concerned with the left hemisphere of the brain alone in right-handed persons, and this is explained by the major potential of the left hemisphere for receptivity and education associated with the major use of the right hand through the countless ages of humanity. Left-handedness is usually associated with a transfer of the speech function to the right hemisphere, but there are exceptions to this rule.

The possibility of the transference of the speech function from the left to the right hemisphere is great during childhood, to the extent that no lesion of the speech region of the left hemisphere, however extensive, causes lasting loss of speech in a child under the age of six years, provided sufficient intelligence remain. After this age the possibility of such compensation by the right hemisphere for lesions in the left hemisphere seems gradually to diminish and to occur but little after adult life is reached, but even in adult life remarkable exceptions to this rule are seen.

The descending paths from the brain by which speech is executed are the pyramidal paths. The speech area of the cortex seems to command both right and left pyramidal systems equally, so that no lesion of one pyramidal system is ever productive of speech defects, either asphasic or dysarthric.

From this it follows that aphasia, word-blindness, word-deafness, amnesia, etc., only result from lesions of the convolutions and of the white matter closely underlying the convolutions, and never from lesions of the deeper parts of the corona radiata and capsules.

When, however, both pyramidal systems are involved, as, for example, by bilateral lesions of the brain, or by lesions of the brain stem which involve both pyramidal systems where these are contiguous, or by neuronic degeneration of the pyramidal systems in general, then defects of articulation arise comparable to the spastic paralysis of hemiplegia. These do not concern the pattern of speech, but solely the articulation, which becomes slow, clumsy, and slurring and indistinct, from weakness of movement, stiffness of the muscles concerned, and inability finely to adjust the stop positions at which the consonants are made. This condition, which is known as " spastic dysarthria," is commonly met with in double hemiplegia, in lesions of the brain stem involving both pyramidal tracts, and also in the tonic form of progressive muscular atrophy. In older writings it is often referred to under the most inappropriate name of " pseudo-bulbar paralysis."

When the lower motor neurons subserving the speech mechanism are bilaterally affected, a very similar dysarthria results, from the weakness and inaccuracy of the movements thus entailed, which is known as " flaccid or atrophic dysarthria," and which is met with in lesions of the medulla oblongata of all kinds, in progressive muscular atrophy, and in peripheral neuritis.

Lesions responsible for Aphasia.—By far the most common cause of aphasia, in all its degrees and varieties, is vascular disease, usually thrombosis, less commonly embolism, and only in the rarest cases hæmorrhage—

for the reason that the two former lesions often affect the vascular supply of the superficial parts of the hemisphere, whereas hæmorrhage is generally situated deeply; moreover, cases of cerebral hæmorrhage rarely survive the occurrence for more than a few hours. Cerebral tumour is the usual lesion causing aphasia of gradual onset, and is perhaps the only known cause of isolated "word-deafness" and of "voluble jargon aphasia," for it is the only conceivable lesion which can undercut and, therefore, isolate the temporal convolutions without otherwise interfering with their function.

Physiological Considerations.—Within a short time after birth the child begins to recognise the nature and uses of some of the objects in the world around it, and to express its simple conscious process by gestures, and it early appreciates the "gesture language" of those around it. The "mimesis," or gesture language, thus early impressed and expressed, remains throughout life the most stable, the least vulnerable, and the longest lasting of the methods of receiving and communicating ideas. Long before it is able to utter any articulate sound, the infant learns to connect certain sounds which it hears with certain objects and with certain events, and the memories of these auditory patterns first implanted serve by far the most important function in the processes and expressions of thought throughout life. Whereas we rely upon our visual memories for our remembrance and intelligence in general matters almost exclusively, yet as regards speech we rely upon auditory memories to a very large extent, and of course those who have never learned to read do so exclusively. The process of recall, both in silent thought and in speaking, is the revival of auditory patterns. We are, therefore, strong "visuals" as regards general memory, but strong "auditives" as regards speech memory, and the relative strength of the two functions varies somewhat in individuals, according to personal idiosyncrasy and to education, and this individual variation is sometimes apparent in the phenomena of aphasia. From the original connection with hearing, the memories of speech patterns come to be located in that part of the brain associated with the auditory function—in and around the temporal lobe. Later, guided by the auditory memories, the child begins to express himself in articulate speech and he does so by the revival of auditory memories.

All living motion is sensory-originated, sense-guided and sense-governed, and a motor process of itself has no proved conscious concomitant. Our consciousness is that of the sensations which accompany the movement, or which result from the movement. The knowledge of correct execution so gained fortifies and increases the functional stability of the speech area, and is of immense importance in the speech function. If it be absent owing to a lesion isolating the speech area on the incoming side, speech degenerates into a jargon and soon becomes impossible; just as in tabes the walking becomes irregular from loss of the muscular sense conveyed in the posterior columns, and ultimately standing becomes impossible.

When at a considerably later age the child learns to read and to write, certain visual patterns (letters, words, sentences) become connected with certain objects and ideas, and become linked on to the already well-established auditory memories of speech. The meaning of the visual symbols is learned by the child from the meaning of the word or pattern spoken, which he already knows well, and the already developed auditory speech

function serves as the instructor of the visual speech function, and throughout life remains the more potent, more dominant and less vulnerable function of the two.

Later still, in learning to write, the child relies upon his visual memories, and as his knowledge of correct execution in writing is largely visual and only in minor degree common sensory from the movements of the hand in writing. It follows that the function of exteriorising speech by writing becomes intimately connected with and a part of the visual speech function, and is usually depressed or lost with the visual speech function as the result of disease. It will thus be seen that there are not separate regions of the speech area in which the auditory memories of language and the execution of spoken speech on the one hand, and the visual memories of language and the execution of written language on the other hand, are represented, but that there are four functions intimately coupled in pairs, which have their seat in the same anatomical substratum.

It is a general principle that when the speech area is damaged the speech function becomes depressed as a whole, with the result that function is lost in order of its depth of impression.

Symptoms.—Small lesions of the convolutions seem to produce no defects at all, and this is perhaps true of all the regions of the cortex of the brain. There can be, therefore, no narrow localisation of function, and there must be capacity for compensation for such small lesions in the surrounding undamaged cortex. With larger lesions of the cortex, and in proportion to their extent, mutilation of the patterns of speech, slowness of utterance, inability to find the words (inability to recall), especially nominals, and above all isolated nominals, and finally confusion of speech intelligence occur, in that order.

In the mutilated speech of the aphasic may be sometimes noticed stammering. This condition is at once distinguishable from true jargon aphasia, since the former is slow and halting whereas the latter is facile and voluble. Misplacement of words and the use of wrong words is common and is called " paraphasia." A tendency to repeat a word once pronounced is sometimes present and bears the name " echolalia." The same faults occur also in writing, as faulty spelling, misplacement of letters and words, wrong words, " paragraphia " and " echographia." Much defect of general intelligence always accompanies severe damage to the speech area, and this will be readily understood from the very large rôle which speech patterns play in the working of thought. Difficulty in the recall of words and speech patterns, which has been termed " verbal amnesia " or " nominal deficiency," is a characteristic feature of lesion of the speech area. This difficulty is greatest with spontaneous revival than with recall, which is " kicked up " by direct sensory stimulation. For example, an aphasic person who is unable spontaneously to utter a word, may repeat the word at once when it is spoken to him, when he sees it in writing, or when the corresponding object is shown to him. It is important in this connection to bear in mind that we do not speak in the letters of the alphabet, nor in the words of our dictionary, but in a running pattern of sound. The pattern or context provides the meaning, while the individual words are negligible and have no meaning. The power of the pattern in aiding revival is very great both from sequence rhythm and musical quality. As examples, an aphasic who

has no utterance spontaneously is told to count with his interlocutor. The interlocutor begins counting, the aphasic joins in. The interlocutor then stops, but the aphasic continues counting, carried by the sequence rhythm.

The confusional defects of speech function are met with in extensive damage to the speech area, and are usual as immediate and transient phenomena in all suddenly occurring lesions of the speech area. There is general mental dullness, with varying degrees, usually severe, of depression of speech function, and much confusion, both on the acceptive and expressive side, when any of these functions remain, and the results of the examination of the speech faculty are apt to vary very much from moment to moment, for attention is very difficult to hold and the patient is easily fatigued and bored. Severe degrees of this form of defect may be associated with inability to recognise objects—"object-blindness," and with loss of ability to convey ideas by gesture—"amimia."

Prognosis.—In attempting to estimate the degree of recovery which is likely to occur in cases of aphasia, it is necessary first to bear in mind that sudden cerebral injury is apt at first, by the process which has here been described as functional depression or "diaschisis," to cause very wide loss of function, though the lesion may not be very extensive. A total aphasia, for example, is often the immediate result of a lesion of moderate size. Such phenomena last usually not longer than a week, and until they have passed off it is impossible to make a definite statement, either as to the extent of the lesion or the likely degree of recovery. Speech may be regained by two entirely separate processes—either by recovery of function in partly damaged and functionally depressed areas, or by compensatory activity in the potential speech area of the undamaged hemisphere. The possible recovery of function will depend upon the nature of the lesion and upon its extent. It will be greater when a lesion may be judged to be one of pressure rather than of actual destruction, if such pressure be removable, as in subdural hæmorrhage, abscess and gumma, and least when widely spread arterial disease and a failing heart suggest that the lesion is a thrombosis, and when an irremovable tumour is present. The greater the extent of the lesion if it be presumably from vascular occlusion, as judged by the associated signs, paralysis, anæsthesia and hemianopia, the less is the chance for functional restitution, as there is then little hope of any useful restoration of the circulation through collateral vessels. In children under the age of six years, unilateral lesions produce no permanent speech defects, provided sufficient intelligence remains, but even to this rule some important striking exceptions have been recorded. When adult life is reached, transference seems to occur but little, yet in a few recorded instances destruction of the posterior half of the speech area has been followed by an almost complete restoration of speech function.

Treatment.—A careful and patient system of re-education in speech, such as is used in teaching mentally deficient children, is often of great value in all forms of speech defect. From the amount of labour that the teacher has to expend for very little progress made, this treatment is not often given a fair trial. A fair degree of intelligence must be present, and care must be taken that the lessons are not prolonged to the production of the boredom, with accompanying inattention and confusion, which occurs so readily in aphasic patients. The utterance of a simple vowel sound should

first be taught, then that of the several vowel sounds, and afterwards that of consonants and their combinations, and the patient should be directed while learning to watch the movements of the lips, etc., of the teacher. The simultaneous presentation of an object with its spoken and written name is often helpful in stimulating the remains of speech function into activity. An intelligent patient soon comes to recognise under such tuition that he has no paralysis of the articulatory mechanism.

Testamentary Capacity.—No rule can be laid down as to the capacity of a person suffering from aphasic speech defects to exercise civil rights and to make a will, and each case must be judged upon its own merits. The first and all-important consideration is the degree of intelligence, and when this is good it is essential for such capacity that there should be some mode of cognition and of expression left. Pure word-blindness and the extremely rare condition of pure word-deafness do not interfere with the exercise of civil rights, for the patient can understand what he hears in the first case, and what he reads in the second, and in both conditions can express himself both in speech and writing. In cases of pure aphasia and pure agraphia there is complete civil capacity, but when, as usually happens, the two conditions co-exist, though intelligence and the receptive side of speech may be but little impaired, yet the expressive side of speech is reduced to gesture, and extreme difficulty may be met in ascertaining the patient's wishes. Auditory amnesia, and combined auditory and visual amnesia, and confusional defects, except in the slightest forms, interfere seriously with testamentary capacity and with capacity for exercising civil rights. In such cases there is great loss both on the acceptive and on the expressive sides of speech, with confusion of memory and impairment of intelligence. Most satisfactory results have, however, many times been brought about in apparently hopeless cases by careful, sympathetic and repeated procedures, in which the properties to be bequeathed and the likely legatees are assembled before the patient, thus allowing the testator to match the gift with the recipient. The proceedings should be conducted in the presence and under the direction of a physician thoroughly conversant with the subject of aphasia. All concerned should bear two points in mind, the one being that the wishes of the legator must be paramount, and the other that an obviously just will is most difficult to upset in a court of law.

The Method of Examination of patients suffering with speech defects should be in accordance with some definite scheme so drawn up as to test each function of the complex physiological process of speech.

The following scheme is convenient: (1) Is the patient right- or left-handed, and, if the latter, did he write with the right hand? (2) What was the state of education as regards reading, writing and foreign tongues? (3) Does he understand the nature and uses of objects, and can he understand pantomime and gesture, or express his wants thereby? (4) Is he deaf? If so, to what extent, and on one or both sides? (5) Can he recognise ordinary sounds and noises? (6) Can he comprehend language spoken? If so, does he at once attempt to answer a question? (7) Is spontaneous speech good? If not, to what extent and in what manner is it impaired? Does he make use of wrong words, recurring utterances, or jargon? (8) Can he repeat words uttered in his hearing? (9) Is the sight good or bad, is there hemianopia, or papillœdema? (10) Does he recognise written or printed

speech and obey a written command ? If not, does he recognise single words, letters, or numerals ? (11) Can he write spontaneously ? What mistakes occur in writing ? Is there paragraphia ? Can he read his own writing some time after he has written it ? (12) Can he copy written words, or from print into writing ? Can he write numerals or perform simple mathematical calculations ? (13) Can he read aloud ? (14) Can he name at sight words, letters, numerals and common objects ? (15) Can he write from dictation ? (16) Can he match an object with its name, spoken or written, when a series of objects and names are simultaneously presented ? (17) Any other tests, emotional, rhythmical, or musical, which may raise the physiological level of the speech centres. (18) Any other means of proving in what way he can receive and express ideas.

OTHER DEFECTS OF SPEECH

1. Stammering or Stuttering.—A spasmodic defect of articulation leading to a sudden check in the utterance or words, or to a rapid repetition of the consonantal sounds in connection with which the difficulty arises. To the trouble with articularion are often added spasmodic movements of the face and head, or indeed of any part of the anatomy.

Except in the rarest instances this condition is not associated with any structural changes in the nervous system nor in the organs of articulation, but it has been observed as the end-result of a lesion of the speech area. The disorder seems to consist in a lowering of the functional stability of the executive speech mechanism by a physiological embarrassment in consciousness. It is begotten of shyness and self-consciousness. It is never congenital, nor met with in early infancy, but arises at the age when shyness and self-consciousness trouble youth most. It is infinitely commoner in boys than in girls, for the latter are much less liable to self-consciousness. The stammerer never stammers in the speech of thought, nor when talking aloud to himself alone, nor at any time when singing, for in the two former cases the embarrassment of self-consciousness is absent, and in the last case the element of rhythm and music greatly increases the stability and confidence of the function. It not uncommonly appears in conditions of debility, and especially after measles and diphtheria. It has a frequent origin in sudden fright. It is the historical utterance of fright and of those who find themselves suddenly "inflagrante delicto." In rebellious cases the element of self-consciousness seems to disappear, while the stammer persists as an ineradicable habit, and it is remarkable how many sufferers of this class have strong aspirations towards public speaking.

In articulate speech three muscular mechanisms are concerned—(1) the respiratory mechanism for supplying the blast of air, (2) the larynx for producing the voice, and (3) the muscles of the lips, tongue, jaw, and palate for articulation. For distinct speech there must be absolute co-ordination of these mechanisms one with another. Consonants are in nearly all cases the source of the difficulty in stammering, and while these are all buccal sounds, yet some begin with a laryngeal sound, while others are purely buccal. The former are termed "voiced consonants," and are B, W, V, Zh, Z, Th (as in "thus"), D, L, R, G, Y; and the latter "voiceless consonants,"

and are P, F, Th (as in " thin "), S, Sh, T, K ; while N, M, and Ng terminal, are " voiced nasal resonants." If one articulates these consonants it becomes at once clear that it is the presence of the initial laryngeal element or " voicing " which makes the difference between B, V, Z, D, G, and P, F, S, T, K, respectively.

A careful attention to the manner in which the letter sounds are produced is absolutely essential in the investigation and treatment of stammering. The difficulty occurs most commonly with the explosive consonants, P, B, T, D, G, K, and nearly always where these occur as initial letters—that is, in starting the articulatory mechanism ; and to avoid this difficulty which arises after every pause, most stammerers speak in a rapid monotonous fashion. The fault chiefly lies in the direction of energy to articulation rather than to phonation. The patient held up by his stammer usually remains silent, but occasionally, having produced the first sound, he continues to repeat it—the reduplication stammer which has been the origin for the names " stammer " or " stutter " by which the malady is known.

Often the patient uses a trick or contortion to prevent the stutter or to relieve the feeling of nervous tension and embarrassment in consciousness which the defect causes, and these tend to become engrafted on him, as (1) associated sounds—whooping, grunting, crowing, etc. ; (2) habit spasms—contortions of the face, limbs, or body, which sometimes take a complicated form and exactly resemble the co-ordinated forms of tic.

Prognosis.—The majority of the cases tend to a spontaneous cure, and recovery is hastened in all cases by systematic treatment. In every class of case the results of treatment may come slowly at first, but perseverance will in almost every case bring success.

Treatment.—Attention should be paid to conditions of general health, and to the mental well-being and satisfaction of the child, with plenty of scope for pleasure and satisfying occupation.

It is well for the patient to speak, read, or recite in a large room alone, loudly, slowly and distinctly. The following system for such exercises is useful : (1) The chest must be kept well filled with air. This most important point is often most difficult to the patient. (2) He must speak slowly, with a full resonant voice. (3) When he comes to the word on which he tends to stutter, he should raise his voice and direct his energies to vocalisation, and not to articulation. If the difficulty be over a voiced consonant, he must be directed to voice it firmly. If the consonant over which he stumbles be a voiceless one, attention must be directed to the vocalisation of the subsequent vowel sound ; for instance, in " pat " he must attempt to vocalise the " at," and he will find little difficulty in prefixing " p " as the syllable is uttered. (4) Gymnastic and singing exercises are valuable additions to treatment. Should associated movements be present, the speaking exercises may be carried on in front of a mirror, so that the patient may see these himself and endeavour to suppress them.

The development of confidence and self-reliance is everything in the treatment of stammering. The skilled teacher first gains the liking, respect, and submission of his patient. He then assures him that his defect will disappear, and that he can cure himself, and demonstrates to him by correcting the faults that he can speak normally.

2. Lalling.—A defect due to want of precision in the action of the oral

articulatory mechanism. It characterises the speech of many children before the art of articulation is completely learnt. It is only a persistent condition in some cases of defective intelligence.

3. Lisping.—A defect due to the indistinct enunciation of certain consonants, or to the substitution of wrong consonants. It usually occurs in connection with the sounds of Th, R, and S, which change to V, L, and Th respectively. The condition, which is almost usual in infants learning to speak, is due to faulty articulation, and may become a habit, in which case the subject has probably a bad "ear" for sound. Defective conformity of the mouth may cause it; for example, a "tongue-tied" person can never pronounce the English R correctly.

4. Idioglossia.—A condition in which from the first moments of learning to speak, a child uses wrong consonants, or rather he tends to substitute three or four consonants for the whole series. Very slight degrees of idioglossia are common in little children, whose early speech is intelligible only to their nannies. In marked cases the child comes to speak a language entirely its own.

The course of time and education removes the defects of lisping, lalling, and idioglossia, and the prognosis in all these conditions is invariably good.

Any deformity of the articulatory organs should be remedied if possible.

James Collier.
Revised by F. M. R. Walshe.

APRAXIA

Definition.—A disorder of cerebral function, characterised by inability to perform certain familiar purposive movements, in the absence of motor and sensory paralysis and ataxia (Kinnier Wilson). This disorder does not depend upon defective perception (agnosia) nor upon general reduction of intelligence.

Ætiology.—Apraxia may result from both general and local diseases of the brain. It may be met with in general paralysis of the insane, in cerebral sclerosis and in several forms of dementia, and in paralytic chorea. It occurs in its purest form from local lesions of the brain, and may then be confined to one region of the body. It may result from lesions of the posterior part of the prefrontal area of the left side, the so-called "motor or verbal" aphasia and agraphia being good examples of apraxia of speech, and lesions in this region may also cause apraxia of the limbs on one or both sides. Lesions of the anterior half of the corpus callosum have been associated with conspicuous apraxia, as have also bilateral lesions in the posterior parts of the hemispheres. In the latter cases, the apraxia is likely to be associated with some degree of lack of recognition of an object, and of its uses (agnosia), and this causes apraxia from a loss of correct comprehension of the act required. Apraxia is sometimes met with in cases of hemiplegia in which, notwithstanding the complete recovery of motor and sensory paralysis, the performance of familiar acts—from the highest skilled movements, such as the fingering of the pianoforte or of the violin, or the use of his tools by a craftsman, to the simplest act—may be no longer possible. The features of the condition may be well demonstrated by the consideration of left-sided

hemiapraxia. There is neither loss of power nor loss of sensibility in the left upper extremity. When such a patient is asked to perform some familiar act with the right hand, he at once does so correctly, but when ordered to perform the same act with the left hand he is unable to do so. Either he makes aimless wandering movements with the left hand, or he may succeed in making movements somewhat resembling those required of him, with much slowness and clumsiness. Sometimes he may perform some act which is entirely different from that required of him, and this phenomenon is called parapraxia. When the apraxia is partial, the patient may be able to perform some acts and not others, his inability usually, but not always, increasing with the complexity of the act required. Or he may be able sometimes to perform an act in which he commonly fails. Not infrequently such a patient, wearied with the unsuccessful attempts of his left hand, will abruptly perform the act correctly with his right hand, to get rid of it. And he will define his defect by saying, "I know quite well what you want me to do, but I cannot do it." Spontaneous volitional movement is similarly affected, and this leads invariably to a marked loss of initiative in the use of the affected limb—the patient will not try to use it. The apraxic patient is often to an astonishing degree unaware of his disability, and frequently becomes conscious of it for the first time when it is pointed out to him by another person.

Diagnosis.—Apraxia may be confused with astereognosis, with agnosia and with cortical ataxia. A correct conception of the nature of the two former conditions will exclude the possibility of error. In cortical ataxia the patient obeys the word of command at once and succeeds more or less with the act required, the defect being clumsiness of execution. The clinical examination of patients for apraxia must include—(1) the general psychical condition as regards attention, memory and reasoning; (2) an inspection of sensory appreciation for defects of simple perception in the regions of smell, sight, hearing, taste, cutaneous sensibility and muscular sense; defects of recognition of sensory impressions in these regions (agnosia); defects of memory; and (3) an examination of executive power for any defects in the movements determined by visual, auditory, tactile and kinæsthetic stimuli. What response does the patient make to objects held in front of him or to gestures made to him? Can he imitate movements? Can he when requested make simple and purposive movements, with and without the objects in his hands? When given an object, how does he hold it and use it?

AGNOSIA

In certain conditions of cerebral disease, it is found that each and all of the sensory organs, when called into play, may fail to arouse an intelligent perception of the object exciting them. This inability to recognise the import of a sensory stimulus is called agnosia. Those patients who present apraxia and agnosia, often show other interesting phenomena which are of importance; these are (1) inattention, (2) defective capacity for retaining recent impressions, (3) lack of initiative, and (4) perseveration. Perseveration consists in the repetition of an already executed movement when and only when the patient desires to make a fresh movement.

CEREBRAL DIPLEGIA

Synonyms.—Congenital Spastic Paralysis; Lobar Atrophic Sclerosis.

Definition.—A series of clinical conditions, dependent upon lack of, or imperfect development, or degeneration of the nerve cells of the cerebral cortex, basal ganglia or cerebellum. This agenesia of nerve cells may affect those cells of the pyramidal system which are the latest to develop before birth, namely those for the supply of the lower extremities and the resulting clinical condition is cerebral spastic paraplegia or Little's disease, or all the cells of the pyramidal system may be affected, producing generalised spastic rigidity. Again, the higher regions of the cortex may be affected, and the result is congenital idiocy. Similar affections of the cells of the basal ganglia result in congenital bilateral athetosis, and congenital chorea. When the cerebellum is involved, congenital cerebellar ataxy results. Further, there may be any combination of the above conditions.

Ætiology.—The malady may be apparent at the time of birth, as the child may be born with contractures present. More often, the signs of deficient or perverse movement, or of mental deficiency, appear during the first year of life, as the signs of cerebral activity commence to be exteriorised. In other and rarer cases, the degeneration of the nerve cells seems to be truly post-natal in onset, as in amaurotic family idiocy. In most cases no heredity can be traced, but sometimes several children of the same mother may be affected, and direct heredity has been known. Amaurotic family idiocy is always familial, and is almost, but not quite, limited to the Hebrew race.

Abnormalities of birth are frequent. Premature, or precipitate birth, prolonged birth from uterine inertia rather than from dystocia, and asphyxia neonatorum are all common. The child is frequently the first born of its mother.

Collier has expressed the probable pathogenesis of cerebral diplegia as follows: "If we regard the brain from the time of its earliest stages of development as a field sown with seeds (neuroblasts), which germinate at different periods of fœtal life, and the germination is not even complete at the time of birth, the germination of all the elements in due time and their complete development being necessary for the formation of the perfect brain, then we may liken the cause of diplegia to some baneful influence, such as a frost, which acting at a particular time, may spare those seedlings which are well developed and able to withstand it, and those seeds as yet not germinated, but which causes havoc among the tender germinating seedlings, either to their death or severe maiming. In some cases, as, for example, in Little's disease, the neuroblasts thus affected may, after a period of retarded development, ultimately become strong plants and complete their development. It is of interest that in the highest degrees of cerebral agenesia—anencephaly, pituitary abnormalities seem to be constant."

Pathology.—The essential histology of the affected regions is that of non-development, paucity in numbers and degeneration of the nerve cells, with corresponding absence, poor development, degeneration or a combination of these states, of the tracts which spring therefrom. The pyramidal tract, for example, may be found absent throughout, or it may reach to the medulla,

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or to the cervical region only, and so show at what period development was arrested. The changes in the nerve cells are followed by secondary gliosis. The final result is termed atrophic sclerosis. More often certain regions are profoundly affected, while others escape relatively or completely; but the distribution is always symmetrical upon the two hemispheres. The convolutions are unduly hard to the touch, and their surfaces often present a worm-eaten and faceted appearance. This irregular form of the convolutions, with wide, separating sulci, gives the brain a characteristic appearance, like that of a walnut kernel.

Symptoms.—The clinical picture of the several forms of cerebral diplegia presents a combination in varying degrees of certain characteristic symptoms, always bilaterally distributed, though sometimes more severe on one side than on the other. These symptoms are: muscular rigidity, paresis, perverse movements, contractures and increased deep reflexes. Mental deficiency, optic atrophy and ataxy are other important symptoms. The signs of the disease become obvious during the first year of life or soon after. In severe cases, soon after birth, the nurse, in washing the child, is the first to notice the stiffness of the limbs, or the regular assumption of a curious bodily attitude. Otherwise, the abnormalities may not be obtrusive, until the child should sit up or learn to get about, when weakness, rigidity, perverse movements and pes cavus may call attention, or backwardness in learning to walk and to talk, and mental deficiency may first suggest that there is something wrong with the child. The following are the common types of the disease, but it must be remembered that any combination of, or transition between, the types may be met with. Cerebro-macular degeneration has certain peculiar features which necessitate a separate description for this malady:

1. *Generalised rigidity; general congenital spastic paralysis.*—There is extensive defect of the pyramidal system. The rigidity and weakness affect the whole of the musculature.

2. *Paraplegic rigidity; congenital spastic paraplegia; Little's disease.*—The pyramidal deficiency is confined to that supplying the lower part of the trunk and lower limbs.

3. *Congenital bilateral athetosis and congenital chorea.*—The agenesia affects the cells of the basal ganglia, with the appearance of irregularity of movement, and of spontaneous involuntary movements, which may be of an athetotic, choreic or irregular type. A certain variable degree of general rigidity is present in these cases.

4. *Congenital cerebellar ataxy.*—The agenesia affects the cerebellum with the appearance of cerebellar ataxy. In this type, the limbs are flaccid, and in mixed cerebral and cerebellar types there is a tendency to hypotonicity of the muscles, instead of rigidity.

5. *Congenital idiocy; restless idiocy.*—The agenesia affects those parts of the brain concerned with the higher functions. These children are emotionless, restless and unteachable. The skull often shows frontal or occipital microcephaly.

6. *Microcephalic idiocy*—where the agenesia is of the whole brain and the skull very small.

7. *Cerebro-macular degeneration.*

Paresis and Rigidity.—Except in severe cases, in which the weakness

amounts to complete paralysis, there is more rigidity than weakness, and it is often astonishing that there should be so much power in the presence of such a degree of rigidity. The lower extremities are generally the most affected, the upper to a less degree, and the facial region still less. Movement is slow and clumsy and resembles that of the tardigrade animals, and spontaneous involuntary movements are often present in the limbs. Contractures accompany the rigidity, and if walking is possible the gait is digitigrade from contraction of the calf muscles, the knees are flexed from contracture of the hamstrings, the thighs are rotated inwards, and the knees pressed together, rubbing against one another. More severe adductor spasm gives rise to the cross-legged progression. The rigidity and contractures, when severe, may give rise to peculiar attitudes and deformities. A mask-like expression of face, with wide palpebral apertures and large open mouth, is not infrequent. Slobbering is very common. The head may be rigidly retracted, but more commonly the chin is pressed down upon the chest. The spinal column generally shows some deformity in the way of kyphosis, lordosis or scoliosis, and pes cavus or equino-varus is the rule.

Perverse Movements.—Under this heading must be grouped the very constant maladroitness of voluntary movement, the facial over-action and grimacing in speech and in mimetic expression, choreic movements, athetotic movements and intention tremor. Common sensation and the muscular sense are unimpaired. The sphincters are unaffected. The deep reflexes are increased, but are often difficult to obtain when rigidity is very marked. The trunk reflexes are often absent, the plantar reflexes usually are extensor in type. Since the growth of the skull follows and conforms with that of the brain, cranial abnormalities are common. There may be microcephaly, asymmetry and flattening in the region of the central convolutions, or a furrow corresponding with the interhemispheric fissure, or frontal or occipital smallness and flattening. Every degree of mental reduction may be met with, from precocity and slight mental dullness to complete amentia. But this by no means corresponds with the severity of the bodily symptoms, for the mental defect is often most severe when the bodily symptoms are slight, and conversely. In some cases, very high intelligence persists, when there is utter uselessness of the limbs, and when speech is hardly intelligible. Primary optic atrophy occurs in a small number of cases. Inequality of the pupils and slowness of light reaction are not uncommon. Nystagmus is often met with. Convergent strabismus occurs in about one-third of the cases. Convulsive attacks are of common occurrence, and in about one-eighth of the cases epilepsy becomes established.

Diagnosis.—When the symptoms are well marked, the diagnosis presents little difficulty, since the disease dates mostly from birth, or is discovered during the first year of life. Paraplegic rigidity may possibly be confused with other forms of paraplegia, and, especially, with that resulting from spinal caries. Certain cases of pontine tumour may closely resemble generalised rigidity. The occurrence of such conditions during the first two years of life is, however, very rare.

Prognosis.—In many cases of generalised rigidity, and in all cases of paraplegic rigidity, there is a tendency to slow amelioration of the rigidity, an increase of voluntary power and control of the muscles in the course of time, especially under the influence of careful training, and in paraplegic

rigidity, if the mental acuity be not seriously impaired, laborious treatment may result in an almost normal condition of the limbs by the age of puberty. On the other hand, some cases of generalised rigidity become progressively worse, and succumb, usually before the end of the fourth year. Bilateral athetosis and choreic diplegia, as a rule, follow a very slowly progressive course, without tendency to a fatal result. Paraplegic rigidity apart, a great many of the cases of all forms of diplegia succumb before the sixth year, and in those who survive this age, the tenure of life is short, few reaching far into the third decade of life.

Treatment.—In those cases with a marked degree of mental impairment, and in those which show a course of progressive degeneration, no treatment is of avail. In slighter cases of generalised rigidity, and in paraplegic rigidity, treatment is to be directed to the prevention of the rigidity, to regaining of voluntary control, and the improvement of mental acuity. There is, perhaps, no disease which demands greater patience and persistency in carrying out of suitable treatment, and there are few diseases in which more brilliant results may be produced from apparently hopeless cases by pertinacity in treatment. It is in the early years, when treatment is for the most neglected, that good results are more quickly and readily obtained. From the first, regular massage and passive movements should be employed. Voluntary movement should be encouraged, as far as possible, and as power and movement increase, gymnastic exercises of every kind should be employed. Rigid apparatus for prevention of deformity and to reduce contracture is harmful, for it increases the weight of the limb, and interferes with movement, which is the remedy with which paralysis is to be combated. Tenotomy is of great service in the relief of deformity and contracture, and should be soon followed by passive movements. It should never be performed, unless a fair degree of voluntary power is present. Many of the patients seem to improve more rapidly if thyroid be administered in moderate daily doses.

CEREBRO-MACULAR DEGENERATION: AMAUROTIC FAMILY IDIOCY

1. WAREN TAY-SACHS' DISEASE: THE INFANTILE FORM

Definition.—A family disease of infancy occurring chiefly, but not entirely, in the Hebrew race, affecting children during the first year of life, who are apparently quite healthy when born, and characterised by—(1) progressive mental impairment, ending in absolute idiocy; (2) progressive paralysis of the whole body; (3) progressive diminution in sight, ending in absolute blindness. Pathognomonic retinal changes are constantly present, consisting of a large and conspicuous "cherry-red spot" in the region of the macula, and, in addition, optic atrophy occurs later and (4) a fatal termination in the marasmic state before the age of 2 years.

Ætiology.—Nothing is known of the ætiology of the disease apart from its familial and racial incidence. The tendency to the disease is unquestionably congenitally installed.

Pathology.—This is very striking. It consists of a progressive degeneration of the nerve cells from the highest to the lowest, and ultimately there may be no normal cells remaining anywhere in the nervous system.

The degeneration takes the form of swelling of the cell protoplasm, and of the dendrites with chromatolysia, swelling of the hyaloplasm and destruction of the cell fibrils, followed by disappearance of the nucleus, and finally by absorption of the remains of the cell. Every cell of the central nervous system both of the brain, spinal cord and spinal ganglia is in the end similarly affected.

Symptoms.—There are few diseases in which the *clinical manifestations* are so perfectly uniform as in this malady. The children have all been born at full term, and in perfect health. They thrive well during the first 3 to 6 months of life, when they gradually become listless and apathetic, cease to take interest in the surroundings, and begin to show signs of the visual failure which ends in blindness. Later, the child is unable to sit up, or to hold up its head. The limbs, which may be slightly spastic at first, become flaccid and motionless. There is a gradual increase of all these signs. The mental defect becomes more and more noticeable, the paralysis more extreme, complete blindness follows, and the patient sinks into a condition of marasmus, in which he dies. Convulsions, nystagmus and strabismus are sometimes present.

The retinal changes are pathognomonic and are due to a degeneration and disappearance of the nerve cells of the retina and their processes, which constitute the fibres of the optic nerve. This change is most intense in the region of the fovea centralis, where the retina thins and disappears over a circular area, exposing the vascular choroid. This gives rise to the characteristic appearance, on ophthalmoscopic examination, of a cherry-red spot in the region of the macula. This spot is actually a hole in the retina exposing the choroid. The optic disk shows progressive atrophy.

Diagnosis.—Distinction has to be made between this and other forms of progressive diplegia. The symptoms are so distinct that a physician, who is acquainted with the disease, and able to recognise the retinal picture, can hardly fail to make the correct diagnosis.

Treatment.—No treatment is of any avail.

2. OTHER FORMS OF CEREBRO-MACULAR DEGENERATION

In addition to the classical infantile form described in the preceding article, two other forms are well known in which the pathological changes are similar but much less severe than in the Waren Tay-Sachs' disease, and there is a similar familial incidence, but the incidence of the malady occurs later in life and the course is less rapid and the result far less serious. The later the onset in life the slighter and less progressive are the symptoms. The cherry-red spot at the macula, so constant in the infantile form, does not occur in the later forms. The characteristic retinal change is a disturbance of the retinal pigment commencing in the macular region, rather like retinitis pigmentosa, accompanied by honeycomb changes at the macula and sometimes by optic atrophy. The *juvenile* form occurs in later childhood and is characterised by the association of the retinal changes and visual defect with some degree of mental deterioration. The *adult* form is the least progressive of any, and the clinical manifestations are the visual defect and retinal changes in the absence of mental deterioration.

INFANTILE HEMIPLEGIA

While in childhood hemiplegia of slow onset is due to the same causes as in adults, cerebral tumour being the common cause and chorea not an infrequent one, yet the majority of the cases of infantile hemiplegia of rapid onset are examples of diseases peculiar to children, to which no comparable disease occurs in adults, and to such cases the term "infantile hemiplegia" is restricted. These conditions are due to gross organic lesions of the brain, and for this reason must be strictly separated from the cerebral diplegias which are the result of cell lesions and not of gross lesions.

Ætiology.—In two-thirds of all the cases, the onset occurs within the first three years of life. The malady becomes increasingly rare as childhood advances. A few of the cases are of prenatal origin, and some of these have been proved to have been due to injury to the fœtal brain from a blow upon the mother's abdomen, while others are due to syphilitic fœtal vascular disease. In a third class of mysterious origin, mothers have given birth to several hemiplegic children, examples of which we have recorded. Some of these children are born with definite hemiplegia and contractures. Again, a very few cases are due to obstetrical events during birth, by which the cerebrum is injured. Acute infective diseases play a very important rôle in the causation of the disease, for about one-third of all the cases develop the malady during the course of a known infection. By far the most important of such fevers are measles and scarlet fever, but hemiplegia may occur in the course of pertussis, small-pox, rötheln, diphtheria, dysentery, pneumonia, typhus, typhoid, mumps, malaria, chorea and endocarditis. While there can be no doubt that primary vascular lesions are responsible for a few of the cases in which this condition complicates the specific fevers, whooping-cough, for example, may cause cerebral hæmorrhage; marasmic conditions in any fever may cause thrombosis of cortical veins, and chorea and endocarditis may cause embolism, yet it is certain that in the majority of cases, an inflammatory focal lesion of the brain or encephalitis is the pathological lesion. In cases which arise with no definite ætiological connection, it seems clear that a primary encephalitis is responsible, but there is no evidence at present as to its causal factors.

Pathology.—The following lesions are met with, either alone or combined in order of frequency: (1) Atrophic sclerosis; (2) cyst formation; (3) shrunken patches resembling wet wash leather, with some degree of atrophic sclerosis in their vicinity, and (4) porencephaly. Of these, the atrophic conditions seem to be the results of encephalitis, which may also cause some cyst formation; the cystic conditions may result from the above, or from hæmorrhage or thrombosis, and porencephaly is certainly due to embolism.

Symptoms.—The onset is rapid, and in two-thirds of all the cases the disease is ushered in by convulsions, which may be unilateral, but are more frequently general, and are frequently repeated during a period of from a few hours to 24 hours, after which the patient sinks into a subconscious state, from which he gradually emerges in the course of a few days, to show the signs of some cerebral defects, usually hemiplegia, sometimes hemianopia, or aphasia, or any other sign of local cerebral or cerebellar lesion. Pyrexia

often accompanies the convulsion, and vomiting is common. The onset may be without convulsions or loss of consciousness.

The relation of the onset of the paralysis to the convulsion varies. It may reach its height immediately after the initial convulsion, or slight hemiparesis may occur which deepens after each subsequent convulsion. Sometimes the early convulsions leave no paralysis, but this appears towards the end of the first week, either suddenly with fresh convulsion, or gradually, as the patient recovers from the comatose state. The paralysis at its onset is flaccid, and involves the whole of one side of the body to a greater or smaller extent. An initial monoplegia is of extreme rarity. The paralysis may not reach the greatest intensity until the end of the second week. Subsequently it lessens, in some cases disappearing completely in from a few weeks to 3 months; in others, it may show no signs of improvement. The limbs, at first flaccid, subsequently become spastic and develop contractures. In the course of years there may be great arrest of growth on the affected side, and this is not in relation with the degree of paralysis, but apparently depends upon the degree of destruction which has occurred in the parietal lobule. Post-hemiplegic spontaneous movements of an athetoid, choreic or irregular kind are common, and are attributable to lesions in the corpus striatum and subthalamic grey matter, for which regions encephalitis shows an especial predilection. Epileptic fits recur at varying intervals in about half of all cases of infantile hemiplegia. These always commence upon the affected side and are sometimes confined to it. Mental deficiency is met with in all degrees, in relation to the position and extent of the cerebral cortex which is involved in the lesion.

Diagnosis.—The nature of the malady at the onset, with convulsions, may be possibly suggested by prodromal pyrexia, by the severity and long duration of the convulsions, and by the prolonged subconscious state that often follows. Convulsions occurring several days after the onset of specific fevers should strongly suggest the diagnosis. When the signs of hemiplegia or of other local cerebral lesions appear, the diagnosis presents no difficulty.

Course and Prognosis.—In a very small proportion of the cases the patient does not survive the initial manifestations of the disease, and dies in convulsions. Apart from this event, infantile hemiplegia has little tendency to destroy life. The initial flaccid hemiplegia tends to improve and gives place to a slowly improving spastic hemiplegia, which, with the return of some power, shows perversity of movement, stiffness and slowness, ataxy, athetosis and choreic movements or tremors according to the position of the lesion. The spontaneous movements appear within a year of the onset. Slow improvement may go on for years, but cases with much mental reduction or when recurring epilepsy is frequent, improve but little.

Treatment.—We know of no measures that avail to prevent the occurrence or lessen the severity of the cerebral destruction which occurs from encephalitis. Too often the damage to the brain has happened as soon as a diagnosis is possible. When the paralysis has developed, treatment is to be directed to the prevention of rigidity and contractures by regular passive movements, to regaining voluntary control by encouragement and patient exercises, and to the improvement of mental acuity. Where there is much contracture and deformity, tenotomies are of great service, provided there be some voluntary power in the muscles, the tendons of which are

to be divided. Recurring convulsions should be treated as idiopathic epilepsy.

SYPHILIS OF THE NERVOUS SYSTEM

Of the many problems presented by syphilis of the nervous system one may be chosen for special reference, namely, the alleged dual nature of nervous syphilis and of the causative organism. It has been maintained that there are two distinct pathological forms of nervous syphilis, namely, primary *parenchymatous* syphilis, as exemplified in tabes and general paralysis, where the initial lesion is held to be in the nerve elements themselves, and primary *meningo-vascular* syphilis, in which the initial lesion is in the blood vessels and meninges. But the dual nature of syphilis implied by these distinctions is subversive of pathological principles, for the initial and fundamental lesion of syphilis, wherever found and at all stages, is a lymphangitis or an arteritis, and very strong evidence would be needed to enforce the conviction that the reactions of nervous tissues to the presence of the spirochæte differs essentially from that of all other tissues of the body. Nor is this view supported by the morbid anatomy of the diseases concerned, for in every case of tabes and general paralysis, vascular and meningeal lesions can be found after death. Moreover, in the vast majority the increased number of cells in the cerebro-spinal fluid shows that the meninges are attacked even in the earliest stages.

For these reasons the trend of opinion is to deny the existence of parenchymatous syphilis as an initial lesion of syphilis in the nervous system, and to hold that the vessels and meninges are first injured in all forms of syphilis of the nervous system.

The contention that the organism of syphilis exists in two forms next demands consideration. Of all syphilitics the proportion in whom the nervous system is attacked is small. To explain this low incidence it has been assumed that neuro-syphilis results from infection by a biological variant of the *Spirochæta pallida* with special affinities for nervous tissues—the "neuro-tropic variety," while other forms of syphilis follow infection by the "dermo-tropic variety." At first sight this attractive conjecture seems to be supported by numerous clinical observations. These are, that in some instances several persons infected from the same source have later developed syphilitic nervous diseases; that the superficial manifestations of syphilis are often mild or absent in those who ultimately develop neuro-syphilis, and that secondary and tertiary syphilis, outside the nervous system of these patients, is rare; also that in Oriental countries where syphilis is common, some forms of neuro-syphilis, namely, tabes and general paralysis, are seldom seen.

But it has never been shown that the persons who formed the source of infection for several cases of nervous syphilis have themselves developed this disease; it can no longer be held that tabetics and paralytics are free from secondary and tertiary lesions—witness the frequency of aortitis in these cases; finally, Europeans who contract syphilis in the East are just as likely to suffer from tabes and general paralysis as if they had contracted

it at home. It cannot be denied that the secondary phenomena are often so slight as to pass unnoticed by patients who later become tabetics or paralytics, or that patients with severe integumental lesions rarely develop tabes or general paralysis. These facts, however, together with a large amount of additional evidence, suggest that the ultimate result of infection depends rather on the individual attacked than on any peculiarity of the infecting agent, and they lend no support to the notion of the duality of the syphilitic organisms.

For the purpose of description it is still convenient to describe syphilitic diseases of the nervous system under two headings; Interstitial or meningo-vascular syphilis and parenchymatous syphilis. To avoid misunderstanding it must be emphasised that these are merely clinical aspects of one disease—neuro-syphilis, and that in both forms the primary lesion is in the vessels and meninges.

The Blood and Cerebro-Spinal Fluid in Syphilis of the Nervous System

A normal fluid may be regarded as one with a pressure equal to 150 to 180 mm. of water, a cell count not exceeding 5 per c.mm., an albumin content of from 0.025 to 0.05 per cent., and negative Wassermann, globulin and Lange's gold tests.

In *secondary syphilis*, without nervous symptoms, changes are found in the fluid in 80 per cent. of the cases. The infection of the nervous system occurs early in the second stage of the disease and it is a common happening. In many of the cases this infection dies out in the course of time either spontaneously or as the result of treatment and the cerebro-spinal fluid reverts to a normal condition. In other cases the infection remains and the W.R. continues positive in the cerebro-spinal fluid, and it is exclusively in this class of patient that tabes, general paralysis and the other degenerative maladies of the nervous system which are due to syphilis arise. Increased pressure, lymphocytosis, excess of albumin or a positive Wassermann reaction are found with a frequency which diminishes in this order. If the blood and fluid are both normal at the end of a year, neuro-syphilis is not likely to arise.

In *latent syphilis*, without nervous symptoms, the blood is positive in about 70 per cent., but changes in the fluid are found in 20 per cent. only. A fluid which is normal in the latent stage almost never becomes pathological later; if it deviates from the normal it is highly probable that neuro-syphilis will develop later.

In *early cerebro-spinal syphilis* the blood is usually positive, but it is sometimes negative when treatment has been thorough or recent. This indicates that an examination of the fluid is essential when the blood is negative in a case where the diagnosis is doubtful. Cells and albumin are usually greatly increased, the gold test is usually positive, and the Wassermann reaction is positive in almost every case when 1 c.c. of fluid is used in making the test. The blood and fluid often become normal after the first course of treatment, but a relapse occurs frequently and long before the recurrence of symptoms. Vigorous mercurial treatment and 4 or 6 full courses of arsphenamine at intervals of 3 months usually render the blood and fluid persistently negative. If both are normal a year after the fourth course, recurrence is unlikely.

In *cerebro-spinal syphilis* of longer duration, the reaction in the blood is

almost always positive, and the fluid is seldom normal in active cases. A positive reaction in the fluid probably indicates an active process, even in the absence of recent symptoms. A normal fluid indicates a healed process. The inference is that all cases with a positive fluid and a history of cerebro-spinal syphilis should be treated energetically whether fresh symptoms are present or not. The treatment outlined above under early cerebral syphilis usually renders the fluid negative and the indications for prognosis are the same.

In *tabes* Wassermann's test is positive in the blood in about 70 per cent. of cases; it is often negative in the fluid when the test is done by the original method with 0·2 c.c. of fluid, but with 1 c.c. it is positive in almost 100 per cent. An increase in the number of lymphocytes in the cerebro-spinal fluid as well as an increase in the total albumin with a relative increase of globulin is almost constant. In some cases in which the disease had remained stationary for a long time the cerebro-spinal fluid was normal in every respect.

Lange's colloidal gold test gives useful information when the diagnosis lies between tabes and general paralysis, for the latter gives a typical reaction, but the test is of no value by itself in distinguishing tabes from other diseases of the nervous system (see page 1558).

Treatment by mercury and intravenous injections of neoarsphenamine sometimes renders the fluid normal. It is stated that in such instances relapse is less likely to occur than in other cases, but no exact correlation has been shown to exist between the clinical course of the disease and the presence or absence of changes in the blood and fluid.

General paralysis of the insane.—The Wassermann reaction is strongly positive in the blood and in the fluid practically in 100 per cent. of cases, and an increase of cells and a positive globulin reaction are almost constant. Lange's gold test gives the characteristic paretic curve.

Treatment by mercury and arsphenamine may produce slight modification in the reactions, but it has very little effect in checking the progress of the disease.

The Essential Lesion of Syphilis

Every lesion in syphilis commences with the collection of spirochætes in the lymphatic spaces surrounding small arteries. This is followed by an inflammatory reaction with œdema and exudation of many lymphocytes and plasma cells around the small vessels, and the "cuffing" or "muffing" of these vessels with such cells is characteristic. These cells may wander freely into the nervous tissue away from the vessels and may form clumps, often containing giant cells, and these are miliary gummata. Such a perivascular lymphocytic exudation is typical of syphilis, poliomyelitis, tuberculosis and lethargic encephalitis, but the distinction can be made by the nature of certain histological elements present. Syphilis is distinguished by the presence of numerous plasma cells among the lymphocytes, poliomyelitis by the large admixture of polymorphs, tubercle by the absence of plasma cells and the presence of Koch's bacilli, and lethargic encephalitis by the absence of any elements except the lymphocytes. The initial periarteriolitis of syphilis is often followed by invasion of the whole vessel wall (panarteritis), and often proliferative endarteritis which may give rise to thrombosis is the most conspicuous feature in the panarteritis. Later, the wall of the vessel may scar and may develop patchy calcareous deposit. The lymphocyte

deposit goes into fibrosis or increases to gumma formation, and there is neuroglial felting. Further thrombosis of the vessel may cause the softening and infarct conditions which necessarily follow vascular obstruction, and local necrosis results. The hyperproteinia and pleocytosis of the cerebro-spinal fluid are expressions of this essential lesion upon the surfaces and spaces of the nervous system, and the meningeal scarring and adhesion are its results.

So far the pathology of nervous syphilis is simple, but the so-called " parenchymatous " or degenerative lesions which are apt to be widespread and progressive are as yet inexplicable. They are commonly found in the absence of any findable spirochæte, or of any sufficient inflammatory lesions in their locality, and have been observed also by Carey Coombs in the heart muscle and the aorta, and may be progressive when all signs of active syphilis such as the W.R., hyperproteinia and pleocytosis have died out finally. These degenerative lesions may not be improved or stayed in their progress by any form of treatment. The slowly oncoming progressive and unarrestable optic atrophy and the systemic lesions of the spinal cord in tabes are good examples of the degenerative lesions, and in them spirochætes have rarely or never been found, while the inflammatory lesions are absent or minimal and cannot be the factors of so wide a destruction. The nearest locus where spirochætes are commonly found in tabes is the bronchial glands.

CEREBRO-SPINAL SYPHILIS

Ætiology. — Cerebro-spinal syphilis (excluding tabes and general paralysis) occurs in about 4 per cent. of all persons who acquire syphilis. The onset of symptoms is commonest from 1 to 5 years after infection, but it may be as early as 2 or 3 months, or as late as 30 or 40 years. The brain is affected more often than the spinal cord, and usually when the main symptoms point to the latter some signs will be found to show that the brain is also attacked.

1. CEREBRAL SYPHILIS

Pathology.—The disease may begin in the meninges, in the blood vessels or in the bones of the skull. In cases where the main incidence falls upon the *blood vessels*, the arteries at the base of the brain forming the circle of Willis or arising from it, together with their branches, are most often attacked. To the naked eye they show irregularities in size, due to thickening of their walls in circumscribed areas. Proliferation of the intima with a round-celled infiltration of the outer coats—*endarteritis obliterans*—is the characteristic microscopical change. The same changes occur in smaller arteries within the brain or on its surface, and these vessels, as well as those at the base, may be compressed or invaded by disease beginning in the meninges. In each case their lumen is narrowed or obliterated, thrombosis occurs readily, and softening may result in parts cut off from their blood supply. Obliterative changes also occur in the veins and lymphatics, and lead to further impairment of the nutrition of the brain.

The commonest form of *meningeal syphilis* is a diffuse gummatous lepto-meningitis at the base of the brain. On the convex surface of the brain

it begins most often over the frontal and parietal lobes. The meninges may be affected alone, but more often the vessels are also diseased. In severe cases a gelatinous exudate fills the sub-arachnoid space and extends along the vessels and nerves. Later, the newly-formed tissue organises, and forms sclerosed masses of thickened adherent membranes containing numerous small gummata.

Gumma of the brain is rare. When present it arises from the meninges, and may be multiple. The convexity of the hemisphere in the motor region is the site of election. A gumma may spread so as to involve the overlying bone.

Many important results of cerebral syphilis are due to impaired nutrition of parts not directly affected. Thus softening, hæmorrhage, cyst-formation, atrophy of cells and tract degenerations may occur, and non-syphilitic diseases may be simulated.

Symptoms.—The main incidence of the disease may fall upon vessels or membranes, the lesions may be diffuse or circumscribed, any portion of the brain or any cranial nerve may be affected alone, and every combination of lesions and, therefore, of symptoms, is possible. In many cases their multiplicity, their presence in unusual combinations, and the changes in their intensity and distribution from time to time give a clue to their nature.

Headache is a common prodromal symptom. It is often severe, and is usually worse at night. Sustained mental and physical effort becomes difficult, the memory is impaired and the character changes. Irritability, intense excitement or delirium may follow, but more often the patient becomes lethargic. At this stage paralysis and localising signs may be absent. In many the pupils are unequal or irregular, or they contract sluggishly to light, and in some the optic disks show blurring of the edges and other signs of early papillœdema.

At any time, with or without prodromata, more definite signs of vascular disease or of paralysis of one or more of the cranial nerves may appear. *Arterial thrombosis* is usually preceded by prodromal symptoms, but it may come on in one apparently well. Its seat of election is the middle cerebral artery or its branches, and weakness of one arm or of one side of the body with or without aphasia is a very common early symptom. The weakness is often slight and transient. If hemiplegia occurs, it takes several hours or a day or two to develop. It is more often a paresis than a paralysis, and consciousness is usually retained. Sometimes the affected limbs are rigid and tremulous. The symptoms of thrombosis in other arteries are given on p. 1559.

In *vertical meningitis*, headache is usually severe, and the skull is often tender over the affected part. It frequently attacks the motor areas, and convulsions are common. They may be confined to one limb or to one side of the body, consciousness being retained, but more often they become generalised and consciousness is lost. In more chronic cases mental symptoms may predominate, the patient becoming slowly demented.

With *basal meningitis* severe deep-seated headache is almost always present. Later, a characteristic lethargy with severe impairment of the mental functions may appear. Whilst in this stuporose state the patient can usually be roused, when he answers questions in a sleepy fashion and obeys simple commands, but his memory is bad, and he is unable to give an

adequate account of himself. Variations in the degree of the stupor are a striking feature. In some cases profound torpor may persist for several weeks.

Soon after the onset, signs of implication of the cranial nerves appear. Any one of them may be affected alone, but, as a rule, several are attacked, where they lie close together after their exit from the brain, or as they leave the skull through the foramina. Ocular symptoms are rarely absent. Inequality in size, or irregularity in the outline of the pupils, may be the only sign, but diminution of the light reflex, ptosis, squint, diplopia and weakness of the movements of the eyeball are frequent, and papillœdema is common. It is characteristic of the cranial nerve palsies in syphilitic basal meningitis that the symptoms often show great variations in degree and distribution at different times.

The symptoms produced by large *gummata* are those of any cerebral tumour—headache, vomiting and papillœdema.

Diagnosis.—The aphorism, probably justified 25 years ago, that syphilis should be thought of in every case of nervous disease that is not quite clearly non-syphilitic in origin, has long outlived its usefulness as a generalisation. But it still lingers and is responsible for the practice, far too general, of throwing the burden of neurological diagnosis upon the shoulders of the clinical pathologist to make blood and cerebro-spinal fluid examinations, as a substitute for that careful history taking and clinical examination that would usually suffice for a complete diagnosis without these accessory investigations. Neuro-syphilis should not be guessed at in a haphazard fashion, but the attempt should be made by the clinical methods mentioned above to assess the pathological nature of the lesion or disease process in any case of nervous disease, and to use serological methods to confirm clinical diagnosis, or to clear up uncertainty when this still obtains after full clinical consideration. A history of syphilis or signs of the disease elsewhere are of first importance. Obstinate headache alone should arouse suspicion, and when signs of vascular or cranial nerve troubles follow a prodromal period of headache and mental impairment, syphilis is the most likely cause.

Jacksonian epilepsy or fits of any kind in patients without an epileptic history are suggestive of syphilitic meningitis or gumma, even though these are not the commonest causes of these symptoms. As a rule, these convulsions are readily distinguished from those of idiopathic epilepsy, by their partial distribution, by the weakness which remains in the parts which were convulsed, and by the presence of papillœdema, of cranial nerve palsies, or of other signs of organic disease which are found in the intervals between the fits. Cerebral new-growths produce similar symptoms, but this diagnosis should not be finally accepted until syphilis has been excluded. In all cases an examination of the blood *and cerebro-spinal fluid* is essential (see p. 1629) because a positive Wasserman or Kahn reaction in the blood may be taken to indicate no more than that the subject has at some time had syphilis. It does not usually mean that the tumour is syphilitic in nature. It is on the whole less rare to find a glioma in a syphilitic subject than to find a gumma of the brain. Only the presence of the changes characteristic of neuro-syphilis in the cerebro-spinal fluid, as well as in the blood, can justify the diagnosis of cerebral gumma.

Prognosis.—The outlook in cases with mild symptoms is good if the treatment is efficient. In severe cases of syphilitic arteritis it is grave. The vessels most often invaded are large end-arteries, and the softening which results when their lumen is occluded is not amenable to anti-syphilitic remedies. Relapses are common, and patients apparently cured are often seized in a few months with fresh cerebral troubles. The lesions in the meningeal and gummatous forms of the disease are mainly cortical, and large areas of softening are not produced. The prognosis is much better in this form, and complete cure is almost the rule when treatment is begun early. It is often impossible, however, to decide from the clinical signs whether the vessels or the meninges have suffered the more. In the absence of this knowledge the prognosis depends on the results obtained by the use of appropriate remedies.

Treatment.—See p. 1636.

2. SPINAL SYPHILIS

Pathology.—The disease may begin in the bony or membranous coverings of the cord, in the blood vessels on its surface, or in the interstitial tissues within its substance, and spreading from one to the other, usually attacks several of these structures in various combinations. As in cerebral syphilis, many of the changes in the cord are secondary to disease in the vessels or meninges, and appear in parts not directly attacked by specific processes. The commonest form of spinal syphilis is *meningo-myelitis*. The meninges are thickened and adherent, while the spinal and meningeal arteries and veins show obliterative changes, and are surrounded or infiltrated by small round cells. The same changes are apparent in and around the vessels and pial septa within the cord. In severe cases, the membranes are united to form a thick fibrous sheath around the cord, and the outlines of the nervous structures as seen in transverse section are almost obliterated by the presence of numerous small gummata or of myriads of small round cells. The nervous elements are compressed by the cell infiltration, or undergo softening or necrosis as a result of obliteration of the blood vessels. Meningo-myelitis is usually confined to a narrow area in the dorsal region, and is often associated with a more extensive meningitis.

In some cases with severe arterial changes, extensive softening results from thrombosis or hæmorrhage and produces severe paralysis of sudden onset—*acute syphilitic myelitis*.

Large gummata are rare. They occur in the cord, or on its surface, and produce the signs of compression.

In another rare form in which the membranes alone are affected—pachymeningitis and leptomeningitis—the dura and pia-arachnoid unite to form a thick fibro-gummatous sheath around the cord to which they become adherent.

Syphilitic disease of the vertebral column is very rare. It produces changes which resemble those of tuberculous spinal caries, with osteitis and periostitis, and the formation of granulation tissue and gummata on the outer surface of the dura. Necrosis of the bones may lead to deformity of the spine. It is seen most often in the cervical region, where it begins in the spine, or spreads from a syphilitic ulcer in the throat.

Symptoms.—In *meningo-myelitis*, pain in the back, tenderness of the spine, and radiating pains or a feeling of constriction in the limb or around the trunk, are often present in the premonitory stage. After these have lasted several days or weeks, cord symptoms appear. They may come on rapidly, or very slowly. Often the first complaint is of numbness or tingling in the lower limbs, or of weakness or stiffness after exertion. Several attacks of temporary weakness may precede severe paralysis, and in different cases every degree is seen, from slight stiffness to complete paraplegia. When the paralysis comes on slowly the lower limbs become spastic, the knee- and ankle-jerks are exaggerated, and the plantar response is "extensor." In severe acute cases the limbs are flaccid and the tendon reflexes are at first diminished or lost, spasticity and increased reflexes developing later. In both forms the abdominal reflexes are diminished or lost below the level of the lesion. In most cases bladder control is impaired, and in some this is the first symptom. Sensory troubles may be slight when the paralysis is severe. Numbness and tingling are common, and some objective loss can usually be detected, the temperature sense, especially for cold, and the sense of vibration being most often at fault.

In one group of cases—*Erb's syphilitic spinal paralysis*—spastic weakness develops slowly in the lower limbs, without meningeal symptoms. The bladder is usually affected, and sensory loss is slight. In this form the spinal disease appears later after infection than is usual in other forms of meningo-myelitis.

Pachymeningitis (diffuse gumma of the theca) as an isolated disease is usually found in the cervical region. The earliest symptom is pain in the neck, radiating down the upper limbs and between the shoulders. After a time, usually several months, weakness, wasting and loss of sensation appear in the arms. Still later, spastic paraplegia may develop from compression of the cord. When the lumbar region is attacked, the same symptoms appear in the lower limbs.

In *syphilitic caries* tenderness over the diseased bones, pain on movement of the spine, and radiating pain in the distribution of the sensory roots at the level of the lesion, are the chief symptoms. When the cord is compressed, power and sensation are diminished in the parts below.

Diagnosis.—Spinal syphilis appears in many clinical forms and often resembles other diseases. Hence it must be considered in every case of spinal disease without an obvious cause. The diagnosis may be founded on—(1) a history of syphilitic infection; (2) the presence of syphilitic lesions in other parts of the body; (3) Wassermann's reaction in the blood or pathological changes in the *cerebro-spinal fluid* (see pp. 1629, 1630); (4) signs of associated cerebral syphilis; (5) rapid improvement under treatment by specific remedies.

Prognosis.—The outlook for recovery of power is good when the meninges only are attacked, but bad when the symptoms are due to softening, hæmorrhage, atrophy of motor cells, or tract degenerations, for these are secondary changes and are not influenced by anti-syphilitic remedies. In a given case, however, it is not possible to assess accurately the amount of damage sustained by different structures, and the prognosis is always doubtful. Complete recovery occurs in about one-third of the cases of slight or moderately severe meningo-myelitis. The majority make a partial recovery, and are able to

walk fairly well, in spite of the weakness and stiffness which remain. In cases with a sudden onset of severe paralysis, the prognosis is very bad, and death from bedsores or bladder and kidney infection is the usual result. On the other hand, the outlook for recovery of power is better when slight troubles come on rapidly than when they develop extremely slowly, as in Erb's form of the disease, in which many years pass before the paralysis becomes severe ; for in the first case the lesions are interstitial and they respond well to treatment, whereas parenchymatous degeneration of the nervous elements themselves is present in the latter, and treatment is of less avail. The prognosis in early cases is determined by the effects of anti-syphilitic treatment. In cases of long standing, the most that can be expected is that appropriate treatment will arrest the course of the disease.

Treatment of Cerebro-spinal Syphilis.—As soon as the diagnosis is made, vigorous anti-syphilitic treatment should begin. The drugs used are mercury, bismuth, the arsphenamine derivatives and potassium iodide. In the opinion of some authorities mercury still holds pride of place in the treatment of neurosyphilis, especially when administered by inunction. Treatment will vary according to the acuteness and nature of the lesion present.

In *acute syphilitic meningitis*, unless the condition is grave, it is best to begin with mercurial inunction (60 grains of the ung. hydrarg., B.P., well rubbed in) for the first week, and then to give a course of neoarsphenamine (0·6 g.), at five or six day intervals, until 6 or 8 injections have been given. Simultaneously with this, intramuscular injections of a bismuth preparation (salicylate, or iodobismuthate of quinine, each dose containing 3 grains of bismuth) are employed. Subsequently, courses of bismuth or mercury and of arsenic may be given alternately until examination of the cerebro-spinal fluid shows cessation of the active disease.

In *chronic syphilitic meningitis* treatment may be started with inunctions of mercury or injections of bismuth, followed by a course of arsenical injections. A full course of mercurial inunctions consists of sixty inunctions if signs of mercurialism do not develop. Potassium iodide in large doses may also be given. Treatment must at the same time be correlated from time to time with cerebro-spinal fluid examinations.

In *vascular syphilis* also treatment is best begun with either mercury or bismuth, and arsenic not given for the first two weeks. Iodides should also be administered.

Massage and passive movements should be carried out daily, when the limbs are weak. When sensory loss is present, careful nursing is necessary to prevent the formation of bedsores ; and when control of the bladder is defective, the usual precautions must be taken for the prevention of infection of the urinary tract.

GENERAL PARALYSIS OF THE INSANE

Synonym.—Dementia Paralytica.

Ætiology.—As in tabes, the essential factor in the causation of general paralysis is previous syphilitic infection. Males are affected much more frequently than females. The onset is commonest between the ages of 30 and 50 years, from 10 to 20 years after infection. As a result of congenital

syphilis or of early innocent infection, it may appear in childhood, youth or even adult life. It has been estimated that about 5 per cent. of syphilitics develop general paralysis, but the incidence in those who have been well treated in the early stages is not more than 1 per cent. The incidence varies in different races, and seems to be greater with increasing civilisation. It is more apt to occur in town and city dwellers, and in those who have led a strenuous intellectual or business life.

Pathology.—The skull-cap is thickened, especially in its anterior part, its density is increased, and the diploë is obliterated. The dura mater is thickened and adherent to the skull, and may show the changes of pachymeningitis hæmorrhagica. The arachnoid is tough and thick, and white lines are seen between the sulci and along the vessels. The pia is thickened, its meshes are distended by pale yellow fluid, and on attempting to strip it off portions of the cortex are torn away. The amount of cerebro-spinal fluid is increased. The brain looks wasted and shrunken, and its weight is abnormally low. The sulci are wide and the convolutions are narrow. The ventricles are dilated, and their ependymal lining presents a granular or a frosted appearance. On section the grey matter of the cortex is seen to be thinner than normal—decortication. On histological examination gross changes are found in the membranes, in the blood vessels, in the neuroglia, and in the true nervous elements. The earliest changes are found in the cortical vessels and membranes. Nuclear proliferation occurs in the walls of the smallest pial vessels and in the perivascular lymphatics. There is overgrowth of the endothelial cells in the capillary walls, and around them lie peculiar cells—the so-called plasma cells. Small lymphocyte-like cells, mast cells, and many others of doubtful nature appear in and around the perivascular channels, and by blocking them interfere with the nutrition of the cortex. The larger vessels also show proliferation of the endothelium, degeneration of the muscular coat and perivascular infiltration. The spirochætes are readily demonstrated in the brain substance.

The fibres of the neuroglia proliferate, its cells multiply, and some assume an abnormal size or shape. These changes in the interstitial tissues are followed by degeneration of the cortical cells and atrophy of their processes. The changes are most marked in the cortical cells and association fibres of the anterior part of the cerebrum, but similar degenerations are found in the basal ganglia, the cerebellum, the brain stem and the spinal cord.

Symptoms.—The disease is characterised by progressive deterioration of the mental and physical powers.

Mental Symptoms.—The most recent acquisitions are usually lost first. Hence the earliest sign of mental failure will differ according to the intellectual and emotional make-up of the individual attacked. Memory, judgment and reasoning are impaired from the first, the æsthetic, moral and intellectual attributes alter early, and changes occur in the domains of conduct and emotion which astonish or distress the patient's friends. To one who sees the patient for the first time the defects may not be apparent, but those who know him will speak of the *changes* in his intellectual capacity, character or behaviour. Cheerfulness has given place to depression or irritability. the quiet and unassuming man has become passionate and boastful, the good father has turned against his family, promises are no longer kept, a good

business is neglected, money is spent unwisely, high artistic skill is lost, the moral code is transgressed, and so on. There is no end to the variety of the early symptoms, but in each case they represent a change for the worse.

In the classical form of the disease, elation and expansive delusions concerning health, wealth, social position or physical and athletic powers are prominent, but in a larger number of cases the patients are depressed in the early stages, and the delusions when they appear may be melancholic or hypochondriacal. Unlike the paranoiac, who may refuse to disclose his delusions or who may reason skilfully from his false premises, the paretic reveals his delusions readily, and can be made to betray their falseness by his own words. To the direct question regarding his occupation the Emperor, the possessor of untold wealth, the world's greatest general, will reply unconcernedly that he is a boot-black, or the champion athlete of the universe will give answers showing a complete absence of familiarity with any branch of sport.

In the course of time dementia increases, memory is abolished, delusions are forgotten, emotion disappears, and in a year or two the patient is unable to move from his bed where he lies speechless, paralysed and incontinent. The various concomitants of the delusions are described in the following paragraphs.

The most constant and most characteristic signs are changes in the pupils, tremors of the face, tongue and hands, and disorders of speech. Changes in the pupils occur early, indeed they are often present as signs of past syphilis before symptoms of general paralysis appear. Inequality in size, irregularity in outline, and the complete or incomplete Argyll Robertson phenomenon, are very common pupillary signs. Primary optic atrophy is frequent, but except in tabetic cases it is rarely complete. Paralysis of the external ocular muscles sometimes occurs as a result of associated tabes or cerebral syphilis. Tremor is often an early sign. In the face and hands, though often present when the parts are at rest, it is best seen in speaking or when movements, such as showing the teeth and holding the arms outstretched, are carried out to order. The typical tongue tremor is a backward and forward "trombone" movement of the organ, when the attempt is made to protrude it. Speech is often affected early. At first it is merely hesitant. Later it becomes blurred, syllables are omitted, interpolated or slurred, and the voice becomes feeble and lacks intonation. As the memory fails, confusion arises in the construction of long sentences, proper names are forgotten, the choice of adjectives and verbs becomes more and more limited, and the vocabulary diminishes until only interjections are left. Written language suffers in the same way, and may show defects of execution and of ideation before spoken speech is noticeably altered. At the onset voluntary power in the muscles is usually maintained, but undue fatigue after moderate exertion is a common early symptom. As the disease progresses, weakness appears in the lower limbs and soon affects all the muscles. Some of the signs of injury to the pyramidal tracts, such as increased tendon reflexes, diminution or loss of the skin reflexes, and Babinski's plantar response, are found sooner or later in almost every case. In a small number the tendon reflexes are abolished and other signs of tabes, such as sensory disturbances, are present. Retention of urine or incontinence sometimes

occur in the early stages. Towards the end, control of the bladder and rectum is always lost.

Epileptiform seizures of various kinds are common. They may be the first obtrusive symptom, and may occur at any time in the course of the disease. The attacks may have all the aspects of idiopathic epilepsy, or they may be local and of the nature of Jacksonian fits. Attacks resembling *petit mal* have also been observed. In the so-called "congestive" apoplectiform attacks, paralysis of one limb or of one side of the body comes on suddenly with or without convulsions and passes off in a few days or weeks. The patient may become comatose and breathe stertorously, or he may be merely somnolent or confused.

Insomnia is frequent in the prodromal period, but in the early stages sleep is often excessive. Later, sleeplessness and motor restlessness are often troublesome symptoms.

CLINICAL TYPES.—*Exalted or expansive form.*—This form includes the cases in which elation, euphoria and grandiose ideas are prominent.

Demented forms.—The patients often seek advice of their own accord, complaining of diminished mental and physical power or failing memory. Mental deterioration runs its course without marked depression or exaltation.

Depressed form.—This common form is characterised by melancholic and hypochondriacal delusions. Some have delusions of persecution. Very often the patient exaggerates his afflictions to a degree not seen in other forms of insanity, melancholic megalomania. Remissions are common.

Maniacal form.—The features of this form are attacks of acute maniacal excitement, which may resemble acute delirious mania. Remissions are common, and apparent complete recovery may be made; but the attacks recur, each one leaving the patient more demented.

Many other varieties have been described, the stuporose, the convulsive, the tabo-paretic, and so on. The characters of these types are sufficiently indicated by the names.

Diagnosis.—It is upon the detection of character alterations in the patient that the early diagnosis of general paralysis commonly depends. As has been said, these alterations vary from subject to subject, but constant components are impairment of judgment, defects of memory, and signs of impaired emotional control. Emotional tone may be one of depression, or one of exaltation, and while the latter is the more striking it is probable that the former is the more frequently encountered. It is the patient's family and his fellow-workers who first notice the insidiously developing change, and their evidence may be essential to early diagnosis. It is, however, important to remember that an altered emotional tone is invariably accompanied by some indications of mental deterioration, and this latter component serves in the differentiation of the psychoneuroses from general paralysis. Commonly the patient himself has little or no insight into his altered state, and may express his subjective sense of well-being and of intellectual acuity in glowing terms that arouse a suspicion of the true state of affairs in the trained observer.

Accompanying these essential alterations are a number of somatic physical signs, such as a slurring articulation, some tremor of the lips and tongue, perhaps some tremor of the hands. Pupillary anomalies are almost constant,

but fall short of those seen in tabes dorsalis. Thus, myosis is uncommon, but irregularity of outline, inequality and sluggishness of the light reaction are usual. There may or may not be changes in the tendon reflexes and plantar responses, but diagnosis in the initial stages of the malady has often to be made in the absence of many of these somatic signs. In doubtful cases confirmation must be sought, and can be obtained from the examination of the cerebrospinal fluid and from the Wassermann reaction (see pp. 1629, 1630).

Course and Prognosis.—After an insidious onset, the disease progresses steadily and usually ends fatally in about 3 years. Acute forms may run their course in a few weeks. When convulsions are frequent, death usually results in about 6 months. When periods of extreme restlessness and excitement alternate with depression, one year is the average duration. In simple demented and depressed forms, the duration is usually about 3 years. The course is most prolonged in those who have attacks of wild excitement or mania, as remissions are very common in this form. During the remissions, patients may be able to return to work, and 10 years may elapse between the first attack and the fatal termination. The course is often prolonged in women, in congenital cases, and in cases of taboparesis.

Treatment.—As some cases of cerebral syphilis simulate general paralysis, in every instance where the latter disease is suspected rigorous anti-syphilitic treatment should be tried in the hope that the patient is suffering from the more curable condition.

Malaria therapy in general paralysis.—Encouraging results have been obtained by infecting paralytics with benign tertian malaria. Blood is obtained from a patient suffering from malaria (not necessarily during a rigor), and is injected intramuscularly, or infected mosquitoes may be applied to the skin in a wide-mouthed jar, the orifice of which is covered with muslin. The incubation period may be as long as a fortnight or more after subcutaneous injection, but failure to infect with 5 c.c. of blood is rare. If the blood has to be transported it should be received in a sterile test-tube containing glass beads; after defibrination it is transferred to another sterile tube and packed in ice, when it will remain active for 6 hours or more. The recipient is allowed to have six, ten, or more rigors, the number depending on his general condition during the treatment; the infection can be cut short at any moment with quinine; relapses rarely occur in this experimental malaria. In favourable cases a remission occurs, improvement continuing for several months; the end result of the treatment cannot be assessed until 6 months or more have elapsed. When the patient has recovered from the debilitating effects of the malarial infection, antisyphilitic treatment should be initiated. For this purpose tryparsamide has been successfully employed, after an initial injection of 1 g., a course of weekly injections of 2 g. may be carried out—15 injections being given. This drug has been known to cause optic atrophy and therefore the visual function must be carefully watched during its administration.

Malarial therapy is not without risk and should be employed only by those experienced in its use, and under institutional conditions where adequate nursing is obtainable. Malarial therapy owes such efficacy as it possesses to the severe and recurrent pyrexia it produces, which is very destructive of spirochætes in the brain. Recently attempts have been made to bring

about a more readily regulated hyper-pyrexia by mechanical means, such as prolonged retention in electrically heated cabinets. This procedure, not less than malarial therapy, calls for considerable experience and the requisite apparatus, and even on these terms it cannot be said to be free from danger.

TABES DORSALIS

Synonym.—Locomotor Ataxia.

Ætiology.—Tabes is more frequent in men than in women (10 to 1), and begins most often between the ages of 30 and 45. The essential factor in its causation is previous syphilitic infection. The interval between infection and the onset of symptoms varies from 2 to 20 years; commonly from 5 to 10 years. As a result of congenital syphilis, or of infection in infancy, it sometimes begins in childhood, youth, or early adult life—infantile or juvenile tabes. Occasionally husband and wife are both affected—conjugal tabes.

Pathology.—Despite what has been said earlier (p. 1630) of the essential lesion in syphilis of the nervous system, it has to be admitted that all we know with certainty of the lesion in tabes is that there is degeneration of exogenous fibres in the posterior columns of the cord. At various times it has been suggested that the primary lesion is a form of local meningitis of the posterior roots proximal to the posterior root ganglion. Recently, Richter has described a peculiar type of granulation tissue in this situation, and he believes that this "strangles" the entering nerve fibres, and thus leads to their secondary degeneration. But Stern has shown that this tissue is present in the normal subject, and therefore the hypothesis of a primary local meningeal lesion remains unsubstantiated. It is known that toxins may ascend afferent nerve fibres from a peripheral focus of infection, and that degeneration of exogenous nerve fibres *within* the cord may result, the peripheral portions of the nerve fibre showing no lesion. It has been suggested that the toxins of syphilis may thus ascend from a peripheral focus, and that the essential and primary tabetic cord lesion is thus a degeneration of nerve fibres within the cord. Some of the degenerated fibres end around cells in the grey matter soon after they enter the cord, while all the fibres with a long intraspinal course enter the posterior columns, and ascend in them to the nuclei of Goll and Burdach in the medulla. As a secondary change the neuroglia around the degenerated fibres increases in amount and density. Hence the characteristic feature in sections of the cord in tabes is sclerosis of the posterior columns. The sclerosis usually appears earliest in the postero-lateral columns of the lower lumbar and upper sacral regions. In the dorsal and cervical cord it is confined at first to the postero-internal columns, which contain the degenerated fibres from the lumbar and sacral regions, but in advanced cases when the dorsal and cervical sensory roots are also affected the posterior columns are sclerosed throughout.

In advanced cases the endogenous tracts of the posterior columns show degeneration, and in some the afferent tracts in the lateral columns are also affected. In sections stained by the Weigert-Pal method the diseased areas are paler than the rest of the white matter. By the Marchi method parts containing recently degenerated fibres show numerous black dots, which represent fatty material in the degenerating myelin sheaths.

In cases of long standing, atrophy of the entire sensory root with degeneration in the peripheral parts of the sensory nerves, and atrophy of cells in the ganglia are frequent findings. The ocular palsies of tabes are probably mainly due to gummatous meningitis, but it is probable that in the case of the third nerve there may be a degeneration of the nerve cells in the nucleus. Tabetic optic atrophy is also the result of a combined interstitial gummatous inflammation and primary degeneration of optic nerve fibres.

Symptoms.—The inadequacy of current descriptions of the clinical manifestations of tabes is shown by failure on the part of those who depend upon them for guidance to diagnose the disease before it has reached an advanced stage. So long as tabes is described as a disease characterised by severe lightning pains, absent knee-jerks and Argyll Robertson pupils; so long as the diagnosis is withheld until these symptoms are found together; so long as patients without ataxy are stated to be in the *early* or preataxic state—just so long will valuable years be wasted, as they are at present, before patients receive treatment at a time when it might be expected to arrest the course of the disease. It is true that these important symptoms appear ultimately in a very large proportion of the cases, and they are often present when the patient is seen for the first time. It is equally true, however, that many of these patients have complained of symptoms which, if they had been appreciated by the physician, would have betrayed the disease many years before, and that throughout these years they have presented physical signs which, although the knee-jerks and pupillary reactions were still present, would have made the diagnosis of tabes certain. In the following paragraphs stress will be laid on the signs that appear early and allow the diagnosis to be made at the onset of the disease. Chief amongst these early symptoms are disturbances pointing to interference with the functions of the posterior nerve roots.

Sensory Disturbances.—*Subjective.*—Following a general law the first manifestations of altered function are subjective—the patient complains of sensory troubles before any changes can be discovered by objective examination. The most important of these subjective troubles in tabes are the so-called lightning pains. These pains merit the closest attention. They are rarely absent, they often precede other symptoms by 5 or 10 or more years, and most important of all they possess peculiar features which render them pathognomonic of tabes and allow the diagnosis to be made in a syphilitic on their presence alone. Although they are rarely absent careful interrogation may be needed to disclose them. To the question, "Have you had any pains?" the patient may answer "No." If then he is asked if he has rheumatism, he will often answer "Yes," and proceed to give an account of characteristic tabetic pains of several years' duration. In other cases the patient mentions his pains, but their significance escapes notice because it is thought that they are too slight for tabetic pains. It must be made clear at once therefore that the peculiarity of the pains in tabes does not lie in their severity, for they vary from a trifling sensation of discomfort to almost intolerable agony, but in their distribution, in their direction of propagation and especially in their arrangement in time.

As a rule, they come on in attacks, in which single momentary pains are repeated at intervals of a few seconds or minutes for several hours, the whole bout lasting several days or weeks. Between the attacks there may

be long intervals of complete freedom from pain. The pains are felt most often in the lower limbs, but any part may be affected. They may be referred to the skin, to the muscles or to the bones. They are very common in the bony prominences around the knee and on the foot. The direction of radiation varies. In some the pain seems to shoot up or down a limb, but in a larger number it seems to strike the limb vertically as if a sharp object were piercing it from without. Some patients experience both kinds of pains. The onset of each pain is always sudden. If it is severe the patient may cry out, and if it overtakes him whilst walking he is forced to stop and he may fall. The duration of each pain is usually momentary, but sometimes it lasts a second or two and fades away gradually. During a given bout the pains usually recur in the same place each time for several hours on end, and then appear in another part, say on the following day. In a few cases, however, they confine themselves to two or three points, now appearing in one and now in the other. In a still smaller number the site varies from moment to moment, so that the patient never knows where the next one will strike him. In one group the pains are repeated very rapidly in one place for a few seconds, and then after an interval in another, so that the timing recalls the sound of a machine-gun firing short bursts—tap, tap, tap, pause, tap, tap, tap, pause, and so on with a longer interval now and then during which the gun is trained on a new objective.

After a bout the skin is often tender, and ecchymoses may appear over parts in which the pains were felt, though this is exceptional. Cold, changes in the weather, anxiety and especially over-exertion make the pains worse. They are often more severe for a day or two after treatment by intravenous or intrathecal injection of specific remedies. Other pains with characters which are not peculiar to tabes are common. They are described as aching, burning or gnawing pains. Like the lightning pains, they alter with changes in the weather and are usually attributed to rheumatism. Other common subjective sensory symptoms are "pins and needles" in the extremities, a feeling of walking on a soft substance, and of constriction around the trunk or limbs. More important than these, because it often appears very early, is hyperæsthesia of the trunk, especially in its lower part. Light touches or applications of water at certain temperatures are almost unbearable.

Objective sensory disturbances.—Signs of damage to the posterior nerve roots appear in the earliest stages of the disease, and are demonstrable in many cases long before the classical signs appear. The detection of this early sensory loss is of great importance, for its distribution is pathognomonic. The parts in which sensation is first impaired are—(1) a band on the chest and along the inner border of the arms; (2) the feet; (3) around the anus; (4) on the nose.

As the disease advances, sensory loss extends upwards from the feet, downwards from the chest, and outwards from the nose and anus in concentric circles. Ultimately these areas coalesce, and in the later stages sensation is diminished all over the body. All forms of skin sensation are not equally affected Sometimes the defect is first discovered on testing with light tactile stimuli, but more often pain and temperature are first impaired.

The senses of deep pain and of position and passive movement, as well as the vibration sense, are often diminished in the legs in the early stages. In advanced cases these defects are present in all the limbs.

In cervical tabes sensory disturbances occur first, and are most severe in the arms.

In severe cases sensation of all kinds may be almost completely abolished. No cutaneous stimuli are felt and the deep structures are insensitive to pain. To this is added loss of the sense of position, not only in the limbs but also in the trunk, so that the patient is unaware of their position when his eyes are closed. If he sits up with the arms outstretched, on closing his eyes the arms "wander," the fingers execute slow "piano-playing" movements, and the body sways. In extreme cases the patient falls on his side as soon as the eyes are closed.

Muscular Hypotonia and the Tendon Reflexes.—Loss of muscle tone occurs in lesions of various parts of the nervous system, and is not necessarily accompanied by changes in the reflexes in the limbs, but when it results from interruption of the spinal reflex arc the two signs are found together. Hence in tabes, where the afferent limb of the reflex arc is the first structure affected, hypotonia and diminution of the tendon reflexes are characteristic signs. The decrease in the tone of the muscles is often well marked when lightning pains are the only symptom of tabes, and loss of skin sensation the only other sign. It is shown by flaccidity of the muscles, and by an abnormal range of active and passive movement of the limbs.

The leg can often be raised to an angle of 100° from the horizontal, with the knee extended, whereas a normal person cannot raise it more than 60°, and excessive range of dorsiflexion of the foot is often a striking sign. In extreme cases the legs can be made to encircle the neck, the body can be flexed so that the head touches the bed between the knees, and the patient is able to imitate the tricks of the "double-jointed" man.

The knee-jerks are very often absent when the patient is first examined, and in the later stages they are almost always lost, but compared with the signs already mentioned this one is of late onset, and may be missing even in the ataxic stage. The position formerly held by the knee-jerks in the symptomatology of tabes should be given to the tendo Achillis (ankle) jerks. Loss of the ankle-jerks is indeed an early sign in tabes, for it often precedes loss of the knee-jerks by many years. The tendon reflexes in the upper limbs are lost early in cervical tabes, and are frequently absent in cases of the ordinary type.

The skin reflexes are often exaggerated to a degree rarely met with in other diseases. This is best seen on the abdomen, and is usually associated with hyperæsthesia to touch and temperature. Later, when the tactile sense is lost, the skin reflexes are often diminished. The plantar reflex is usually normal. It is sometimes absent when sensory loss on the soles is severe, and in cases where sclerosis of the pyramidal tracts exists as a complication of tabes the response is "extensor."

Ataxia.—The fibres conveying those afferent impressions which are essential for the proper execution of voluntary movements, are more resistant than those with other functions, and inco-ordination, though extremely characteristic of tabes, is usually a late symptom, or it may be absent throughout the whole course of the disease. Its onset is marked by unsteadiness in walking and difficulty in maintaining the balance of the body. These troubles are first noticed when co-ordinated movements are performed without the aid of vision. As the defect increases unsteadiness appears even

with visual guidance. To maintain their balance the patients walk on a wide base with the eyes directed to the ground. At a later stage some raise the feet too high, throw them too far forward and bring them down forcibly, the whole sole striking the ground at once—stamping gait. Others reel from side to side like drunken men. Still later the support of one or two walking-sticks is required, and ultimately walking becomes impossible. The inco-ordination is not only present in walking, but can be seen in all voluntary movements, *e.g.* in the heel to knee test. The same defects occur in the upper limbs. At first there is merely clumsiness in performing fine movements such as picking up small objects and in adjusting the dress. In the end the ataxia may become so great that the patient is unable to feed himself.

By appropriate tests inco-ordination can usually be disclosed before the patient has noticed it. Some of the tests are: standing with the heels and toes together, standing on one foot, walking backwards, rising quickly from a stooping position and turning quickly in walking. In each instance the unsteadiness is greatest when the eyes are closed and when the feet are bare.

Sphincter Troubles.—These are the result of the lowering of pain sensibility in the bladder which is the afferent element in the reflex of micturition. An increased distension of the bladder becomes essential before the act can be started, and this fails before the bladder is completely emptied, and residual urine is present in slowly increasing quantity. Though this causes little or no inconvenience to the patient it often leads to cystitis and renal complications. Difficulty in starting micturition and nocturnal incontinence are the common complaints. Complete retention and paralytic incontinence are rare, and when retention occurs it has in our experience been due almost invariably to enlargement of the prostate, the removal of which has been well borne and has given complete relief. Sexual desire and power are usually lost early in the course of the disease.

Ocular Symptoms.—Changes in the reaction of the pupils and in their size and form are very frequent and are of great importance for diagnosis. The chief of these is the Argyll Robertson phenomenon, in which the pupil contracts on accommodation but not when exposed to light. This sign appears in both eyes in 70 per cent. of cases, and is one of the earliest to appear. It is sometimes found in one eye with a normal or diminished reflex in the other. It may be present in an incomplete form, the contraction to light being slight and sluggish when the reaction to accommodation is brisk, or the pupils may contract when first exposed to the light only to dilate again. Occasionally the pupils are fixed and do not react to either stimulus. In rare cases the reaction to accommodation is lost while the light reflex persists.

The size of the pupils varies greatly in different cases. Most often they are small, but pupils of moderate size are common, and sometimes they are widely dilated, though this is very exceptional and usually associated with optic atrophy. It is not unusual to see pupils which, when contracted on accommodation, are no larger than the head of a pin, but the "pin-point" pupils are extremely rare. Inequality of the pupils or irregularity in their outline is present in most cases. It is said that the pupils are sometimes normal in every respect even in the advanced stages of the disease. On the other hand, in old tabetics in whom the disease has been present for

very many years the pupils may be found wholly inactive both to light and on convergence.

External ocular muscles.—In the early stages transient palsies of the muscles of the eyeball often cause ptosis, diplopia or squint, lasting a few days. Permanent paralysis may come on at any time, but is most frequent in the later stages. A persistent drooping of the eyelids—tabetic ptosis—is a common sign. This is attributable to a lesion of sympathetic fibres. The patient tries to overcome the defect by contracting the frontalis muscles, and the wrinkling of the forehead with slight drooping of the lids gives the patient an expression—the tabetic facies—by which the disease may be recognised at a glance.

Optic atrophy.—Defective vision from atrophy of the optic nerve is often the symptom for which the patient first seeks relief. It occurs in about one case in ten, and almost without exception ends in complete blindness. The loss usually begins in the periphery of the visual field, and is often unnoticed until central vision begins to fail. Occasionally central vision fails early. At first one eye suffers more than the other, but ultimately, after a period which averages 5 years, all vision is lost in both. Patients sometimes relate that their blindness came on suddenly, or in a few hours or days. In these cases optic atrophy has been present for a long time, but the fibres subserving central vision have escaped until the last. On the other hand, vision may fail very slowly, with periods of arrest or apparent improvement, and total blindness is sometimes delayed for 10 or 15 years. The atrophy is primary, that is, it is not preceded by papillœdema. Pallor appears first on the temporal side, whence it spreads over the whole disk. The edges of the disk are sharply defined and the lamina cribrosa is visible as slightly darker spots, so that the disk stands out clear and bright, like a full moon. When optic atrophy is the first symptom, it is often impossible to detect any incoordination in the lower limbs, and ataxia may be long delayed. The knee-jerks are often brisk, but some of the early signs—lightning pains, sensory disturbances or loss of one or both ankle-jerks—are almost always present, and the Argyll Robertson pupil is a constant accompanying sign. In a number of the patients with optic atrophy the signs of general paralysis are added to those of tabes (tabo-paresis), and the course of their illness is that of the more serious disease.

Other Cranial Nerves.—The senses of smell and taste are sometimes lost. Vertigo, tinnitus and nerve deafness are common. Lightning pains are often severe in the distribution of the trigeminal nerve, and loss of sensation on the nose, especially to pain, is one of the earliest and most frequent signs. Paralysis of the vocal cords, though rarely sought for, is present in many cases.

Visceral Crises.—There are two varieties of visceral crises which are associated with disturbance of the parasympathetic and with the sympathetic innervation respectively. The former, which is confined to the vagus distribution, consists of spontaneous sensory irritation and its reflex results which is never painful since the vagus contains no pain-conducting elements. The examples are the laryngeal crisis and the gastric crisis, which comprises painless vomiting. The latter belongs to the sympathetic distribution, always involves severe pain, and is made up of the painful gastric crises, and the rectal and vesical crises.

Gastric crises.—The organ most subject to crises is the stomach. Attacks of severe abdominal pain with repeated vomiting come on suddenly. They last a few days, or a week or two, and are often repeated every few weeks for long periods. Sometimes pain or vomiting alone is present. There is always complete anorexia. The patient looks very ill during the attack, but it is never fatal. They often occur before other symptoms of tabes appear, and are often mistaken for acute obstruction, and other conditions requiring urgent surgical treatment, but careful examination will rarely fail to reveal indubitable signs of tabes. If attention were paid to the ankle-jerks, and to sensory disturbances, instead of to the knee-jerks, unnecessary operations would be less frequent.

Next to the stomach, crises are most frequent in the larynx (*laryngeal crises*). In the commonest form there is spasm of the larynx, with noisy breathing, cough and dyspnœa. Sometimes the attacks resemble whooping-cough or laryngismus stridulus. They are much shorter than gastric crises, rarely lasting more than an hour. Death in an attack is extremely rare.

Attacks of extremely painful and prolonged tenesmus (rectal crises) are not uncommon. Attacks of frequent painful micturition (vesical crises) and of pain like renal colic (renal crises) are rare.

Cardiac, nasal, bronchial, intestinal and other crises have been described.

Vasomotor and Trophic Disturbances.—The most important of these are changes in the joints and perforating ulcers. Rarer forms are local sweating, loss of hair, nails or teeth, attacks of herpes, hæmorrhages into the skin, necrosis, rarefaction and spontaneous fracture of bones, excessive callus formation and spontaneous rupture of tendons.

Charcot's joint disease.—Arthropathies may develop at any stage of the disease. Occasionally the patient seeks advice for the first time with this complaint. The first sign is usually rapid swelling in and around a joint, with effusion and œdema. The effusion, in slight cases, subsides slowly and the joint recovers, but more often the enlargement is followed by destruction of the cartilages, wasting of the ends of the bones, peri-articular new-bone formation and destruction of the ligaments. The joint becomes disorganised, the range of movement is increased, and crepitations of startling coarseness are heard and felt when the part is handled. The characteristic feature is the complete absence of pain. Dislocations occur readily, especially at the hip. The diseased joint sometimes becomes infected. This is commonest in the foot. The joints most often attacked are, in order of frequency: knee, hip, shoulder, elbow, ankle, small joints of the hands and feet, the spine.

Perforating ulcers are commonest on the sole of the foot. Patches of hard thickened skin are frequently seen on the soles of the feet. Sometimes blisters form beneath this thick epidermis, and on bursting leave an indolent sore. Once formed the ulcer is very indolent. It is usually painless.

Complications.—Tabes is frequently complicated by other syphilitic affections of the nervous system, of which the commonest and most important is general paralysis of the insane. Some tabetics develop general paralysis, and many paretics present some of the signs of tabes. Indeed, these conditions are merely different aspects of the same disease, and are named according to the predominant features. Sometimes it is difficult to decide the category of given cases, and the name tabo-paresis is used to describe them. At the same time it may be observed that tabo-paresis

runs a much slower course than uncomplicated general paralysis, and apart from any question of treatment the survival period is longer in the former than in the latter. Occasionally the pyramidal tracts degenerate and signs of spastic paraplegia are added to those of tabes. Atrophy of the anterior nerve roots with consequent wasting of the corresponding muscles is a fairly common complication. Outside the nervous system the commonest complications are aortitis, aortic regurgitation and aneurysm.

Diagnosis.—Most tabetics come under observation for the first time when one of the many symptoms of the disease begins to cause serious trouble. The obtrusive symptom may be: lightning pains, failing vision from optic atrophy, double vision from paresis of ocular muscles, attacks of vomiting, tenesmus, unsteadiness in walking, painless joint disease, impotence, troubles with micturition, or some other less common complaint. In these the diagnosis rarely causes difficulty. A history of characteristic pains, or evidence of syphilis in the past, justifies the diagnosis of tabes on the symptoms alone. In almost all of these cases, moreover, unequivocal signs will be found which make the diagnosis certain. Two signs—the Argyll Robertson pupil and absence of the ankle-jerks or knee-jerks—are of supreme importance, for although one is often lacking, the absence of both in the kind of case we are discussing is rare. To one or both of these several of the following confirmatory signs are usually added: inequality or irregularity of the pupils, diminished sensibility to pinprick of the skin on the nose, on the chest and feet, absence of pain on compressing the calf muscles, loss of vibration sense in the feet, muscular hypotonia, defective sense of position in the limbs and unsteadiness when the eyes are closed.

When the symptoms and signs are slight and few, or when suspicious signs are found during a routine examination, the diagnosis is sometimes difficult, and may require for its elucidation a careful inquiry into the history, an examination of the blood and cerebro-spinal fluid, and a meticulous investigation of the nervous system. These cases are discussed in the following paragraphs.

The Diagnosis of Early Tabes.—1. Since Westphal, some 60 years ago, described loss of the knee-jerks as an early sign of tabes, and established the existence of the pre-ataxic stage, the profession, apart from neurologists, has altered its views but little, and still hesitates to diagnose tabes while the knee-jerks are present. Consequently mistakes in diagnosis are common. The diagnosis can and should be made when lightning pains are the only symptom. Pains with the characters already described occur in no other disease, and their presence calls for a careful investigation for evidence of past syphilis. In this first stage of tabes the diagnosis is founded on (1) characteristic pains; (2) evidence of syphilis in the past, obtained from the history or by examination of the blood and cerebro-spinal fluid (see pp. 1629, 1630).

2. Only rarely need the diagnosis be made on these grounds alone, for in almost every patient with lightning pains careful examination will reveal confirmatory signs. The most important of these are sensory disturbances and alteration in the pupils. Hyperæsthesia to touch and temperature on the lower part of the trunk is very common, although few patients mention it until their memory is refreshed by careful interrogation. In a patient who has had syphilis and suffers from lightning pains, a clear demonstration

of sensory impairment confined to the characteristic areas makes the diagnosis still more certain. Other signs to which a high value may be given are absence of pain when the calf muscles are compressed, loss of the vibration sense in the feet, and muscular hypotonia. Irregularities in the outline of the pupils without an obvious explanation, or pupils which react well to accommodation but sluggishly to light, are very strong evidence of past syphilis and should be duly appraised. This may be called the second stage of tabes in which the diagnosis is founded on (1) evidence of syphilis; (2) tabetic pains; (3) sensory disturbances with a characteristic distribution.

3. If to these sensory disturbances there is added an Argyll Robertson pupil, or if one ankle-jerk or knee-jerk is absent or definitely diminished when compared with its fellow, the diagnosis is established beyond doubt. This may be called the stage of the fully developed disease. The diagnosis rests on—(1) evidence of syphilis; (2) lightning pains; (3) characteristic sensory signs; (4) the Argyll Robertson pupil in one or both eyes; (5) absence of one or both ankle- or knee-jerks, or a definite diminution in one of them.

Lightning pains probably indicate that the disease is active. In the absence of pains tabes would still be suggested by the combination of an Argyll Robertson pupil with an absent ankle or knee-jerk, or by the combination of one or both of these signs with characteristic sensory loss. In such cases, however, it would be impossible to say whether the patient was suffering from tabes which was likely to progress, or whether the disease had been arrested in its earliest stages.

Differential Diagnosis.—*Peripheral neuritis.*—The signs common to both diseases are loss of reflexes, hypotonia, inco-ordination and sensory loss. Wasting, loss of power and tenderness of the calf muscles distinguish peripheral neuritis. A complete history and examination will usually reveal the cause of the neuritis, or disclose certain signs of tabes.

Friedreich's disease.—Loss of tendon reflexes and inco-ordination occur in both diseases, but the age of the patient, the family history, the speech defects, nystagmus and the deformities of the feet and spine make the diagnosis easy. Juvenile tabes is sometimes mistaken for Friedreich's disease.

Course and Prognosis.—In most instances the disease is well established before some serious symptom brings the patient under observation. For this reason it is usually impossible to determine the sequence and duration of the signs that are found, but if the onset of lightning pains and of ataxia are taken as landmarks, an idea of the extreme variability of the course of tabes in different cases will be obtained. In many patients the disease remains stationary in the earliest stage and causes no disability. In a larger number inco-ordination appears after a pre-ataxic stage of 10 or 20 years. Some become ataxic within five years of the onset of pains, a few within a year. Once ataxy appears, its rate of increase varies within wide limits. It may be so rapid that walking becomes impossible in a few weeks; it often increases very slowly, and only interferes seriously with walking after several years, and in a large number periods of increase in the ataxy alternate with long periods in which it is stationary or undergoes temporary amelioration.

The course of the other symptoms is equally variable. In general, irritative phenomena—pains and crises—tend to diminish, while the signs of destruction of sensory nerves — diminished sensation, hypotonia, etc. —

increase. Ocular palsies are frequently of short duration, and bladder and rectal symptoms are often temporary. It is impossible to foretell how any given case will progress, but there seems to be some connection between the period which has elapsed since syphilis was contracted and the rate of evolution of the disease—the longer this period the more benign the course. If the symptoms have increased slowly in the past, the future course is likely to be slow, whereas cases of rapid onset often progress rapidly. When optic atrophy occurs, blindness results almost invariably, and a proportion of these cases develop general paralysis of the insane.

The prognosis as to life is variable. Most tabetics die of intercurrent maladies or of some cardio-vascular complication, but life is constantly menaced by cystitis and ascending infection of the urinary tract. It should be remembered that in many cases of tabes, the malady undergoes arrest, and the patient may never become ataxic or grossly disabled. Such arrest may be found in persons who have at no time had any anti-syphilitic treatment. Conversely, tabetics who have been rigorously treated in this way may become progressively disabled. On the whole the prognosis as to both working capacity and life is best in those cases where the bladder can be kept free from infection.

Treatment.—This falls under three heads: treatment by anti-syphilitic remedies, general treatment, and treatment of individual symptoms.

ANTI-SYPHILITIC TREATMENT.—Mercury and bismuth are the most valuable drugs. Several courses of daily inunctions should be given at intervals, until 60 inunctions have been applied. This may be supplemented by injections of arsphenamine. Between the courses, which may be repeated at 6-monthly intervals, mercury should be taken by the mouth in a pill or mixture. Most observers agree that all forms of intraspinal therapy are useless, and many will doubt whether any form of anti-syphilitic medication can be conclusively shown to influence the course of the malady. Nevertheless, patients should be given the benefit of such doubt on this point as there is, and it is this attitude, rather than one of unreasoning optimism, that really determines the adoption of anti-syphilitic treatment in tabes dorsalis. It should be remembered that long continued and repeated treatment of this order is apt to evoke an unfortunate psychological reaction in the subject of such a chronic malady as tabes, and to produce in him a syphilophobia that is not less distressing than syphilis. In few circumstances can it be more essential to remember that one is treating a sick man and not merely a disease.

GENERAL TREATMENT.—In early cases the patient should be encouraged to continue at his work and avocations, so far as this is consistent with the avoidance of undue mental or physical stress. Strict moderation in the use of alcohol and tobacco should be enjoined. The diet should be generous, and efforts should be made to prevent the rapid loss of weight which is a feature of many cases. Strict attention to the bowels is necessary. In many tabetics the normal call to stool is not felt, and if regular efforts to open the bowels are not made, stasis develops readily. This should be treated by enemata or by glycerin suppositories. Purgatives should be used with discretion. They are of little use in stasis, and should not be given if there is any tendency to rectal incontinence, as this is always worst when the motions are soft. A change from purgatives to enemata or suppositories

will often relieve this distressing symptom. The bladder should be emptied at regular intervals, regardless of the call, which is apt to be less insistent than in normal persons. In general, rest in bed is to be deprecated. In some instances, however, where ataxy develops rapidly, it is advantageous, provided that daily treatment by massage and exercises is instituted at once.

TREATMENT OF SYMPTOMS.—*Pains.*—Of the many drugs that have been tried for the relief of pains the following either in single or in various combinations have been found useful: aspirin, phenacetin, phenazone, amidopyrine, cannabis indica, colchicum, ammonium chloride and sodium salicylate. After one has lost its effect another will often give some relief. Morphine is the only drug that is certain in its action, but it cannot be allowed except on isolated occasions, when for some special purpose it is essential that the patient should be free from pain for a few hours. In no disease is the morphine habit more rapidly acquired or more difficult to break. External applications rarely do any good. Chloroform on lint sometimes gives relief. Hot baths, hot applications to the limbs and blisters to the spine are worthy of trial.

The clothing should be warm, and sudden changes of temperature should be avoided. Residence in a warm country is an advantage. Attention to small details, such as the avoidance of constipation and abstinence from alcohol, often has a favourable effect.

Crises.—Gastric crises, like the pains, are very resistant to treatment. Chlorbutol in cachets containing 10 grains is often useful. It may be given twice or at most thrice in 24 hours. The effect of the drug should be watched carefully, as it sometimes produces alarming depression of the heart and respirations. When chlorbutol fails cerium oxalate and tincture of iodine should be tried. The use of morphine is not justified. Rectal crises are sometimes relieved by small doses of grey powder with opium or pulv. ipecac. et opii. The lower bowel should be emptied daily by enemata. In mild cases with morning diarrhœa an enema or a suppository should be used before the first evacuation. Thereafter the patient should try to resist the desire to defæcate, which soon passes away, and with a little training this troublesome symptom can usually be overcome. Laryngeal crises though very alarming are practically never fatal. They are usually relieved at once by an inhalation of nitrite of amyl.

Bladder disturbances.—When there is any difficulty in passing water a mixture containing 5 minims of liq. strychninæ thrice daily will be found useful. When the bladder is imperfectly emptied the use of the catheter should not be delayed. Only too often neglect of this matter leads to death from pyelo-nephritis. It is well to remember that serious infections may run a painless course. Their presence must be sought for even when pain is absent. This entails an examination of the urine from time to time for evidence of inflammation in the urinary tract. If pus-cells are present in the urine, urotropine and acid sodium phosphate should be given by the mouth. If this does not remove them, the bladder should be irrigated daily until the urine becomes normal. True incontinence of urine is often diminished by 5 minim doses of tincture of belladonna thrice daily, or by the use of the following pill: ℞ Ergotin (Bonjean) gr. 1, Ext. Belladonn. gr. 1–4. Ft. Pil. Sig. i t.d.s.p.c.

Ataxia.—Just as a normal person by practice and effort can learn to perform feats of balance and muscular co-ordination which are impossible for one untrained, so the tabetic by concentrating his attention on his movements can be taught to make greater use of his remaining powers. The results of appropriate re-educative treatment are often astonishing. It is no uncommon thing to see patients who had been confined to bed for months able to get about freely again. Permanency of the result is often a gratifying feature.

As long as the patient is able to get about the necessary re-education can be acquired, if he is taught to pay particular attention to each movement of his limbs, and to attempt to carry it out accurately. In more severe cases, and when the patient is confined to bed, re-education should be given along the lines devised by Fraenkel. Constant supervision is necessary at first, and the treatment should begin in an institution, or under the supervision of a skilled attendant.

No remedy is of avail in checking the progress of optic atrophy.

The condition of the feet often requires attention. Corns should not be cut. Perforating ulcers should be curetted and dressed with a paste of iodine and starch. A cradle should be placed over the feet to prevent deformities, and over-extension of the knee-joint should be prevented by wearing a suitable splint.

Charcot's joints.—As soon as this condition is discovered, the patient should be put to rest, the joint immobilised, and those measures used which tend to relieve the œdema and the effusion into the joint; and if occasion demand, the joint should be aspirated. When the joint becomes dry it should be rested for a long period. For example, the patient with a Charcot's foot should use a peg stump for six months, when the condition will be found to have healed. The knee is a difficult joint to support, and the best treatment is excision of the joint, with the production of a stiff knee.

CONGENITAL SYPHILIS OF THE NERVOUS SYSTEM

Affections of the nervous system are much less frequent in congenita syphilis than in the acquired disease. Viewed broadly, the pathological changes and the clinical manifestations are the same in both. Regarding the first, meningitis, endarteritis and gummata are common to both forms; but while *central softening* from arterial disease is characteristic of acquired syphilis, *cortical cell atrophy and subsequent sclerosis* are prominent features in congenital cases. As for the symptoms, mental defects, with convulsions and spastic weakness of the limbs, are typical of congenital syphilis in contrast to the hemiplegias and monoplegias, with or without convulsions, which occur in the acquired form. It is noteworthy that the combination of obvious visceral and integumental lesions, with parenchymatous degeneration of the nervous tissue, is very common in the congenital, but not in the acquired disease.

Symptoms.—Many syphilitic infants suffer from *convulsions* during the first two years of life and in many cases these are given as the cause of death. In those who survive, fits may continue or they may begin again towards the end of childhood. The latter is more common. The fits in some

cases have all the aspects of idiopathic epilepsy, and may continue throughout life without the addition of any symptoms suggestive of local brain disease. In another group, convulsions are followed by symptoms of *hemiplegia* or of *spastic diplegia*. The same defects may appear apart from convulsions.

Mental impairment is one of the common features of the disease. Idiocy is rare. More often the defect is first noticed between the ages of 5 and 15 years. The child may merely cease to learn, and retain any acquirements he posses, or he may lose his memory and become slowly demented.

Vision is often defective as a sequel of atrophy of the optic nerve or of choroido-retinitis, and bilateral deafness is not uncommon. Affections of the remaining cranial nerves are rare.

Juvenile general paralysis appears most often between the ages of 10 and 17 years. It has been seen as early as the eighth, and as late as the thirtieth year. In some cases it results from congenital syphilis, in others from syphilis acquired in infancy or in childhood. The physical signs are the same as in the adult form. The mental symptoms, as might be expected, differ from those in adults, when mental decay sets in before the appearance of the instincts and passions which form the content of the delusions in older patients. A boy of 12, for example, is not likely to have delusions regarding his wealth or his intellectual capacity or his sexual powers, although he may well have grandiose ideas concerning his physical strength. Optic atrophy is very common in juvenile cases, and as in adults, signs of tabes are present in many cases.

Juvenile tabes presents the same features as in adults. It is important to remember that in rare instances, tabes in an adult owes its origin to congenital syphilis or to syphilis acquired in infancy.

The diagnosis of congenital syphilis of the nervous system rarely causes any difficulty, as the patients almost invariably present some of the stigmata of their malady.

Treatment by mercury should be carried out perseveringly. The results are disappointing.

DISSEMINATED SCLEROSIS

Synonyms.—Multiple Sclerosis; Insular Sclerosis.

Ætiology.—Disseminated sclerosis disputes with neurosyphilis and intracranial new-growths for primacy as the commonest organic nervous disease in these islands and throughout Europe. It is said to be less frequently observed in North America.

Cases have been recorded in which the disease was noticed after acute illnesses, such as scarlet fever, influenza and rheumatism; but it is probable that these simply made more prominent a condition already present. Febrile illnesses are usually followed by increase in the symptoms, and many patients with disseminated sclerosis relate that they became much worse after an attack of influenza. In the great majority of the cases there is nothing in the family or personal history to which the disease can be attributed. In one instance, confirmed by examination after death, it attacked a mother and her child, and a few similar cases, as well as the affection of several members of a family, or of a household, have been recorded.

The onset is most frequent between the ages of 16 and 30, the sexes being affected equally. It is rare for the disease to begin after the age of 55.

The cause is still wholly unknown. Weston Hurst has recently expressed the considered view that there is no sure evidence that any of the demyelinating diseases of the nervous system are directly due to the action of a filtrable virus. The signs of inflammatory reaction in this disease are compatible with the view that it is infective in origin, but it may be added that it behaves like no known infective disease.

Pathology.—The disease has been described by Nageotte and Riche as "an affection constituted by multiple inflammatory foci, varying greatly in size and number, disseminated irregularly throughout the length of the cerebro-spinal axis. The chief features of these foci are (i) their sharp outline, (ii) their irregular and capricious shape, (iii) the fact that they do not interrupt the axis cylinders, which are only demyelinated and deformed as they traverse the focus. Hence the absence of Wallerian degeneration. The abundance of neuroglia in the foci justifies the name sclerosis which has been given to the process."

These foci are visible on naked eye examination, the fresh ones as greyish translucent foci, the older ones as greyish or pinkish shrunken areas. Grey and white matter are both affected, the foci having some predilection for the walls of the ventricles. The foci bear no necessary relation to blood vessels.

Under the microscope the older patches are found to contain proliferated neuroglia and nerve fibres which have lost their myelin sheaths. The axis cylinders in the sclerosed areas escape destruction for a long time. For this reason secondary degenerations do not occur in the spinal tracts, and sections of the cord between lesions at different levels present normal appearances. Ganglion cells are also spared; hence wasting of the muscles supplied by the affected segments is not a feature of the disease. In recent patches, œdema is present with infiltration by small lymphocyte-like cells, plasma cells and compound granular corpuscles around the blood vessels, especially in the adventitial sheath of the veins. It is highly probable that these inflammatory changes represent the initial lesion, and that the alterations in the nerves and in the neuroglia are secondary to them.

Symptoms.—In the early stages the axis-cylinders in the diseased areas are not interrupted completely, but suffer partial and temporary impairment, which alters in intensity with the severity of vascular and other inflammatory changes in the tissues around them. Moreover, as the inflammation subsides in one patch a new one develops and produces a different set of symptoms. Hence it is not surprising that the earliest symptoms are often slight and fleeting, or that they may first appear now in one part and now in another. In spite of this, however, certain symptoms and physical signs appear with remarkable regularity and render disseminated sclerosis, in the more advanced stages at least, one of the most distinctive and most easily recognised diseases of the nervous system.

It is remarkable that though the demyelinating lesions, which are often of considerable size, occur anywhere in the central nervous system and commonly involve the fillet, the lateral fillet, the spinothalamic paths and the peripheral neurones in their intramedullary course and the visual path, yet anything but the most transient loss of function never occurs in connection with these

systems. On the other hand, the phylogenetically newer systems—the pyramidal paths and the proprioceptive system commonly suffer permanent damage. The common transient loss of vision may be determined by an œdematous lesion of the optic nerve as it traverses the optic foramen.

Motor Symptoms.—Weakness in the lower limbs is the symptom for which many patients first seek relief. Beginning with a feeling of heaviness or stiffness in one or both limbs, the weakness, which may be limited at first to one group of muscles, increases, in some uniformly, in a larger number with remissions or with periods of apparent recovery, until at last, after a time which varies from a few weeks to many years, it ends in severe spastic paraplegia. The physical signs are those of pyramidal lesions in general—increased tone in the muscles and exaggeration of the tendon reflexes, diminution or loss of the abdominal and cremasteric reflexes, and Babinski's plantar response. They are of extreme importance, for some or all of them may be present when the patient's complaints are still trivial, and they are found so constantly in all stages of the disease that the diagnosis of disseminated sclerosis is rarely made in their absence.

The paralysis can often be distinguished from that of other pyramidal affections by the variations in its severity from time to time, and by the occurrence of remissions or of apparent recovery, the improvement sometimes lasting for weeks or months, and, in rare cases, for many years. In most cases, moreover, examination will reveal some other sign—nystagmus, intention tremor, or pallor of the disk—which betrays the cause of the paralysis. In one large group of cases, however, the symptoms are those of a steadily increasing spastic paraplegia without remissions and without any indication, either in the physical signs or in the history, of extra-pyramidal disease. The gait may be but slightly altered, even when the tendon reflexes are greatly exaggerated and the plantar responses are "extensor." Later, it becomes spastic or spastic and ataxia. Sometimes ataxy makes walking very difficult, when the power in the limbs is only slightly impaired. In the arms there is often loss of power associated with exaggeration of the tendon reflexes. In some cases the arms are affected before the lower limbs, when astereognosis and loss of sense of position from a lesion in the course of the parietal projection produce one of the commonest of the early symptoms—the "useless arm."

Tremor.—The characteristic tremor in the arms appears on voluntary movement only, and increases in rate and amplitude as the goal is approached. For these reasons it is called intention, volitional, or terminal tremor. It is sought for by causing the patient to touch his nose with the tip of one finger. In its minimal form the tremor appears as two or three jerky movements of the finger just as the goal is attained, or the finger reaches the nose without any abnormal movement and then oscillates, so that it slips away from the nose again or depresses it several times before coming to rest. The tremor may be noticed first in writing or in performing other delicate movements, such as threading a needle. Later, the rate and amplitude of the movements increase, and the tremor, although still greatest at the end, appears almost as soon as a voluntary movement begins. In advanced cases it prevents all useful movements, and the patient is unable to do anything for himself. The arms are affected earliest and most often, but nodding of the head is common, and any part of the body may be affected. Beside

intention tremor, other types of inco-ordination of the limbs are occasionally seen, such as those characteristic of lesions of the optic thalamus or of the mid-brain or of the cerebellum.

SENSORY SYMPTOMS.—*Subjective.*—Numbness and tingling in the extremities and alterations in the sensation of various parts are common complaints. They are often transient, and may be the only symptoms during the premonitory period. Severe pains are rare, but many patients complain of stiffness or of aching in the limbs and in the back. Occasionally intense neuralgic pain of trigeminal nerve distribution is found.

Objective.—Severe sensory loss is not common, but careful examination will often reveal areas of skin in which sensation is impaired. Occasionally the loss is severe, and may show so sharp an upper level as to suggest the presence of a spinal tumour. In many cases the sense of position and passive movements in the limbs is seriously affected, in others loss of vibration sense is the only sensory sign. An isolated loss of the last named, in the legs, is a phenomenon of diagnostic importance. Like the other signs, the sensory disturbances often show considerable variations in extent and degree at different examinations.

OCULAR SYMPTOMS.—Attacks of *double vision* are frequent, and highly characteristic of the disease. Close interrogation, avoiding the leading question if possible, will often elicit an account of these attacks when the patient has not mentioned them at first, either because he has forgotten them, or because it does not occur to him that a symptom so remote or so transient can have any bearing on his present trouble. This diplopia is of the highest importance, because it is often the sole complaint when the patient seeks advice for the first time, and because its presence, or a history thereof, is often the deciding factor in the diagnosis of early cases with spinal symptoms. Double vision in a young person should always arouse the suspicion of disseminated sclerosis, and if it is associated with signs of pyramidal tract disease, the combination makes the diagnosis almost certain.

Strabismus is uncommon. Even when the patient is seen whilst complaining of double vision it is unusual to detect any limitation in the range of the ocular movements.

Ptosis is rare.

Nystagmus is present in more than half the cases, but not so frequently as an early sign. It is usually fine, rapid and horizontal, appearing only when the eyes are directed to the side. In some cases the eyes oscillate constantly whatever their position. Except in rare cases, there is no apparent movement of objects, even when the oscillations are of wide range.

Visual failure.—Diminution of visual acuity due to lesions in the optic nerves—*retrobulbar neuritis*—occurs sooner or later in nearly every case. It may precede all other symptoms by a period of several years. As in the case of the other symptoms, it is subject to exacerbations and periods of improvement. A young healthy person complains of rapidly increasing mistiness of vision, usually in one eye, sometimes in both or in one after the other, reaching its maximum in a few hours or days; this is often preceded or accompanied by pain about the orbit, which is increased on moving the eye. In the common unilateral case the signs are those of a lesion in one optic nerve; the pupil on the affected side is larger than its fellow; its direct reaction to light is impaired, but it contracts well consensually. Tests with

a small object, preferably coloured, reveal a central scotoma. At the onset the disk is usually normal, but in a few instances the inflammation reaches the nerve head, in which event the disk is blurred and swollen. Later the disk may be pale or normal. Rapid improvement of vision is the rule. Special tests may reveal a persistent slight loss of visual acuity, and a partial central scotoma, or, very rarely, a complete central scotoma. Subsequent acute attacks are common. In some cases the onset of visual failure is gradual. Usually the defect is slight, but it may be serious, although complete blindness never occurs. In these cases the disk is pale, especially in its temporal portion, and the field shows a central scotoma or narrowing at the periphery.

MENTAL SYMPTOMS.—Defective memory and slight impairment of intellectual power are common. Some of the patients are morose and subject to fits of depression, but the majority are surprisingly cheerful, and do not seem to suffer mentally even when their physical state is most pitiable. In many cases there is considerable loss of emotional control, and ready laughter or weeping is fairly common. More often there is merely a tendency to laugh at trivial things.

SPHINCTER DISTURBANCES.—These troubles arise from interference with the long path in the spinal cord by which volitional consent and inhibition are held upon the act of micturition. Therefore, lack of control in the form of hesitancy and precipitancy are common, and retention may occur. In rare cases, control over the rectal sphincter is lost.

OTHER SYMPTOMS.—Deafness, giddiness and tinnitus, sometimes with repeated vomiting, are common. Epileptiform convulsions are rare. In most instances the distribution of the signs will indicate that the lesions are multiple; but sometimes, although the patches are numerous, the signs are those of a single lesion, say of the internal capsule, of the midbrain or of the cerebellum.

CEREBRO-SPINAL FLUID.—The colloidal gold test may give a weak paretic curve in association with a negative Wassermann reaction. In a few cases the number of cells is increased. Otherwise the fluid is usually normal.

Diagnosis.—The combination of spastic weakness of the legs with "Charcot's triad" of symptoms—namely, intention tremor, nystagmus and scanning speech—which is so widely and so erroneously regarded as characteristic of the disease and as necessary to its recognition, is rarely seen except in the later stages of disseminated sclerosis. As this malady usually presents itself to us in its initial stages, when it may and should be diagnosed, it commonly consists in a group of signs of involvement of the pyramidal tracts: namely, increased tendon jerks, Babinski plantar responses, absent abdominal reflexes, a little weakness of dorsiflexion of one or both feet, possibly also some weakness of flexion of the proximal segments of the lower limbs, and usually a degree of impairment, or loss, of vibration sense over the malleoli. In many cases, this is all we can find, but in an otherwise healthy young adult, it is a syndrome more likely to be due to disseminated sclerosis than to any other pathological process.

Perhaps there may be confirmatory signs, such as a little nystagmus, slight intention tremor or sensory ataxy of an arm; it may be pallor of the temporal half of one or of both disks—a pathognomonic sign. If some or all of

these signs have, as it were, been arrived at after such a fluctuating course as we have seen to be so typical of most cases of disseminated sclerosis, then diagnosis can be no longer in doubt, and it is comparatively seldom that pathological examinations of blood or cerebrospinal fluid are really necessary for this end.

When, after some years, the disease is fully developed it still retains its individuality. The patient is commonly euphoric, there is frequently tremor of the head, and sometimes of the whole body, when the patient tries to stand or walk. The arms are unsteady, the legs spastic and weak—sometimes showing a tendency to pass into the condition of "paraplegia in flexion." There is little sphincter control left, but cutaneous sensibility is commonly almost or quite intact.

At whatever stage disseminated sclerosis comes under observation, a careful inquiry into the history of the illness is important, and to elicit this requires a knowledge of the natural history of this disease as it has been outlined here.

Disseminated sclerosis has to be diagnosed from various diseases, of which we will consider the following:

Hysteria.—The serious mistake of attributing the early symptoms of this relentless disease to hysteria can be avoided by careful examination of the nervous system. Pallor of the disk, absence of the abdominal reflexes, or a distinct difference between them at corresponding points on opposite sides, unequal exaggeration of one or more of the tendon reflexes when compared with their fellows, Babinski's plantar response on one or both sides —any one of these signs alone would render a diagnosis of hysteria untenable.

Compression of the cord.—When the signs in disseminated sclerosis are purely spinal, the diagnosis from *spinal tumour* presents real difficulties. The first may be mistaken for the latter, when the paralysis increases steadily without remissions and is associated with sensory loss extending upwards to a definite level, while the reverse error may be made when the symptoms caused by a tumour are purely motor, or vary in intensity, or are associated with nystagmus.

Friedreich's ataxy.—This may be suggested by the presence of ataxy in a young patient with disseminate sclerosis. The distinction can be made at once, for in the latter disease the tendon reflexes in the lower limbs are exaggerated, whereas they are lost early in Friedreich's disease.

Course and Prognosis.—Despite the remarkable fluctuations which may mark its course, the disease ultimately disables the sufferer and is the cause of his death. Nevertheless, it is important to remember that after the initial outbreak of symptoms, some patients regain normal physical capacity, lose all abnormal physical signs, and lead a normal life for several years. Five, 10 and 15 year periods of this kind are by no means rare, and in general it may be said that the period of evo'ution of the disease is longer than is generally supposed. On the other hand, a few cases run a rapidly downhill course from the onset. The later in life disseminated sclerosis makes its first appearance, the more benign its course, and sufferers may be found who have reached old age without gross or total disablement. Commonly, after two or three fresh exacerbations with intervening recoveries of greater or less completeness, a slowly increasing permanent disability sets in. It is not

possible to say that those cases which run the longest and less distressing course owe this to treatment, for many untreated cases fare relatively well. But there are certain factors which do appear to influence its course unfavourably in most, though not in all, instances; thus, intercurrent illness, especially if it be febrile, injuries which disable the patient for a short period, all surgical interventions—including the therapeutic interruption of pregnancy which is designed to avert the frequently-seen exacerbations that follow the puerperium—and prolonged or recurrent physical exhaustion.

Treatment.—The behaviour of disseminated sclerosis makes the assessment of any mode of treatment extremely difficult, and a failure to appreciate the wideness of its fluctuations and the length and completeness of some of its remissions is responsible for many therapeutic claims that in the hands of those best acquainted with this malady fail to justify themselves. So far, there is no remedy which exerts any constant or certain influence upon the course of the disease.

Arsenic is the remedy which has the longest vogue, and many believe that it is of value, though the present writer has never been able to satisfy himself that this is the case, and has seen severe exacerbations interrupt the course of a series of injections of arsenical preparations.

Nevertheless, and *faute de mieux*, we may prescribe arsenic either by the mouth, as Fowler's solution, or by intramuscular injection of one of the arsphenamine derivatives. In the former case, some begin with a dose of min. 3, which is increased by one minim per dose on alternate days until min. 8 is taken three times daily. The dose is then reduced again to its original level. If this method is used, it is best to stop all arsenic for a week at the end of each complete curve of dosage. Not every patient can tolerate doses larger than min. 3 or min. 4 three times daily. This method is probably as useful as that of intramuscular injection, but considerations of expediency may dictate the use of the latter method.

A more recent suggestion is that of Brickner, who gives quinine hydrochloride in doses of three to five grains twice daily, continued over a long period. Here, again, intolerance may intervene and prevent this. The present writer has used quinine extensively in this way since its introduction by Brickner, and regards it more highly than arsenic. Other recent forms of medication include liver therapy, pyrexial therapy, protein shock therapy, and vaccine therapy. None of these has justified itself in the writer's experience, and when it is recalled that a febrile illness commonly aggravates the severity of disseminated sclerosis, it is scarcely surprising that pyrexial therapy should sometimes have the same result.

The fact that disseminated sclerosis is sometimes—though not always—adversely affected by a confinement has led to the increasing advocacy of terminating pregnancy at the third month to avert this ill effect. But this procedure is exposed to the same objection as a full-term delivery or any surgical procedure, and sometimes has the same unfortunate influence upon the course of the malady. It is therefore not a therapeutic measure that can be justified by its results. The correct procedure is to take every possible measure to maintain the health and nutrition of the pregnant woman, and to afford her at this time and after the puerperium more than the ordinary amount of rest. This is the rational, if not always the acceptable, line of treatment.

Of great importance is the right ordering of the patient's life, when practicable, and the avoidance of fatigue in the early stages of the disease.

JAMES COLLIER.
W. J. ADIE.
Revised by F. M. R. WALSHE.

ACUTE DISSEMINATED ENCEPHALOMYELITIS

Synonym.—Acute perivascular myelinoclasis (Hurst).

Ætiology.—This is unknown. The malady may follow one of the exanthemata, or may develop without any known exciting factor. A form following vaccination first attracted attention in 1922, and later cases have been recorded after measles, smallpox and varicella. It is doubtful if the meningo-encephalitis of mumps belongs to this category. Whatever be the preceding acute specific fever, or if none has preceded the attack, the symptomatology and pathological lesions are the same. It seems unlikely that a filterable virus is responsible, since no neurotropic virus is known that attacks the white matter. All such viruses so far identified have been polioclastic, that is, they attack grey matter only.

The relation of this variety of encephalomyelitis to other demyelinating diseases, *e.g.* disseminated sclerosis and neuromyelitis optica, is uncertain. There are no grounds for assuming that the pathological process has a common cause.

In conclusion, it seems that acute disseminated encephalomyelitis may occur apart from any exanthem, and is entitled to recognition as a separate pathological process with its own clinical picture.

Pathology.—The lesions are widespread throughout the central nervous system, and consist in perivascular foci of softening involving the entire nerve fibre, axis cylinder and myelin sheath. The foci tend to coalesce. There is proliferation of the microglia cells, and some lymphocytic reaction with a secondary gliosis. The lesion of the nerve fibres is probably primary in the myelin sheath. The lumbar cord tends to be more severely hit than higher levels.

Symptoms.—This is charasticteric and uniform. The onset is relatively sudden, and when an exanthem has been present, the nervous symptoms make their appearance at more or less regular times: thus from 10 to 13 days after vaccination, from 5 to 13 days after the appearance of the rash in smallpox, and at the end of the first week in measles.

In most cases the symptoms are predominantly encephalic, but myelitic forms are also seen. In the former case there is a slight rise of temperature, some unsteadiness of gait if the patient is ambulant. Drowsiness soon develops, and there is headache, stiffness of neck and back, Kernig's sign and tache cerebrale. The abdominal reflexes usually disappear and there is disturbance of sphincter control. The state of the tendon jerks is variable. The drowsiness may deepen into coma. At this stage the limbs become flaccid and the tendon jerks abolished. There may or may not be cranial nerve palsies and some œdema of the optic disks. Death may ensue from bulbar paralysis with hyperpyrexia and a terminal broncho-pneumonia. On the other hand, a dramatic recovery may ensue even when the patient

is in this grave state. With survival there is a gradual return to full consciousness.

In the spinal type unconsciousness, if it occur, is short-lived. A severe paraplegia with incontinence of urine and fæces and sensory loss develop. The paraplegia is usually flaccid with loss of tendon jerks at first. The upper limbs may escape or be less severely affected than the lower. Recovery is the rule, but this may be slow and finally incomplete.

Treatment.—There is no specific treatment and the management of the case should follow the lines applicable to any severe and acute paralysis, with special care to avoid bedsores, infection of the bladder, hypostatic pneumonia and wasting.

NEUROMYELITIS OPTICA

Synonyms.—Diffuse myelitis with optic neuritis; Devic's Disease.

Definition.—A form of disseminated myelitis, preceded or accompanied by retrobulbar neuritis, with or without papillœdema. It is commonly acute in onset, and may end in death or in arrest with residual disabilities. Recovery is rare. Persons of all ages from adolescence onwards may be affected.

Ætiology.—Nothing whatever is known of its causation, and therefore it has been suggested that the disease is infective. None of the neurotropic viruses is known to produce the demyelination which is the characteristic lesion of the disease, nor is there any evidence that this is bacterial.

There are points of resemblance to disseminated sclerosis on the one hand, and to Schilder's disease on the other, both in the morbid anatomy and symptomatology of the disease, but there are equally significant points of difference, and whether or not the three are ætiologically related cannot be affirmed.

Pathology.—The spinal cord shows either diffuse or multiple disseminated lesions. They may be confined to a few segments of the cord, or may be found from end to end of this structure. The essential feature of the lesions is a demyelinisation of axis cylinders. There is also round-celled perivascular infiltration, an intense proliferation of microglial cells, and a multiplication of tiny vessels in the affected areas. The optic nerves present the same type of lesion, namely, an intense demyelinisation of the nerve fibres.

Symptoms.—The blindness which indicates the optic nerve lesion may precede or may follow the appearance of paraplegic symptoms. The latter develop rapidly, and may spread upwards until sensory loss and muscular weakness reach the upper thoracic level. Blindness, with some swelling of the optic disc, and central scotoma may ensue. The patient may become progressively worse and die; or the paralysis may become stationary and then proceed to complete recovery of both power and of vision; or the subject may be left with disability of varying severity.

The paraplegia is that characteristic of a diffuse spinal lesion in that there is sensory loss, paralysis, and loss of sphincter control.

Treatment.—No treatment has any clear influence upon the course of

events. Arsenical preparations have been employed—as for disseminated sclerosis. The management of the case is that of any paraplegia.

F. M. R. Walshe.

SCHILDER'S DISEASE

Synonym.—Encephalitis periaxialis.

Definition.—A malady characterised anatomically by a progressive and massive demyelination of the white centre of the cerebral hemispheres, proceeding from a single focus or from two symmetrical foci, and producing the clinical picture of progressively increasing failure of cerebral function, local at first, but advancing in terms of the functions of the contiguous regions which are next affected, by the spread of the disease from its starting-point.

Ætiology.—Nothing is known of the essential nature of the disease, nor is it certain that all cases included under this heading form a homogeneous group. Originally regarded as an inflammatory, probably an infective, disease, the increasing evidence of its familial incidence suggests that it may be primarily degenerative. It has also been suggested that those cases in which an inflammatory reaction is present may be infective, and those in which it is absent—as it may be—degenerative. Many of the reported cases have occurred in childhood, even as early as the second year. The latest case was in the fifth decade of life. The sexes are equally affected.

Pathology.—The characteristic lesion consists of: (1) A primary demyelination and, later, destruction of the axis cylinders of the central white substances of the cerebral hemispheres, which till very late spares the subcortical zone of white fibres and the radial cortical fibres, and produces a translucent jelly-like appearance of the oval centres. (2) A very early and perhaps primary overgrowth of the neuroglia, forming a feltwork, which is particularly intense round the vessels. (3) A general infiltration of the white matter of the brain with round cells, all of which are of neuroglial origin, and most of which are engaged in the removal of altered myelin or in the formation of neuroglial fibres.

The process commences most commonly as a symmetrical patch of demyelination, in either occipital white centres, less frequently in both temporal white centres or in both prefrontal white centres, and spreads directly thence until the whole of the oval white centres becomes demyelinated. The corpus callosum is involved, and the demyelination spreads downwards through the crura into the brain stem. Sometimes, especially in the central regions, the disease starts on one side, and, after playing havoc with the white centre of one hemisphere, spreads across the corpus callosum into the other. The resulting picture of a brain, normal on the surface, and on section with apparently normal cortex and intact subcortical white bands, but with the oval centre completely changed and translucent, is peculiar to this disease. Not infrequently other patches of the disease may be scattered throughout the central nervous system. This scattered distribution and the prominence of demyelination bring Schilder's disease very close to disseminated sclerosis, and it has actually been described as " disseminate sclerosis in childhood " ; but the massiveness and mode of spread of the lesions, together with their distribution, with predilection for the brain and avoidance of the spinal cord,

its incidence in childhood and its entirely different symptomatology, separate Schilder's disease sharply from disseminated sclerosis. It is largely to Collier that we owe the clinical recognition of this malady.

Symptoms.—The clinical aspect is precisely that which might be expected from a progressive destruction of cerebral function, spreading by contiguity from the initial seat of the disease. In many of the cases blindness—by which is meant blindness without any change in the optic disks and with pupils reacting normally to light—has been the first symptom, and is the result of the symmetrical demyelination of the occipital white matter. As the disease spreads forwards into the temporal regions, bilateral deafness appears; and, later, bilateral ataxy and astereognosis—due to parietal involvement, bilateral spastic paralysis—the result of central involvement, and complete amentia—due to callosal and prefrontal involvement, develop.

In those cases in which the initial seat of the disease is in the temporal, central or frontal regions, the first symptom to appear is obviously determined by the location, and the order of development of symptoms will be changed, but the mode of progress is the same in all. Where the disease starts on one side only, hemianopia or hemiplegia is the first symptom, and these are followed by the train of added signs produced by the extension of the disease into other regions. Complete mindlessness and paralysis always dominate the clinical picture in the end. The disease-process within the brain sometimes causes swelling with increase of intracranial pressure, and signs of the latter may appear in the form of headache, vomiting and papill-œdema. Such cases are not common, and most of them have been regarded in life as cases of intracranial tumour. Fits are by no means uncommon. Sometimes they constitute the initial manifestation of the disease, and they may occur at any time during its course, and may be local or general. Fever is usually absent, but there may be irregular pyrexia and some of the more acute cases have been pyrexial throughout. The cerebro-spinal fluid is normal in the majority of the cases, but sometimes there is an increased protein content and a small excess of lymphocytes.

Diagnosis.—The onset with cerebral blindness or with bilateral deafness, followed by signs of progressive cerebral destruction, is so rare in any other disease as at once to suggest the diagnosis of Schilder's disease, indeed no less than two-thirds of the reported cases have shown this picture. When the disease begins unilaterally, and more particularly when headache, vomiting and papillœdema are present, the distinction from intracranial tumour is difficult or even impossible, for in both diseases the local commencement and the progressive destruction occur. In Schilder's disease, however, high-grade papillœdema is not met with, and consecutive optic atrophy does not occur. It should be borne in mind that any locally commencing progressive destruction of the brain may be an example of this malady.

Course and Prognosis.—In most cases Schilder's disease is regularly progressive to a fatal termination. In some, however, periods of stand-still have been noted, while in a few others marked improvement for a time has occurred, as the result of administration of mercury, arsenic and iodides. The duration has varied from 7 days to 36 months, with an average of 9 months.

Treatment.—No treatment is at present known that will influence the course of the disease.

THE PRIMARY CEREBELLAR ATROPHIES

In the present state of knowledge a satisfactory description or classification of the primary cerebellar diseases is not possible. They are extremely rare, and in the recorded cases the nature and the incidence of the pathological change varies so from case to case that in all probability what have been described as distinct "types" are in many cases no more than different stages of a single process.

Of all the primary atrophies of the cerebellum it may be said that their ætiology is unknown, but the cause probably endogenous. In some forms there is clear evidence of heredo-familial factors, but not in all. Some of them appear in early infancy, others in later life. The lesion is bilaterally symmetrical, essentially an atrophy, and in the late cases is slowly progressive.

The most useful working classification is as follows:

(i) Atrophy of the cerebellar cortex.
(ii) Atrophy of the central white matter of the cerebellum.
(iii) Atrophy of the spino-cerebellar tracts.

Of these the least rare is Friedreich's ataxy, in which there is also a lesion of the posterior column fibres, but nevertheless this disease is most conveniently dealt with here.

(i) *Atrophy of the cerebellar cortex.*—This may be total, or may be confined to particular cortical regions. It may be found as a post-mortem discovery in idiots dying in infancy, or may develop slowly in middle-aged or elderly persons (Marie's delayed cortical atrophy). The last-named form is most marked on the upper anterior parts of the cerebellum. There is a characteristic loss of Purkinje cells. The clinical picture is that of a slowly developing ataxy of gait, severe disorder of articulation, and later ataxy of the upper limbs. Nystagmus is rarely present.

(ii) *Atrophy of the central white matter of the cerebellum.*—This is commonly known as olivo-ponto-cerebellar atrophy, and is characterised by a severe loss of nerve fibres in the central white matter, with a secondary proliferation of glia fibres and nuclei, the cortex being relatively intact. In addition there is degeneration of the pontine nuclei and their fibres (middle cerebellar peduncles) and of the olives. This also is a slowly progressive lesion of middle-aged and elderly persons, occasionally familial in incidence. It can only with difficulty be distinguished clinically from cortical atrophy, except when it is accompanied by Parkinsonian symptoms or by dementia, as is sometimes the case.

Scherer has found that a similar type of lesion is constantly found in the substantia nigra and corpus striatum in these cases, and when severe is responsible for the Parkinsonism sometimes observed. Similarly, focal atrophy in the cerebral cortex may be present, and may account for the dementia which may be present. Scherer suggests that all these changes have the characters of a focal, premature senile change, and points out that the lesions of Pick's focal atrophy and Huntington's chorea also belong to this category.

(iii) *Atrophy of the spino-cerebellar pathways.*—A rare form is the so-called spino-cerebellar ataxy, which may vary in its clinical expression from a con-

genital tremor, to gross ataxy of all four limbs, accompanied in some cases by optic atrophy, and ocular palsies. The lesion is a degeneration, falling most severely upon the dorsal-spino-cerebellar tract and less severely upon Gowers' tract and upon Clarke's column. It is a malady of children and adolescents.

More familiar is Friedreich's ataxy, which is described below under its own heading.

1. FRIEDREICH'S ATAXY

In addition to the slow, clumsy ataxy, Friedreich's type is characterised by the absence of the knee-jerk and other deep reflexes, and by the presence of the extensor plantar response and of contractures, especially in the form of pes cavus, and by the presence of curvature of the spine in the later stages of the disease.

Ætiology.—The first signs of the disease usually appear in early childhood and before the sixth year; but symptoms may not be evident until a few years later. In a considerable number of cases, however, the onset is delayed until the time of puberty, while in a few examples the onset may be delayed until after the age of thirty years. As a rule the age incidence is approximately the same in each child-rank of the same family; but sometimes the phenomenon of "anticipation" is well marked, the disease appearing at an earlier age in each succeeding generation as a whole, or in successive children of the same parents. The disease is said to be slightly more common in males. Isolated cases in which no heredity can be traced are not rare. Indirect heredity is the most common, for the reason that the subjects of this disease are usually afflicted in childhood and incapacitated by the time adult life is reached, and that they therefore do not procreate. Transmission occurs both through the males and through the females. Direct heredity is, however, by no means so uncommon as has been supposed, and in one family under my observation the disease had been transmitted from father to son for seven generations.

Pathology.—The spinal cord is unusually small, and apparently this smallness may be congenital, and the posterior roots tend to be small, grey and poorly myelinated. The essential change is a primary degeneration of certain neurones in the dorsal column of the spinal cord, of the pyramidal tracts and of the spino-cerebellar tracts, both dorsal and ventral. This degeneration commences first in the periphery of the axon, which slowly dies back towards the nutrient nerve cell, as the branches of an aged tree tend to die back towards the trunk.

The degeneration of the dorsal columns is usually the earliest change, and remains the most prominent feature throughout. The degeneration of the fibres of the pyramidal tract appears later. It has its origin in the ascending frontal convolutions, where atrophy and disappearance of the giant pyramidal cells have been shown.

The spino-cerebellar tracts are constantly degenerated, the direct cerebellar tract being the most seriously involved. The cells of Clarke's column, from which the direct cerebellar tract takes origin, and around which the pyramidal tracts end, degenerate and disappear, as does also the network of collaterals which surrounds these cells. Consequent upon these degenerations, and secondary to them, well-marked neuroglial proliferation or sclerosis

occurs. The cerebellum may be normal, or it may show varying degrees of atrophy of Purkinje's cells, or of any other of its cell elements, and of the tracts connected therewith.

Symptoms.—The onset is always insidious, and physical signs of abnormality usually precede any complaint on the part of the patient or his relatives. The first symptoms generally appear between the sixth and the tenth year of childhood; but if a careful examination be made of the younger members of the families upon which Friedreich's disease is incident, physical signs of the disease, especially the extensor response in the plantar reflex, the retraction of the great toe and some degree of pes cavus may often be found before the sixth year. Not infrequently the onset of symptoms does not occur until puberty, and in some families it is delayed until after the age of 30 years.

Ataxy is always the first sign to appear, and this is shown by an awkwardness of gait and a tendency to stumble and fall readily. Sometimes it is obvious from the history, that the ataxy dates from the earliest years of infancy when it is said that the child was never strong on his legs from the time of learning to walk, and that he could never run properly or join on equal terms with other children at play. As the disease progresses, the gait slowly becomes more irregular and clumsy. The patient walks with his feet upon a broad base, and staggers and reels from side to side; but, notwithstanding this, he keeps a fairly direct line of progresssion. He takes short steps which are unequal, and which are irregular in relation to the line of progression, and the movement of each foot as it is raised is poorly coordinated. There is never the undue excursion and noisy stamping of the feet which are so characteristic of the gait of tabetic patients.

In standing the body oscillates from side to side in slow and clumsy fashion, and coarse tremors of the head and trunk are constant features in advanced cases (titubation). Sometimes Romberg's sign is present; but this is never so well marked as in tabes, and it is frequently absent. The ataxy invades the upper extremities, as a rule, later than the legs. There is first clumsiness with the finer movements, and then little by little with all the movements. It closely resembles the ataxy due to gross disease of the cerebellum, and differs from that which occurs in tabes, and that irregular breaking of a movement towards the end of its accomplishment, which has been long termed "intention tremor," is frequently seen.

Very characteristic of the disease, and highly important in diagnosis, is the occurrence of irregular involuntary movements, which are often described as like those of chorea or of myoclonus. They differ entirely, however, from the movements of chorea, etc., in that they occur only when the limb or some of its segments are unsupported. In advanced cases such movements are constantly seen in the head and neck as nodding movements and tremors, and in the trunk as swaying instability, when the patient is sitting unsupported or standing. Similar ataxy and irregular movements affect the muscles of the eyes, of the face, tongue, larynx, etc., and the respiratory muscles. In the eyes they are seen as fine, regular nystagmus and as coarse, irregular jerkings, chiefly upon lateral deviation. There is no other disease in which ataxy of the facial muscles is so conspicuous for, in engaging the patient in conversation, all the facial muscles may be observed in irregular contraction. The ataxy of these muscles causes an invariable impairment

of articulation, which gradually becomes indistinct, clumsy, drawling and slurred. The syllables tend sometimes to be separated, adding a staccato element. Explosive utterance is almost constant, and from the irregularity of the respiratory movements short inspiratory whoops are not uncommon. Articulation thus closely resembles that of advanced disseminated sclerosis, the cause being identical in the two diseases, namely, interference with the cerebellar co-ordinatory mechanism of speech.

The strength of movements is at first little impaired; but as the disease advances and the pyramidal degeneration increases, the power is gradually lost in proportion to the degree of the pyramidal degeneration, which varies greatly in different cases. The lower extremities are affected first and most, and later the arms, and in severe cases at a late stage paralysis may be almost universal.

The condition of the muscular tone depends upon the relative degree of degeneration in the posterior roots and in the pyramidal tracts respectively, the former tending to abolish and the latter to increase it. As a rule the influence of the posterior root degeneration is preponderant and, therefore, the limbs are flaccid and hypotonic, but occasionally they are somewhat rigid. Contractures are the rule, but these are confined to the lower extremities. The most constant of these produces the deformity of the feet characteristic of Friedreich's disease, and known as "pes cavus." The great toe is strongly retracted, the tarsus is pulled up, and the metatarsus is dropped and the plantar arch is increased. The outline of the inner border of the foot comes to resemble the letter Z, the tarsus, metatarsus and great toe forming the three limbs of the Z. Sensibility is but little affected; but in most cases minute examination reveals slight relative loss to touch, pain and temperature, most marked at the periphery of the limbs and diminishing upwards. Similarly there may be slight loss of sense of position in the limbs, with diminution of osseous sensibility to the slowly vibrating tuning-fork.

The ocular movements are almost always intact apart from the already described nystagmus. In rare instances strabismus, diplopia and ptosis have been recorded. The pupils are not affected. Optic atrophy is a rare phenomenon in Friedreich's disease, yet it has been reported in quite a number of otherwise typical cases.

Mental symptoms are usually not conspicuous, but some of the patients are of poor mentality from the first, while others show a tendency to severe mental degeneration in the later stages of the disease. Emotional instability, irritability and outbursts of temper may occur.

Absence of the tendon reflexes is a most characteristic feature, and is often the first objective sign of the disease. When one considers, however, that the absence or presence of the tendon reflexes depends upon the relative degree of affection of the posterior columns upon the one hand, and upon the pyramidal degeneration upon the other, it is not surprising to find in cases where there is a major degeneration of the pyramidal tracts, that the knee-jerks may persist or even be brisk into the advanced stages of the disease. The abdominal reflexes gradually disappear. The plantar reflex is invariably an extensor response. The sphincters usually escape. The cerebro-spinal fluid presents no abnormality.

Spinal curvature is very common, and may reach a severe degree. It consists of a scoliosis of the dorsal region, and often with some kyphosis, and

with a compensatory reverse lumbar curve. The cause of this deformity is probably the defect in the postural tone of the muscles, which occurs when the afferents subserving the function of postural tone, and which are contained in the spino-cerebellar tracts, are severed.

Diagnosis.—In uncomplicated cases the diagnosis is a matter of no great difficulty on account of the strikingly distinct nature of the symptoms. Friedreich's disease can hardly be mistaken for tabes, since the history of heredity, the peculiar deformity of the feet and spine, the extensor response, the speech affection and the nature of the ataxy contrast strongly with the loss of pain sensibility and of deep sensibility, the pupillary changes, the sphincter trouble, the abnormal Wassermann reactions and the abnormal cytology of the cerebro-spinal fluid in tabes. The distinction from disseminated sclerosis presents more difficulty; but in this disease the onset never occurs in childhood, there is no heredity, the deep reflexes are never lost, and the spinal deformity does not occur.

Course and Prognosis.—The course of the disease is usually progressive in slow and irregular fashion, and the prognosis is therefore in every case serious; but the average duration of the disease is over 30 years, and in some cases it seems to have no tendency to shorten life. The prognosis is worse and the course more rapid in those patients who have shown disability from the time of learning to walk. In some cases the disease appears to become arrested, as, for example, in one family which came under my observation, twelve members in three generations were affected with typical Friedreich's disease, yet none of them was incapacitated from following a normal life, and those that were deceased had all survived the age of 70 years. Intercurrent maladies, febrile illnesses and debilitating influences generally, may have a strong effect in hastening the advance of the disease, and bringing about a fatal termination. Confinement to bed from any cause whatever has a most derogatory influence upon the ataxy, and upon the capacity for walking. It is therefore of great importance that these patients shall be kept off their legs as little as is possible. Cases in which the ataxy becomes extreme, or in which paralysis from pyramidal degeneration becomes severe, necessarily become bedridden, and in this condition the patients may survive for many years. In other cases rapid increase of the symptoms of degeneration within the nervous system is followed immediately by drowsiness, asthenia and coma, and death ocurs in that peculiar toxic state which is commonly the end-result of all degenerative nervous diseases.

Treatment.—No treatment is known which specifically affects the malady. General tonic treatment, and all measures which improve the general health and mental well-being, often have a surprising effect in improving the ataxy. Re-educational training of the limbs and trunk in the form of Frænkel's exercises are most beneficial. Properly designed boots to ensure the most advantageous use of the deformed feet must be provided.

2. FAMILIAL SPASTIC PARALYSIS

This malady is here described with the hereditary ataxies, since it seems to fall naturally into the group of diseases in which primary degeneration of the pyramidal tracts is a usual anatomical feature, and of which a familial and hereditary incidence is the rule. Moreover, among the hereditary

ataxies every grade of transition is seen to the type of pure familial spastic paraplegia. Whilst in the majority of the hereditary ataxies cerebellar, spinal and cerebral lesions coexist, yet there are the purely cerebellar and the purely spinal type; and the purely cerebral type, in the form of familial spastic paralysis, forms a natural end to the series.

Ætiology.—The disease is sometimes hereditary, but is more commonly familial and incident upon several children of the same parents. Sporadic cases are not very rare. The onset is gradual in early life, and usually occurs after the sixth year.

Pathology.—The pathological changes consist in a primary degeneration of the pyramidal neurones which apparently takes place in terms of the length; those supplying the lumbo-sacral region, being lower and longer, are earliest affected; those supplying the brain stem, being shortest, are the last to be affected. Degenerative changes in the neurones of the posterior columns of the spinal cord are often present, showing the transition to the pathological type of the hereditary ataxies.

Symptoms.—The clinical aspect consists in the slow development of spasticity and weakness, first and most in the legs, which gradually increases and progresses to the trunk and upper extremities, and involves the face last and least. The usual signs of pyramidal involvement are present in the loss of abdominal reflexes, increased deep reflexes and extensor type of plantar reflex. The malady is progressive, increasing to complete paralysis, and in its course contractures of the spastic muscles occur, that of the foot and leg producing some degree of pes cavus, while, above this, flexor contracture at hip and knee is met with. Optic atrophy is by no means uncommon. Mental symptoms do not occur in uncomplicated cases, neither is epilepsy observed.

Diagnosis.—This malady is most easily confused with cerebral diplegia; but the latter disease appears much earlier, so soon after birth, in fact, as defective movement in the child can be ascertained. Further, cerebral diplegia is not a progressive disease in the majority of the cases, and it is often associated with mental deficiency and recurring convulsions.

PARALYSIS AGITANS

Synonym.—Parkinson's Disease.

Definition.—A progressive disease of insidious onset and slow course, usually occurring in the second half of life, and characterised by a peculiar stiffness of the muscles, which tends to fix the body in a certain posture, which can be changed less speedily than in health, and which gives rise to a distinctive facial expression, bodily attitude and gait. The stiffness is accompanied by weakness, and often by rhythmic tremors, which have earned for this malady the name "shaking palsy."

Ætiology.—Little is known of the causal factors of this malady. It is essentially a disease of the decline of life, and though in rare instances it is met with as early as the eighteenth year, the maximum incidence is from the fiftieth to the seventieth year. Men suffer twice as frequently as women. Heredity seems to play no part in the causation; but it is remarkable that longevity in one or both parents is common.

Pathology.—No naked-eye changes are to be found other than the vascular and degenerative changes which are common in senile conditions. The facts that tremors and rigidity, almost identical with those of this disease, may be met with in tumours involving the substantia nigra of the crura cerebri—two striking cases with autopsy having been under my own care—and still more importantly, the frequent appearance of a paralysis agitans-like end-result in lethargic encephalitis, where the subthalamic region and substantia nigra are conspicuously picked out by the lesions, make it probable almost to a certainty that the locus morbi of paralysis agitans is the basal ganglia.

Symptoms.—The onset is always insidious, and the muscular rigidity is almost always the first sign to appear. This rigidity affects the face, neck and trunk to a greater extent than the limbs, and when the limbs are affected then the proximal muscles present a greater degree of rigidity than do those of the periphery. The oncoming rigidity of the facial muscles does away with the usual play of the emotional movements in facial expression, and the face assumes a fixed, anxious and mask-like expression, with absence of the usual involuntary nictitation. The voice loses its inflexions, and becomes monotonous, from rigidity of the muscles of larynx, tongue and lips; but there is no other defect of articulation. Very striking is the effect of the rigidity of the muscles of the neck, for the patient carries his head and neck in one piece with his trunk as if he were a statue, never inclining or raising it in the customary expressive manner, and if he turn round to look at anything he tends to move the whole trunk round with the head. In looking sharply to one side the eyes move before the head, whereas, under normal circumstances, the coarse adjustment of this movement is done first by the neck muscles, and the fine adjustment subsequently by the eye muscles. The stiffness of the trunk muscles gives a stooping attitude with the head inclined forwards, while that of the upper extremities causes the shoulders to be rounded, and the arms carried with the elbow semiflexed, and pressed into the sides. The gait is highly characteristic in marked cases since, on account of rigidity of muscles, it is deprived of spring and suppleness; the patient, in the characteristic attitude above described, takes small gliding steps, displacing his centre of gravity as little as possible. If, by any circumstance, such as catching the feet against an unevenness of the ground, or a push, the centre of gravity is much displaced, the patient often has a difficulty in regaining it, and in moving to recover his centre of gravity is unable quite to catch it up, and so continues the movement of necessity until he fall or come in contact with some object by which he can arrest himself and restore his balance. This phenomenon is more often seen in advanced cases, and is known as "propulsion," "retropulsion" and "lateri-pulsion," according as the centre of gravity is displaced and the movement occurs in a forward, backward or sideways direction. Festination is the term used for the quickening of the pace sometimes seen in this attempt to overtake the displaced centre of gravity. In the hand the rigidity is greater in the interosseal muscles, and the hand therefore tends to assume the "interosseal position" with the fingers pressed together and the thumb adducted, the metacarpophalangeal joints being flexed, and the interphalangeal joints extended. From this rigidity of the hand the writing becomes small as well as tremulous, and the patient finds it difficult to write in a straight line. Muscular weakness always accompanies the rigidity and the tremors. It is slight until the late

stages of the disease, when it may increase rapidly and render all useful movement impossible. On account of the rigidity and consequent slowness of movement, the sense of weakness which the patient experiences is much greater than the actual weakness as tested by the dynamometer. Tremor is present in the majority of cases. It usually commences in the hand and forearm, and is most conspicuous in this situation; but it may be seen in the face, tongue, jaw, neck and feet, while, in rare cases, it may be universal. The nature of the tremor is peculiar, and is highly characteristic. It is a regular rhythmical contraction of the muscles, alternating in the opposing groups with a frequency of from four to six oscillations per second with a range of from an $\frac{1}{8}$th to $\frac{3}{4}$ths of an inch. Its rhythmic nature, its slowness and its course range distinguish it from other varieties of tremor. In the hand the characteristic movement of the tremor is the rolling together of the opposed thumb and fingers, cigarette-rolling, bread-crumbling or drum-tapping movement. There is nearly always in addition a peculiar pronator-supinator tremor. The tremor is increased by excitement and by self-consciousness, and ceases during sleep. A highly characteristic feature of the tremor in about one-half of the cases is that it continues during repose, and is temporarily arrested by the execution of volitional movement. In the other half of the cases, however, the tremor appears or is increased on voluntary exertion, and tends to be less during repose. There seems to be an antagonism between the tremor and the rigidity, for in cases where the rigidity is very conspicuous the tremor is little marked or absent, and conversely, when tremor is universal or is of early onset, rigidity is a less noticeable feature.

Other symptoms of the disease which are very commonly complained of are—(1) difficulty in turning over in bed, which is the obvious result of the rigidity of the trunk muscles; (2) flexion of the toes into the sole of the foot, so that they are trodden on, from spasm of the plantar muscles; (3) pain of a dull aching character in the trunk and limbs, which is presumably produced by the long-continued traction of the rigid muscles upon their attachments; (4) abnormal sensations of heat and cold; and (5) hypersensitiveness to changes of temperature—the patient cannot bear to be near a fire nor yet in a cold room. Mental symptoms are conspicuous by their absence, except in the last stages of the malady, when profound asthenia overtakes both mind and body. The constant bodily discomfort, restlessness, sensations of fatigue, which the rigidity and the tremors engender, and the consciousness of a malady which is found only too soon to resist every effort to lessen or arrest it, often result in gloomy and lasting mental depression. Objective sensibility is unimpaired. The special senses and the cranial nerves are not affected. The sphincters and the reflexes are normal. Trophic changes in the periphery of the limbs, thinning and glossiness of the skin, with fluted nails and vasomotor disturbance, are common. Bed-sore is commonly met with in the late stages of the malady.

Diagnosis.—There are three points which can be surely relied upon to render the diagnosis of paralysis agitans certain in every case, namely—(1) the aspect of the patient when he is walking, when the fixed mournful expression, the stooping attitude with round shoulders, the elbows pressed into the side, and the hands carried across the abdomen in the interosseal position, the immobility of the head and neck, and the curious gliding gait which cannot fail immediately to arrest the observer's attention; (2) the rhythmic rolling

tremor which is quite unlike any other form of tremor, and which often continues during rest; and (3) the absence of any of the usual signs of organic disease of the central nervous system. Difficulty may perhaps be experienced when the aspect is little marked, and the tremor is confined to some unusual situation, such as the face, tongue or neck; but, if the possibility of tremor in any situation being that of paralysis agitans be borne in mind, its rhythmic rolling nature will give the diagnosis. When paralysis agitans is confined to one side of the body, the appearance of the patient may superficially resemble that of hemiplegia; but in these cases the peculiar aspect of paralysis agitans is marked, and the organic signs of hemiplegia, such as the extensor response in the plantar reflex, the increase in the deep reflexes, and the absence of the abdominal reflex upon the paretic side are not present. In senile tremor the rhythmic rolling quality is absent, and the aspect is not that of paralysis agitans. In post-hemiplegic tremor the organic signs of hemiplegia are present. Toxic tremor is irregular and never rhythmical, and is (mercurial tremor excepted) a fine tremor. The intention tremor of disseminated sclerosis, cerebellar disease and lesions of the red nucleus are so peculiar, and so widely different from the tremor of paralysis agitans, as to render confusion impossible.

The one clinical condition, which may so closely resemble paralysis agitans as to be superficially indistinguishable, is a not uncommon end-result in lethargic encephalitis, where from a lesion in the basal ganglia the same weakness, rigidity and tremors appear as occur in paralysis agitans. The distinction is not difficult, for the onset of lethargic encephalitis is usually acute, and the symptoms are definite. Moreover, the paralysis agitans-like syndrome of lethargic encephalitis sometimes shows a progressive amelioration, whereas paralysis agitans tends to a progressive downward course. The following features present in post-encephalitic Parkinsonism but absent in true paralysis agitans are of value in making a differential diagnosis: (i) a fluttering tremor of the closed eyelids; (ii) tremor of the protruded tongue; (iii) defect of convergence and of accommodation; and (iv) excessive salivation.

Course and Prognosis.—Paralysis agitans often begins in one limb, usually the upper, and spreads thence to the corresponding limb of the opposite, or to the other limb of the same side. In the latter case it has approximately a hemiplegic distribution, and it may remain for years much more evident upon one side of the body. The course is slowly progressive with variable rate. In some cases the malady may remain stationary for years, and this is more often seen in middle-aged subjects, before the disease has reached an incapacitating stage. Such arrest in the early stages is not often seen in young subjects, for in the latter the disease seems to take a more continuously downhill course. Real improvement in the symptoms is never seen. A fatal issue may occur in as short a time as two years; but this is exceptional, since paralysis agitans has little tendency to shorten life. The average duration is from 10 to 15 years, and since the major incidence of the disease is in the sixth decade of life it will be seen that many of the patients are of average longevity. Death may occur from intercurrent maladies, especially from bronchitis; but more commonly, after the lapse of many years, the patient becomes bedridden from increasing weakness and rigidity, and sinks into a condition of sleepy asthenia which is soon terminated by coma. An unduly

high blood-pressure is unusual in the subjects of paralysis agitans, and it is noteworthy that they do not suffer from gross cerebral vascular lesions, such as thrombosis or hæmorrhage.

Treatment.—Paralysis agitans is one of the least tractable of maladies even as regards the relief of symptoms. Hygienic measures and tonic treatment, calculated to lessen the rapidity of the degenerative process, should be employed. Where there is much rigidity, gentle exercise, passive movements and massage are useful. Care should be taken to avoid the falls which the unstable gait is likely to engender, since these are often followed by a marked exacerbation of the symptoms. Pain is best treated with aspirin, and sleeplessness with a mixture of aspirin and small doses of barbitone (grs. 2 and 3). As might be expected, electrical stimulation of the muscles tends to aggravate the tremor, and even in the predominantly rigid cases can do no good. In the latter type of case, some subjective relief may be obtained by the administration of tincture of stramonium or of belladonna (doses of from 5 to 20 minims), or of hyoscine hydrobromide (grs. $\frac{1}{200}$ to $\frac{1}{100}$ by mouth thrice daily in chloroform water). These drugs may render movements freer, but they have no influence upon the tremor. When the patient is bedridden, great care must be taken with the skin, since the immobility of the trunk greatly increases the liability to the formation of bed-sores.

HEPATO-LENTICULAR DEGENERATION

Synonyms.—Progressive Lenticular Degeneration; Wilson's Disease.

Definition.—A rare progressive disease of the nervous system, often familial, characterised by involuntary movements, rigidity and hypertonicity, with contractures, without signs of pyramidal disease; and by dysarthria, dysphagia, emotionalism and progressive emaciation. Several closely related clinical forms of the disease bear distinctive names: *tetanoid chorea* (Gowers), *pseudosclerosis* (Westphal), *progressive lenticular degeneration* (Wilson), and *torsion spasm*, and *dystonia musculorum deformans* (Thomalla). Cirrhosis of the liver occurs in all forms. The Kayser-Fleischer zone of corneal pigmentation occurs in the first three forms, but has not yet been recorded in torsion spasm. The most constant nervous lesions are found in the corpus striatum.

Ætiology.—The disease often occurs in children of the same parents, but there is no evidence that it is congenital or hereditary. The age of onset has been as early as 7 years and as late as 26 years. The primary and essential lesion is in the liver; its cause is unknown. Syphilis is not a factor.

Pathology.—A multilobular cirrhosis, with "hobnail" liver, is always found after death. There is good evidence that the cirrhosis is not slowly progressive, but is the result of a number of attacks of acute hepatitis. The hepatitis has caused death in some members of affected families before nervous symptoms appeared. The nervous lesions are purely degenerative. In Wilson's case they were almost confined to the lenticular nucleus, especially the putamen. Every degree of degeneration was seen, from discoloration and sponginess of the nucleus in rapidly fatal cases, to shrinkage and atrophy, and even to complete disintegration and excavation of the ganglion. Later observers have described lesions in many other parts of the nervous system. The lesions are often most intense in the corpus striatum, but the noxious

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agent has no strictly selective action on any one anatomical group of ganglion cells, or on any limited area of the nervous system.

Symptoms.—In many cases there are no symptoms of disorder of the liver during life. In other cases an account is obtained of symptoms referable to acute hepatitis before the onset of nervous symptoms—attacks of diarrhœa and vomiting, pyrexia, jaundice, migrainous headaches, hæmatemesis and sometimes definite ascites.

The first nervous signs to appear is usually involuntary movement of the extremities, which may be of several kinds. In progressive lenticular degeneration, rhythmical tremors, increasing on voluntary movement, furnish the most common symptom. This is followed by rigidity of the face, the muscles of the neck, and later of the trunk, which rigidity increases steadily until the patient becomes helpless. The rigidity of the face and neck muscles gives rise to a peculiar expressionless appearance. Still later, extensive contractures, usually in the flexed position, in the upper and lower extremities, follow; but sometimes there is extensor contracture of the latter. During sleep the tremors cease, but the contractures do not relax. Dysarthria, of a slurring type, results from affection of the muscles of speech, and may end in complete anarthria. Progressive muscular weakness and general emaciation follow; and the patient becomes emotional, facile, docile and childish. There is no fibrillation or localised amyotrophy. The optic disks and pupillary reactions are normal. There is an absence of nystagmus, cerebellar symptoms, and impairment of sensation. The reflexes are not altered, as in the case in pyramidal disease.

Prognosis.—The disease always ends fatally in a few months or years; the average duration is about 4 years.

Treatment.—None is known to have any effect upon the course of the disease.

JAMES COLLIER.
W. J. ADIE.
Revised by F. M. R. WALSHE.

KERNICTERUS

Definition and Ætiology.—A yellow pigmentation of certain of the basal ganglia, associated clinically with motor disorders of the type known as extra-pyramidal, and found as a rare phenomenon in children who, normal at birth, develop jaundice within the first three days of life.

In neonatal jaundice the brain may be diffusely pigmented, or more rarely the pigmentation may be confined to the putamen, subthalamic and dentate nuclei, the cornu Ammonis and fascia dentata. To the latter variety of jaundice of the brain the name "Kernicterus" has been given by Schmorl. The nerve cells in the affected masses of grey matter show evidence of destruction and degeneration, while the nerve fibres are demyelinated.

Symptoms.—The child is healthy at birth, but within a few days develops intense jaundice, usually the form known as icterus gravis neonatorum, though kernicterus has been found in association with septic jaundice. The onset of jaundice is followed within 24 hours by tonic and clonic movements, muscular rigidity and opisthotonos, alternating with periods of flaccidity.

If the child survive, within a few weeks involuntary movements of choreo-athetoid form develop. Emotional instability and mental retardation appear as the child grows older.

Prognosis.—The cases so far identified and on record are too few to allow of any generalisation as to the expectation of life of the subjects of this malady, but in two cases recently reported by Greenfield, one patient died at the age of three months, the second at nine years.

Diagnosis.—Athetosis and comparable forms of involuntary movement are not rarely seen in children, and are in the majority of instances not associated with kernicterus. Yet when a case of such motor disorder is seen in a child in respect of whom there is a history of neonatal jaundice, the possibility of this disease should be borne in mind. Again, the development of marked symptoms of organic nervous disease immediately after the appearance of severe jaundice in a newly-born infant should lead to a consideration of this condition as the probable pathological basis.

Treatment.—There is no evidence that the condition is susceptible to any mode of treatment.

F. M. R. Walshe.

EPILEPSY

Synonym.—Idiopathic Epilepsy.

Definition.—A condition characterised by suddenly occurring disturbances of cerebral function, prone to occur over long periods of time or even through life. Of the intimate nature of the disturbance all we know with certainty is that a series of characteristic changes in the normal electrical activity of the cortical nerve cells accompanies it. The clinical forms of the disturbance suggest that this involves both loss and release of function in various regions of the brain.

Ætiology and Pathology.—Few problems in medicine have been more obscure, or more provocative of speculation and of controversy than the nature of epilepsy. It has been widely assumed in the past that there is an idiopathic epilepsy, a definite and often heritable disease, with an individuality and natural history of its own, and one of which the characteristic and often the sole expression is the fit.

On the other hand, it has also long been realised that fits clinically indistinguishable from those of idiopathic epilepsy may occur in the course of many and diverse affections of the brain, as, for example, in certain inflammations, degenerations, intoxications and also in association with new growths. Such fits have been placed in a category of symptomatic epilepsy, the relation of which to the idiopathic variety never admitted of clear formulation.

These facts have led some writers to maintain that epilepsy is no more than a symptom, one expression of many and diverse neuro-pathological processes, and because of this manifold causation they prefer to speak of "the epilepsies." Against this view it may be urged that not one of these pathological processes is necessarily, or even commonly, productive of fits and may occur without their development. Such processes cannot therefore be wholly or even primarily responsible for the fits that may, upon occasion,

accompany them. As the late Kinnier Wilson, a strong supporter of the purely symptomatic nature of epilepsy pointed out, "The fit, the fundamental symptom of epilepsy, has no histopathology." In this statement we see that the fit has become a symptom of a symptom. Again, he stated, "The number of epilepsies for which no cause other than that of inherent irritability can be discovered is being steadily reduced." This pronouncement speaks in favour of a unity rather than of a diversity in epilepsy.

It is probable, therefore, and the evidence about to be stated supports the suggestion, that the fit, and the tendency to its recurrence that we call epilepsy, owe their production to some abnormal quality of structure or of function in the brain, and that the many pathological processes that may give rise to fits—as incidental but not essential phenomena—are no more than secondary and contributory factors capable of fit production in the susceptible brain alone. Yet even if there be but a single essential factor common to all fits, it still remains practically useful, if not necessary, to speak of an idiopathic and a symptomatic epilepsy. For purposes of diagnosis, prognosis and treatment the distinction is clearly important. We must separate the two, for example, when we proceed to generalise as to the heritable qualities of epilepsy, and the treatment of a case of uræmia with fits is clearly widely different from that of a case of idiopathic epilepsy. This distinction still allows us to suppose that in idiopathic epilepsy the "fit threshold" of brain, as Lennox expresses it, is so low that the ordinary activities of life and very minor fluctuations in bodily health are sufficient to fire off a fit; while in what we call symptomatic epilepsy, the threshold is higher and is only crossed when some gross superadded disturbance of the brain—of wholly independent origin —is superadded.

The general point of view thus summarised finds a considerable measure of support in the recent researches of Lennox, Gibbs and others upon this subject. They have employed an instrument known as the electro-encephalograph which promises to do for the brain what the string galvanometer of Einthoven has done for the heart. It was originally observed by Berger (1929) that regular oscillations of potentials of a rhythm of 10 per second could be detected if electrodes applied to the scalp were led off to a recording instrument. This work has since been confirmed and very considerably amplified by Adrian in this country and many other observers. It is known that these oscillations, or, as they are called, brain potentials, are due to the electrical activity of cortical nerve cells. The various rhythms, and their sources in the cortex, that come within the normal range of variations in the healthy subject have been studied, and it has subsequently been found that in the epileptic subject these rhythms undergo characteristic variations during the course of the fit. These observations may be summarised as follows (Lennox): Every fit is accompanied by a disturbance of the normal electrical activity of the brain. The three main types of fit have distinct forms of altered rhythm, the distinguishing feature being the frequency of the waves. In the major fit the waves are abnormally fast; in the minor fit they are alternately fast and slow; while in the so-called psychical fit the waves are slow. The pattern for each patient is apt to show individual peculiarities which repeat themselves in successive fits.

The electro-encephalograph also records fits which are clinically invisible ("subclinical") and abnormal variations of rhythms in epileptic subjects may

be found during the intervals between fits. These electrical changes are found alike in "idiopathic" and in "symptomatic" fits, and afford further evidence in favour of a unity in epilepsy rather than of a number of "epilepsies."

Lennox suggests that epilepsy may, therefore, be regarded as expressing a defect in the rhythm-regulating mechanisms in the brain, or in other words as a "paroxysmal cerebral dysrhythmia." He also suggests that the cause of epilepsy is never single, that there is a fundamental cause; namely, an inherent instability of the brain, and a secondary or contributing cause. Of such there are probably very many, and it is the combination of the two that evokes the fit. It should be borne in mind, however, that we can say no more with certainty than that these variations in cortical electrical rhythm accompany the fit. We may not in the present state of knowledge say that they cause it, and the search for the factor or factors productive of the electrical disturbance remains for the future.

This brings us to a consideration of the many factors that in the past have been held responsible for the production of fits. These do not demand or deserve any detailed discussion, for they are predominantly speculative and have always lacked confirmation, either pathological or biochemical. Disturbances of metabolism, of endocrine function, and of acid-base equilibrium have all been invoked. Yet research has failed to find any constant or characteristic disorder of protein, fat or carbohydrate metabolism, or of endocrine function of any kind, nor have studies of the blood in respect of its cellular or chemical composition been other than negative. The uncertain influence of metabolic and endocrine disorders, when these are manifestly present, in the production of fits tend to strengthen the growing view that none of these factors plays any but a secondary and contributory rôle in the malady. There are, on the other hand, certain well-known clinical features of epilepsy that have in the past been deemed to point to the importance of some metabolic variations in exciting fits; thus, the increased incidence of fits in women at the time of the katamenia, and their common cessation during pregnancy have been noted in this connection.

The features of the fit suggest that the functions of the affected regions of the brain may be disordered in several ways, by suppression, as, for example, in the blunting or loss of consciousness which is probably the most constant and invariable feature of epileptic fits of all kinds, and by release, as in the hallucinations (visual, auditory and gustatory, etc.), the delirium and automatism that are sometimes seen. The actual convulsive moments of the generalised or of the Jacksonian fit can hardly be regarded as release symptoms but point from their form and character to direct stimulation of cortical cells.

Morbid Anatomy.—As has already been stated epilepsy has no histopathology, though in the brains of chronic epileptics various minor changes have been noted. Much of the material from which information on this point has been gathered is useless, since the subjects have been aments or dements, and the relation of the changes found to the occurrence of fits during life is uncertain. Among the changes thus found are smallness of the brain, meningeal thickening, convolutional atrophy and fibrosis of the Pacchionian bodies. But none of these is invariably present, and we say that there are no certainly essential macroscopic changes in the epileptic brain. Histological examination has proved equally inconclusive. Sclerosis of the cornu Ammonis,

consisting of degenerative changes in nerves, cells and gliosis, have long since been reported, but of their significance nothing can be said. In short, as has been already stated, " there is no histopathology of the fit." Examination of the endocrine organs has also given no significant results.

Heredity.—In the past great stress has been laid upon the alleged heritable qualities of idiopathic epilepsy, and they have been made the basis of sweeping prohibitions in the matter of the marriage and child-begetting and -bearing of epileptic subjects. Nevertheless, it seems that direct transmission of epilepsy from parent to child is exceptional, and this has certainly been the experience of the present writer in dealing with the abundant material that presents itself at the out-patient clinics of such an institution as the National Hospital. Recently Cobb has expressed the view that on so-called eugenic grounds as high a proportion as 90 per cent. of epileptics cannot reasonably be advised against marriage. Statistical reviews by others (*e.g.* Muskens, Marchand) seem to confirm this view. Marchand maintains that after the exclusion of all those cases of epilepsy in which gross external factors, such as syphilis, injury, etc., can be excluded there is nothing that can be called a familial epilepsy capable of direct transmission without the intervention of adventitious factors. In congenital affections resulting from developmental defects of the ectodermal layer, epilepsy when it is seen is no more than the symptom of a cerebral lesion. In support of these views he has been able to marshal a great weight of evidence. On the other hand, recent electrographic observations of Lennox suggest that in the parents (one or both) of epileptic subjects abnormally wide fluctuations in the rhythm of the brain potentials are unduly frequent, and it may be that while epilepsy as such is not inherited, some instability of cortical cell function may be inherited, which in combination with other factors (when one or more of these chance to be present) lead to the appearance of epilepsy. This is approximately what Marchand maintains in more general terms.

Exciting Causes of the Fit.—In the majority of cases of idiopathic epilepsy no cause whatever can be found for the occurrence of the first fit. It may follow unpleasant emotional excitement, alcoholic excess, or may occur completely unheralded while the subject is in his normal health and environment. In the case of frankly symptomatic epilepsy, metabolic disturbances in early life, and especially rickets, are potent causes. Acute intoxications with absinthe, lead, bismuth and many other poisons may invoke epilepsy, as may also the poisons occurring in the specific fevers in childhood, in uræmia, cholæmia, hyperpiesia and puerperal eclampsia. And although in these intoxications the epileptic phenomena do not usually recur after the cause has disappeared, yet there is not one of the above-mentioned conditions which has not been followed by persistently recurring epilepsy. Injury to the brain of any nature whatever, whether from violence from without or from disease within, may cause epilepsy. Traumatic cases in which the brain has been severely wounded are not associated with epilepsy in a greater percentage than 5 per cent. Cerebral tumours, agenesia, encephalitis meningitis, cerebral syphilis and vascular lesions give a higher percentage, which in children has been placed as high as 30 per cent. Another form of symptomatic epilepsy that should be borne in mind when a previously normal person who has lived abroad, particularly in the tropics, develops epilepsy is that due to cysticerosis. The cysticercus or bladderworm stage

of T. Solium normally develops in the pig, and infestation of man by the adult tapeworm is due to eating pork thus infested. Man may also accidentally eat tapeworm eggs and serve as the intermediate host, the embryos showing a tendency to invade the brain. MacArthur, who has drawn attention to this factor in the development of fits, records 20 personally observed cases of cysticerosis of the brain, 6 of them soldiers invalided from abroad. The fits may be Jacksonian in type or generalised.

Symptoms.—PRODROMATA.—The circumstances which immediately precede the occurrence of an attack are of some importance. Speaking generally, it is uncommon for an attack to occur when the attention is fixed, or when some act is being performed, and from this it follows that the epileptic is relatively or absolutely free from attacks when at work and doing, and only in the rarest cases comes to harm or injury from accident. Some patients are able, by an effort of will in fixing attention, or by the performance of some vigorous action, to arrest attacks which have already begun.

Sometimes a change in the general condition of the patient may make him aware, or may acquaint those around him, that an attack is pending, and such signs of altered metabolism may herald an attack for from a couple of hours to a week. Headache, irritability, restlessness, euphoria, lethargy, somnolence, unusual appetite and a peculiar vacant look may all be met with in this connection.

Not infrequently the attack is preceded by paroxysmal manifestations which are in reality minute attacks, such as partial lapses in consciousness, a sense of strangeness, "dreamy state," jactitations of any of the muscles exactly resembling those seen in uræmia, slight auras, giddiness, sneezing and yawning.

DESCRIPTION OF THE ATTACKS.—The varieties of the epileptic attack are legion, and several types may occur in the same subject—indeed, it is unusual for fits to be always of the same type in one subject. They tend to vary both in degree and nature. They are usually divided into the less spectacular "minor" attacks, in which spasm is not a prominent feature; and "major" attacks, in which spasm is conspicuous. This distinction is purely artificial, for most patients have attacks of both varieties, and the two merge by insensible gradations the one into the other. Further, the minor attack often is the initial manifestation of the major attack.

The following description will serve to illustrate the more definite manifestation of epileptic attacks:

1. *Simple jactitation.*—Single twitching of individual muscles or groups of muscles, occurring, now in one part of the body, now in another, are seen in the majority of epileptics at some time or other. They are conspicuous in the convulsions of childhood, where they often constitute the chief clinical feature. They are well known as the "carphology," or "subsultus tendimum," of uræmic and eclamptic attacks, and in the "typhoid state." They may be not infrequently noticed in the epileptic person when he is otherwise well, and engaged perhaps in conversation or other occupation. Gowers emphasised epileptic twitching as a prodroma of an oncoming severe attack; but while in some instances this is undoubtedly true, yet it frequently occurs when no attack follows. It has been called "epileptic myoclonus."

2. *Simple loss of consciousness.*—In this, the commonest of all minor

phenomena, there is a simple break in the continuity of consciousness. The train of thought and action is suddenly arrested for a few seconds, and there is a sudden stillness of posture and facial expression which attracts the attention of a witness. The face may show sudden pallor, a vacant expression, and curious fixity of the eyes, with large pupils. The patient does not fall, or move, or drop anything that he is holding. In a few seconds the attack is over, leaving the patient unable to describe what has happened, perhaps a little confused for some seconds, sometimes emotional and even hysterical. More often he continues what he was about as if nothing had happened. Such attacks sometimes occur very frequently, even hundreds in a day. They are characteristic of pyknolepsy, in which the prognosis is absolutely good, and also of a form of epilepsy in which rapid mental degeneration occurs and in which the prognosis is equally bad. Further, they may occur in organic disease of the brain.

3. *Simple loss of consciousness with falling.*—The patient suddenly falls, without warning, in the extended position, and almost always prone, so that his head reaches the ground first, and his forehead receives the bruise. He regains consciousness immediately, and picks himself up as if nothing had happened. It is not uncommon to see the forehead one region of scars, as the result of repeated falls; to prevent these a pneumatic protector should be worn. This form gave rise among the ancients to the name "falling sickness," or "morbus caducens." In another form of this type the head, or the head and trunk, alone are affected. The patient does not fall, but simply drops the head forward—"nodding spasm," or "spasmus nutans"; or he drops the head and bends the trunk forward—"salaam spasm."

4. *Simple loss of consciousness with slight spasm.*—This forms a gradation from the above types to the definitely convulsive seizures. The spasm is seen as conjugate deviation of the eyes, and perhaps of the head also, or it takes the form of laryngeal and respiratory action, giving rise to a groaning noise, or may involve any part of the musculature.

5. *Local fits.*—First studied by Hughlings Jackson, these events have the name of "Jacksonian epilepsy," and this term has unfortunately become coupled with common errors that are no part of Jackson's teachings. These are (1) that some local disease invariably underlies the Jacksonian fit, and (2) that the Jacksonian fit necessarily consists of local motor convulsion. Actually, in many cases naked-eye and microscopic examination may fail to reveal any local lesion, and none such may be present. Also, the Jacksonian fit may consist of phenomena involving any possible cortical function. It may be added that local disease of the brain quite commonly evokes generalised fits indistinguishable from those of idiopathic epilepsy, and conversely that the latter form of epilepsy may express itself in the form of Jacksonian fits.

Psychic fits.—These may take the form of peculiar mental states, of instantaneous onset, remembered afterwards sometimes in exquisite detail, sometimes only in vague character. Emotional conditions of fear or horror, which may cause the patient to attempt with violence to escape from his surroundings—"cursive" epilepsy—may occur. Or, the attacks may take the form of a sudden feeling of misery, or an intense sense of personal wrongdoing, a sense of intense familiarity in surroundings which are unfamiliar, a sudden sense of strangeness, as in a patient whose fit was "suddenly seeming

to be somewhere else," a sense of euphoria or of intense mental energy, a dreamy state, often associated with smacking of the lips and champing or swallowing movements, which often has a pleasurable emotional tone. Again, the psychic fit may take the form of a highly complex and detailed hallucination.

Visual Fits.—These may take the form of negative phenomena, such as dimness of vision, complete darkness or hemianopia, or of positive effects, such as flashes of light, scintillating stars or balls of fire, or of both together in the form of blindness with flashes of light. In the last case they may closely resemble the visual phenomena of migraine, and are not infrequently caused by a local lesion of the occipital region. Complex visual hallucinations may occur.

Auditory fits.—The hallucinations of sound may be of any nature—hissing, booming and elaborate musical sensations, as of bells, being common. There is usually a sense of coincident deafness or " far away " hearing, which passes off with or soon after the sound.

In one case the fits could always be produced by sounding the hallucination note upon the open diapason of an organ. No other note or sound produced the fit. (Such directly excited fits, though very rare, are well known in connection with olfactory, visual, auditory and common sensory stimulation, and have been termed " reflex epilepsy.")

Olfactory and gustatory fits.—These hallucinations are always described as of " favour," usually unpleasant. Very often, movements of the lips, tongue and jaw, or swallowing movements are present, and the dreamy state already referred to may be associated. From the location of the functions of smell and taste in the cortex of the uncinate gyri, and from the common occurrence of fits of this character in lesions of these convolutions, this type of fit is often referred to as the " uncinate fit."

Sensory fits.—These hallucinations may have their seat of commencement in any part of the body. They may remain local, but more commonly they spread from the point of origin in terms of the local representations of the body in the cerebral cortex, and usually from the periphery towards the trunk and head, but a sensory fit may spread to the extreme periphery first. For example, commencing in the fingers, it may spread up the arm to the head, or on reaching the shoulder it may invade trunk and leg before ascending to the head. It may be bilateral, confined to the anterior or posterior aspect of the body.

The sensation may be described as " numbness," " tingling," " pins and needles," " vibration," " rushing," " as if the limb were withering," much more rarely actual pain. Sometimes the sensation is indescribable. The sensory attacks have their origin in a local disturbance of the parietal region of the cortex, and may indicate the presence of an organic lesion in that region. They may be accompanied or followed by temporary loss of sensibility, in the form of astereognosis, loss of sense of position, or anæsthesia.

Another group of sensory fits for which it is impossible to give any definite cerebral localisation at present, is that of the so-called visceral auras, which are mainly referred to the distribution of the vagus nerve. Such are the very commonly occurring " epigastric " sensation, and sensations of choking, dyspnœa, nausea and cardiac sensations.

It is quite possible that the sudden feelings of malaise or of faintness

which may constitute the main feature of some epileptic attacks are expressions of the sudden lowering of blood pressure which is known to immediately precede the epileptic attack.

Disturbances in the realm of the vestibular nerve are common indications of epilepsy. Sudden giddiness may be the sole indication of epilepsy, and is a common initial event in major attacks. It may be indicative of the sudden fall of blood pressure, or the feeling of rotation may be consequent upon early spasm causing conjugate deviation of the eyes.

It must be carefully borne in mind that all the phenomena which have been described above may occur as isolated events and so constitute the epileptic attack. Often, however, the disturbance of the cortex spreads widely, involving general convulsion and loss of consciousness; but the initial phenomena are remembered by the patient as the "warning" of the attack and have from ancient times been termed "auras," when preceding general convulsion. In reality, they constitute the essential part of the attack as showing the region of the brain in which the disturbance starts, and in every patient who has such "warnings" preceding his severe attacks, the warnings occur at times by themselves without any such sequel.

Motor fits (*simple paralysis*).—This is the rarest of all forms of the epileptic attack. It consists in a sudden inability, relative or complete, to use a limb or one side of the body or the whole voluntary musculature, with no preceding convulsion. There are the usual signs of cerebral paralysis—at first flaccidity with a tendency for the jerks to fail; a few moments later increased jerks, with absent trunk reflexes and extensor plantar reflexes, all of which signs soon disappear. It may occur as an isolated phenomenon. More often a slight "minor" attack or a local sensory attack accompanies the onset of the paralysis. Sometimes such an attack may result from local disease of the brain. Such attacks when involving the right face or right side of the body may occasion aphasia, or the aphasia may occur alone as the attack of simple paralysis. Such attacks of simple paralysis without convulsion are well known in uræmia, hyperpiesia, metallic poisoning and general paralysis of the insane.

Local convulsion.—The common foci of onset are the angle of the mouth, the thumb and index finger, and the great toe, but the spasm may occasionally begin elsewhere. It rarely produces conjugate deviation of the eyes as a primary movement, but usually in association with, and secondary to, deviation of the head. The convulsive movements may remain confined to their place of onset throughout the fit, or may spread widely so as to involve a whole limb, one-half of the body, or the entire musculature. In fits involving the musculature of the right half of the face and tongue, speech is usually lost during the attack and returns shortly after its cessation. Spasm never affects the muscles of one eyeball alone, but the spasm is in terms of conjugate deviation of both eyeballs in one direction. The same rule applies when the neck is affected, for the head is then either rotated to one side or extended or flexed on the chest. With the other bilaterally associated muscles it is different, for the tongue is affected on one side only, as is also the face. The onset is with tonic spasm, which after a little while gives place to broken or clonic spasm, becoming more and more intermittent and finally ceasing. In some cases, but by no means in all, the convulsion

leaves varying degrees of weakness in the affected muscles—Todd's paralysis or post-epileptic paralysis, with transient signs of loss of function of the pyramidal system, such as loss of trunk reflexes, increase of jerks, and extensor plantar reflexes.

Epileptic spasm usually puts the hand in the position of extension at the interphalangeal joints, flexion and abduction at the metacarpo-phalangeal joints, flexion at wrist and elbow, and adduction at the shoulder. The feet are dropped and inturned, with extension at the knee and hip. Usually the trunk is in opisthotonos.

The sequence of tonic spasm at first, followed by clonic spasm, though usual in epilepsy, is not invariable. Purely tonic fits may occur with no clonic spasm, the tonic spasm remitting suddenly. Such fits are usually of slight severity and duration, and are almost always general and very rarely local.

On the other hand, the spasm may be clonic only. The simple jactitation already described may be taken as a simple clonic fit. Local fits, especially of the face and of the hand, may be purely clonic. Again, some of the most severe of all general epileptic convulsions are clonic throughout so far as the limb and trunk musculature is concerned, but some tonic conjugate deviation of eyes and head is usual.

Loss of consciousness in local fits.—This seems to depend upon the extent of the cortex involved. With narrowly confined fits there may be no impairment at all, as in local convulsion of the face or hand, or as in a patient who vividly described to me a slow visual fit as it was occurring. When the fit spreads, consciousness is usually impaired, and when lost, it is lost late in the fit. For example, it is usual for a convulsion which spreads to one-half of the body to cause some impairment, and if it involves both sides generally consciousness is always lost.

General convulsive fits (*haut* or *grand mal*).—There is some reason for believing that every major attack has a local commencement in some region of the brain, and that it is in reality a local fit which rapidly becomes general. When such an attack commences with a local aura there is proof positive of local commencement. When it commences with conjugate deviation of head and eyes to one side, this is certain indication that the disturbance commences in the opposite hemisphere. When the spread of the disturbance is so rapid as to cause instant loss of consciousness there is no memory to retain the initial event of the attack. The seizure may begin with any of the local manifestations above described, the epigastric aura and giddiness being two of the most frequent. Or the patient may be only aware of his attacks from the condition in which he finds himself after their occurrence. The tonic spasm commences with conjugate deviation of both eyes to one side, followed by rotation of the head to the same side. The blood pressure falls, the countenance is for a moment pallid, the eyes widely open, the pupils dilated, the corneæ insensitive. The march of the tonic spasm usually causes head retraction and opisthotonos; the upper extremities are stiff in flexion and adduction, the lower extremities in extension. If standing, the patient falls usually backwards, but the conjugate deviation of head and eyes may bring his face to the ground first. The respiratory muscles and larynx, going into spasm, produce the epileptic "cry," and the respiratory movements being no longer possible the face darkens with the asphyxia, and the sphincters

may relax, with the evacuation of bowel or bladder. The protrusor spasm of the tongue and the closing spasm of the jaw may cause the tongue to be bitten. After the tonic spasm has lasted some seconds and perhaps has produced such a degree of asphyxia as seems hardly compatible with survival, it begins to break into a series of sudden shock-like, jerky movements—the clonic spasm—which continue for some seconds, becoming less regular and occurring at longer intervals until, with a final jerk, the muscles become perfectly limp. Meanwhile the relaxation of the respiratory and laryngeal spasm have allowed the respiratory movements to return and to churn up the saliva, often bloodstained, which escapes at the nose and mouth in the form of froth. At the end of the attack there is complete and unrousable loss of consciousness, the pupils are dilated and insensitive to light, the corneal reflexes absent, the knee-jerks absent, and the plantar reflexes extensor in type. In a short time the knee-jerks return, the plantar reflexes return to the normal, and consciousness returns. Usually the patient is dazed, feels ill, has marked headache, and if left to himself soon sleeps heavily for some hours. It must be noted that the general convulsive attack almost always leaves the patient face downwards, so that he has drowned in a puddle an inch deep and has been asphyxiated by his own pillow. The latter event is by very far the commonest way the epileptic meets his death from accident in a fit.

The epileptic cry.—There are two quite different sounds that may occur at the commencement of an epileptic attack. The one is a natural, conscious cry of terror at the advent, as in the patient who alternated piercing screams with "It is coming! It is coming!" before the convulsion commenced. It is curious how rarely any memory of such cries or utterances remains with the patient. The other is the epileptic cry proper—a weird, unearthly, hollow sound, produced by inspiratory spasm drawing air over the nearly closed vocal cords. This cry occurs in a minority even of severe cases, for the obvious reason that it is determined by a particular march of the spasm. If the inspiratory spasm occur before the larynx has gone into spasm or after it is in spasm, there can be no laryngeal noise, but only the commonly witnessed pharyngeal and buccal grunting and gurgling. The spasm must be so timed that the inspiratory spasm must occur as the larynx is closing, and this only obtains in a minority of the cases.

Tongue-biting.—Some patients always bite the tongue, others never, and some now and again. The tongue is always bitten at the side and some way from the tip, because it is deviated to one side in the spasm and its thicker part brought between the molar teeth. The same side is always bitten. The tongue cannot be bitten unless protrusor spasm occur either before the jaw has gone into tonic spasm or after it has broken into clonic spasm. If any other march of spasm occur, the tongue escapes. It is remarkable how little scarring occurs even from severe and repeated tongue-biting unless a piece is bitten clean out.

Incontinence.—Though common, incontinence is by no means the rule even in severe attacks. More often it is the urine alone that is evacuated, much more seldom the bowel alone, still more rarely both. A rare phenomenon during an epileptic fit is seminal emission. The occurrence of this has been denied, but the present writer has seen it occur.

Secondary events.—The degree of asphyxia during the attack may

be severe, and blood vessels may give way under the stress, with the production of surface ecchymoses or deep hæmorrhages, including cerebral hæmorrhage. The spasm is powerful and may give rise to much subsequent aching, as if the patient had been beaten all over. It may dislocate joints, rupture muscles and even break bones. A dislocation once produced in a fit always recurs with subsequent fits.

Duration of epileptic attacks.—Two minutes may be given as an outside time-limit for the duration of an individual attack, from its commencement to the end of the active phenomena, and in convulsive attacks to the end of the spasm. Usually the time is much shorter than this, and often is a few seconds only. Sometimes attacks are described as of much longer duration. When analysed, such attacks will be found to be a series of attacks with very short intervals, or slight attacks with post-epileptic functional spasm, or hysterical attacks.

Conditions after attacks. — The epileptic fit may leave no after-effects whatever, even though it be severe, but this is unusual. On the other hand, even the slightest attacks may cause conspicuous sequels. Sleep and headache are very common, especially following convulsive attacks, and they may be alternative effects, in that if sleep occur there is no headache, but if it be prevented there is severe headache. The post-epileptic paralysis of Todd has already been described, and also the aphasia which may follow right-sided attacks. The mental state is usually affected by the attack, and returns to the normal—sometimes quickly, sometimes slowly. Commonly the patient is dull and dazed, speaking at random, unreceptive, irritable, and does not fully recognise his surroundings. During this state of impaired consciousness he may pass into a condition of mental automatism, in which various acts are performed in a conscious manner but of which no recollection is afterwards retained. One patient always prepared for bed after her minor attacks, and proceeded to undress in the stalls of a theatre. The acts performed during post-epileptic automatism may have a true relation to the life and mentality of the patient. He may do spiteful and criminal acts to those he dislikes. This fact has an important bearing as regards the criminal responsibility of the epileptic. In other cases a patient after recovering from the epileptic fit passes at once into a state of hysterical convulsion. Both these post-epileptic conditions occur commonly after minor attacks, but they may also occur after major fits; they seldom occur when convulsion has been severe.

Vomiting may occur after any type of epileptic fit, but it is most often met with after a convulsive attack. As it occurs during the period of unconsciousness, there is some danger of the vomited material being drawn into the larynx. Though Gowers mentions a case in which this event proved fatal, I have not come across any accident from this cause.

Mental Deterioration and Aberration in Epilepsy.—Many epileptics, especially those who have frequent attacks, show signs of mental deterioration, which is often progressive, and which may become severe and end in chronic insanity; while others show no such mental troubles, and some of these fulfil a long life with the highest standard of capacity.

There seems to be no correlation between the type of epilepsy and mental degeneration, though the latter is widely held to be more frequent and more severe when many minor attacks occur.

The tendency to mental failure is greatest in the cases which commence in childhood, and lessens as age increases; while, again, in the epilepsy commencing in the degenerative period of later life, the incidence again increases. In its slighter form there is merely defect of memory, of attention and power of acquisition. In more severe degree there is greater imperfection of intellectual power, weakened capacity for attention, and often defective moral control. Mischievous restlessness and irritability may develop to vicious and criminal tendencies with advancing age. Every grade of intellectual defect may be met with, to actual imbecility. Paroxysmal outbursts of mental derangement may be met with, sometimes transient and immediately following a fit, sometimes without a fit, and sometimes lasting for weeks or months. From what has been written above upon the cause of the mental disturbance in metabolic dyscrasia, these events will be easily explicable.

Periodicity.—While some patients may have fits at any time and at all times, yet there is a tendency in the majority for the attacks to occur at particular epochs and not at others. Epilepsy may be strictly "nocturnal" or "diurnal." It may occur only on rising in the morning, or solely at the menstrual epoch. The fits may come in batches of several in one day, at intervals of many months, while 7-, 14- and 28-day periods are common. A knowledge of the periodicity when present is of great value in the successful treatment of epilepsy. "Rare" fits, which occur at very long intervals, are apt to present the most severe convulsion ever witnessed.

Special Varieties of Epilepsy

Epilepsy from Local Disease of the Brain.—Almost any lesion of the cerebral hemispheres may produce symptomatic epilepsy. But not more than 5 per cent. of all such lesions do this. The convulsions which may occur in cerebral thrombosis, encephalitis and meningitis are examples of epilepsy incident with the onset of an acute lesion. Usually the epilepsy is incident when the lesion has been present some considerable time. Lesions of the brain in childhood seem to be more commonly associated with epilepsy than when occurring in adult life. Agenetic states of the brain of prenatal origin (cerebral diplegias) are associated with epilepsy in 30 per cent. of the cases, and infantile hemiplegia is followed by epilepsy in about the same proportion. Increased intracranial pressure alone seems capable of causing fits, as in hydrocephalus and subarachnoid hæmorrhage, and this may be a factor in the epilepsy of intracranial tumours and meningitis. Abscess seems very rarely to produce fits.

The fits caused by local lesions may be in almost every respect identical with and indistinguishable from the usual type of epileptic manifestation, from the slightest momentary minor fit, all through the local sensory and motor fits, to the severe general convulsion of instantaneous onset and immediate loss of consciousness. There are the same auras and the same sequels. It may perhaps be said with relative truth that the splanchnic auras (epigastric, cardiac, etc.) are uncommon, and that there is a greater tendency for consciousness to be lost late.

The minor attack is the least common fit occurring as the result of a local lesion; the general convulsion by far the most common; while the local fit

holds an intermediate position, and its nature is often indicative of the position of the lesion.

PYKNOLEPSY.—This is a form occurring in children, so called because of the great number of the fits which may occur daily. These are of the slight minor type, any sign of spasm being infrequent. It is rare for any major fit to occur. There is no mental impairment whatever, no deterioration of health, and no result is obtained by any form of treatment. The malady invariably ends in spontaneous cure, usually before or at the age of puberty. Its separation from minor epilepsy is of uncertain validity.

CARDIAC EPILEPSY.—This is a convenient term for the epilepsy which occurs in Adams-Stokes' disease, and in paroxysmal tachycardia, and for the fits which may occur in congenital heart disease and in some forms of cyanosis. They cannot be the equivalents of asphyxial convulsions, for they are not met with in severe chronic cyanosis, and, on the other hand, there is usually no cyanosis at all when fits occur in Adams-Stokes' disease.

VASOVAGAL ATTACKS.—Under this misleading title, Gowers described a recurrent paroxysmal symptom-complex with some or all the following components: a sensation of fullness in the epigastrium; præcordial pain or discomfort; difficulty in breathing; a sense of impending death; a slowness of mental operations but without disturbance of consciousness; a sense of physical fatigue; and coldness of face and extremities. These symptoms wax and then wane gradually, and may be present for as long as 4 hours from onset to disappearance.

Gowers stated that he used the term "vasovagal" as a purely descriptive one, but without implying any theory of causation. Unfortunately, those who have adopted his terminology have overlooked its lack of foundation. Further, the various descriptions of these attacks to be found in the literature are based almost wholly upon hearsay, the attacks themselves being but rarely observed, and do not provide any evidence of vasovagal involvement. Thus, the pulse is said to be accelerated, not decreased or irregular, while the facial pallor and coldness might equally be the result of local vaso-constriction or of splanchnic dilatation. A further vagueness has been lent to the conception by the different senses in which it has been employed. Thus, Collier has used the term for attacks in which convulsions and loss of consciousness occurred, though Gowers expressly stated that consciousness was not disturbed. In short, the term has no precise meaning, no sound basis of observation, and no proper place in neurological terminology.

The alternative term recently suggested for the attacks described by Gowers, namely, "periventricular epilepsy," must also lack value until we have some precise information as to the nature of the attacks themselves. Lewis has pointed out that the term "vasovagal" may rightly be applied to the common fainting or syncopal attacks, and it is better to restrict the term to these.

MYOCLONUS EPILEPSY.—In this group are included: (1) Epilepsy of an ordinary type in which there is much simple epileptic jactitation of the muscles between the fits; (2) cases of Unverricht's myoclonus in which epilepsy is coincident.

STATUS EPILEPTICUS.—In this condition severe convulsion succeeds severe convulsion at short intervals without any return of consciousness during these intervals. It is as if convulsion recurred so soon as the body recovered sufficiently from the exhaustion produced by the last convulsion.

Meanwhile the temperature rises, and may reach a hyperpyrexia. The difficulty in feeding and watering, the severe muscular exertion and the pyrexia add the dangers of acidosis to those of exhaustion, and the patient is very apt to succumb. Status epilepticus must not be confused with frequently recurring fits in which there is some return to consciousness during the intervals, though it frequently develops from such a condition; for the latter are not accompanied by a rising temperature, are more readily subdued, and are not of nearly so severe a prognostic import. If the convulsions cannot be stopped by treatment, the patient usually dies from sudden collapse, or, the fits ceasing, he remains delirious for a while, with rapid heart and high temperature, and dies of cardiac failure. Status epilepticus may be met with in acute lesions of the brain and in chronic lesions such as general paralysis of the insane. It may occur in acute poisoning with lead, bismuth and absinthe. It may develop suddenly in any type of epilepsy whatsoever, sometimes without apparent cause, sometimes as the result of over-exertion and excitement, sometimes when medicines which have been regularly administered and which have kept the fits in check are suddenly cut off.

Diagnosis.—The recognition of epilepsy requires a working acquaintance with the nature of its many manifestations and especially of the slight forms, little exteriorised, which may be easily overlooked or misinterpreted. The sudden unexpected onset, without cause, the transiency, the recurrence, and the circumstances of the moment, are useful aids.

From syncopal attacks (rapid lowering of blood pressure) epilepsy can often be distinguished by the slow onset, the gradually increasing pallor or greyness, the distancing of sound, the nausea and flatulence, the presence of an obvious cause, the length and the stillness of a fainting attack.

The hysterical attack is easily distinguished by the fact that only the convulsion of epilepsy can possibly be confused: the other manifestations of epilepsy are never simulated by hysteria. Hysterical convulsion has not the manner nor the march of epileptic spasm. It never begins with conjugate deviation of head and eyes to one side, there is not the orderly spread of convulsion, and there is never but a poor imitation of the sequence of tonic followed by clonic spasms. The movements in the hysterical fit are purposive, spectacular, violent, and are liable to be increased by restraint and are rapidly abolished by complete inattention. The functional fit never occurs except in the presence of an audience, for it would then be purposeless, and it never occurs during sleep, the tongue is never bitten, though other parts of the body and other people may be. There is no transient abolition of the tendon jerks, nor transient appearance of the Babinski plantar response. The sphincters are never relaxed. Intense converging spasm of the eyes is a common feature of the functional attack, but this sign is not met with in epilepsy. When functional manifestations follow slight and rapidly transient epileptic attacks, the distinction between these and purely hysterical attacks is often difficult and sometimes impossible, except after long observation. For the initial epileptic attack may be practically unnoticeable, and the subsequent events may be typical of hysteria and are usually amenable to the same line of treatment. Often some point in the circumstances under which the attack occurs will settle the diagnosis. Any attack having occurred during sleep, or any attack in which the patient has fallen in circumstances of serious danger, as among the traffic of a London street, or any attack

occurring when the patient cannot attract the attention of others, establishes the diagnosis of epilepsy. The best plan is to regard every hysterical fit as possibly epileptic, and every fit of doubtful type as probably epileptic, until time and circumstance bring definite conviction.

Migraine may sometimes closely simulate epilepsy when sudden paralysis, or sensory auras, or visual hallucinations occur without headache. But while the sensory phenomena of migraine may last for 5 to 30 minutes, those of minor epilepsy have a duration of seconds only.

Careful search must be made in every case for all the bodily conditions with which epilepsy may be associated. Papillœdema, headache and vomiting may reveal increased intracranial pressure from some lesion of the brain; while local paralysis, sensory loss, visual or other defect may indicate a local lesion of the brain, past or present, and this may also be suggested by the nature of a local fit. The presence of rickets, infantilism, undue adiposity, etc., may indicate the presence of some definite metabolic dyscrasia or endocrine disorder. Renal function and the condition of the blood pressure should always be examined, for even in early infancy fits may be uræmic and in the recurring epilepsy associated with small white kidney, and with cystic renal disease, the causal disease is frequently unrecognised. Where syphilis is likely, the reactions in the blood and cerebro-spinal fluid should be examined. Lastly, any evidence of chronic intoxication by metals, alcohol, absinthe, etc., should be sought for.

Cysticercosis epilepsy should be thought of when the patient has lived abroad. Diagnosis depends upon the palpation of cysts in the tissues, or the shadow in radiograms of calcified cysts in the muscles, or within the skull.

Prognosis.—The outlook in epilepsy is so variable that it is difficult to indicate any but the broadest principles in prognosis. Nor can a definite forecast be made in any case until the result of treatment has been watched for some time; for cases apparently favourable may prove rebellious, and those most unfavourable may turn out brilliant successes. Speaking generally, a cheerful outlook is justified in all cases except those in which there is progressive mental deterioration, and in these the outlook is hopeless in proportion to the rapidity of the mental change. Naturally, in those cases which are associated with serious bodily disease, such as brain tumour, renal disease and hypertension, the prognosis involves that of the exciting condition.

The danger to life from the epileptic attack itself, either directly or indirectly, is not great. However severe the fit, it is extremely rare for death to occur, and when this happens it is from turning over and smothering with the wetted pillow or from choking with the aspiration of vomited material. Injury, burning and drowning may cause death, yet the number of epileptics who meet their death in this way is so infinitely small as almost to remove the danger of accident from practical perspective. In the rare status epilepticus, however, the danger to life may be very great. Spontaneous cessation of the attacks occurs in a small proportion of cases. The convulsive attacks of infancy, which continue for some years after all cause to which they can be attributed has passed away, often cease for ever at the age of 4 to 6 years. Again, after 20 years of age spontaneous cessation is met with, and it becomes more frequent as life advances. It is, in my experience, a

much more frequent event than writers upon this subject, with the exception of Gowers, have been willing to admit.

The probability of cure, arrest or amelioration by treatment may be entertained in all cases where no mental deterioration exists and where no insuperable bodily disease determines the epilepsy, in proportion as the only method of cure—the securing arrest of the attacks for a considerable time by drug treatment—can be adequately administered over a long period. It is greater when periodicity in the occurrence of fits allows these to be anticipated by drug administration. It is much greater when the following out of education, or the continuance of regular employment, allows of a fully occupied and satisfying life, and much less when education is stopped, pleasures and sports forbidden, and the patient condemned to social inferiority and ostracism, and to a gloomy, narrow life of inanition because he has a few fits. It is perhaps smallest when severe attacks occur daily or at short intervals and when both major and minor attacks occur in the same subject.

Treatment.—*General treatment.*—The general principles for the maintenance of health if good, or for its improvement if poor, should be adopted. Whenever possible, no change whatever should be made from the régime of life of a normal person. In childhood, education, discipline and pleasures and school life should be continued upon strictly normal lines, and the adult should continue with work and occupation. No advantage has accrued from the adoption of special diets, such as the abrogation of meat, the exclusion of salt or the use of purin-free foods. The production of a low grade of acidosis by a ketogenic diet is occasionally of value in the epilepsy of children. Alcohol seems to be an excitant of the epileptic attack and should be forbidden.

The forbidding of such pastimes as may be fraught with danger should a fit occur, such as swimming, boating, cycling and car driving, is necessary.

Marriage and pregnancy.—The subject of epilepsy sometimes seeks—but rarely heeds—advice as to the expediency of marriage, both in its effects upon himself (or herself) and in respect of any heritable qualities it may possess. Marriage has no necessary effect upon the course of epilepsy, and, as we have seen, direct transmission of the disease is rare. Therefore the sweeping medical prohibitions once so frequent in these circumstances are not in fact warranted by such knowledge as we possess. Every case must be considered on its merits. It has been noted that in the family history of the epileptic subject, migraine is a far more common antecedent than epilepsy, but no one would venture to advise the migrainous subject against marriage or parentage on any so-called eugenic grounds. In respect of pregnancy it is usual, though not constant, for fits to cease in the epileptic woman when pregnant, and in any event the occurrence of fits at this time constitutes no special danger and is not an indication for the artificial termination of pregnancy.

Institutional treatment.—In cases where there is low mentality, much mental degeneration or insanity, and with frequent fits, where no adequate care and occupation can be provided at home, there is every advantage in a colony, institution or asylum for epileptics. In such patients little or no good can be done by medicinal treatment, whereas regular work, discipline and interest often mitigate greatly the burden of the malady.

Surgical treatment.—There still remains a very widespread impression that local fits and fits following upon injury to the skull are likely to be benefited by decompression. There is, however, little evidence that such procedures benefit epilepsy of any kind. Cases are on record in which a cortical scar, or a meningeal adhesion to the cortex, has become an epileptogenic focus the excision of which has been followed by cessation of attacks. The presence and situation of such a scar having been previously determined by the lumbar insufflation of air and the taking of an encephalogram. In general the dictum of Pierce Clark is just, that "all operative measures upon the brain in epilepsy are allowable only when they are indicated by definite physical signs other than the fits." Thus, in a case of cerebral tumour producing epilepsy, operation is justifiable for the relief of the papillœdema, headache, etc., and with the hope of possible removal or of obsolescence of the growth following the decompression.

Medicinal treatment.—Further than the measures above described, the treatment of epilepsy is purely medicinal. There are two groups of drugs which have a remarkable effect in arresting or mitigating the occurrence of the attacks in epilepsy. They seem to have much the same effect, and may conveniently be combined or alternated in the treatment of any given case. Sometimes one group is found to suit an individual patient better than the other. No advantage seems to accrue from administering these remedies more than twice in the 24 hours, nor from using large doses. Moderate doses, such as will cause no deterioration in bodily or mental health, even if taken regularly and for years, seem to bring about the best results. The first group is that of the compounds of bromine, of which sodium bromide seems to have an advantage over the others, both as regards efficacy and toleration. The organic compounds of bromine are not so useful. Sodium bromide should not be given in larger doses than 25 grains (1·5 G.) to an adult, nor should more than 60 grains be given in the 24 hours. It is conveniently combined with arsenic (min. 2 to 3) in the form of liquor arsenicalis, since this has the effect of checking the occurrence of acne. If it be advisable to conceal the fact that bromide is being administered, Gelineau's "dragées," each of which contains 15 grains of potassium bromide, may be prescribed.

Bromism.—Even in ordinary doses, the bromides may cause some acne of the skin, especially in subjects who are prone to acne, but this is the sole derogatory effect of this remedy, which is of common occurrence. The true bromide rash, which was met with in the early days of bromide treatment when huge doses (even an ounce thrice daily) were in vogue, is highly characteristic. It is hardly ever seen in these days, but I have twice met with it from moderate doses of bromides. Mental dulling and conditions of subcoma, which may occur from poisonous doses of the bromides, are rarely met with from appropriate medicinal administration, except in elderly subjects. The mental deterioration due to the epilepsy in certain cases is often attributed by the laity to this cause, but this occurs, and sometimes in much greater degree, in the absence of bromides.

The second group is that of the malonyl-urea compounds, of which phenobarbitone (luminal) and soluble phenobarbitone are examples. These are very powerful drugs, and must be used with care. Phenobarbitone has certainly the advantage over soluble phenobarbitone in being more pro-

longed in its action. It is conveniently prescribed in doses of ½ grain to a child, and 1 grain, with a maximum dose of 1½ grains, to an adult. In larger doses it is a powerful hypnotic, and in patients who have idiosyncrasy it may produce a troublesome kind of frenzy. It appears to be a more certain means of warding off attacks for many hours after its administration than is bromide.

Whatever remedy is chosen, whether it be the bromide or luminal or a combination of the two, it is essential if possible to anticipate the occurrence of the fit by the administration of the drug. Thus, if fits are nocturnal only, the remedy is given in a single dose at night, or if diurnal only, in a single dose in the early morning. Again, if, as often happens, the fits occur soon after waking, then the single nightly dose should be used. Or, if the fits occur or are more frequent at the menstrual epoch, they should be anticipated by increased dosage before and during that epoch. With fits that are diurnal and nocturnal, a night and morning dose should be used. As it is less important in patients who have employment when fits occur by night, and often most disastrous when they occur at work, for with the present Workmen's Compensation Act no company will insure a known epileptic, I prefer to give phenobarbitone as the morning remedy and bromide as the nightly remedy, since I consider phenobarbitone to be the greater safeguard against the occurrence of the attacks. The question at once arises, Why should two remedies be used? The answer is that these drugs are by no means identical in action, and that the nature of the cause of epilepsy certainly varies in individuals. Some patients do best on phenobarbitone alone, others on bromide alone, and others on a combination of the two, and the best course can only be determined after trial.

Recently, Merritt and Putnam in Boston have introduced the use of sodium diphenyl hydantoinate (dilantin, epanutin) for epilepsy. Favourable results are claimed for this in cases that have not responded well to bromide or phenobarbitone, and some confirmation of its value is being obtained in this country. Obtainable here under the names of epanutin and solantoin, it is dispensed in capsules containing 1½ grains. For small children dosage is begun with 1½ grains twice daily, increased to three or even four times daily until optimal results are obtained. For adults 1½ to 3 grains twice or thrice daily may be given. Symptoms of intolerance or of overdosage are tremor and unsteadiness, and these call for reduction of dosage. It seems safe to say that for adults a dose of 3 to 4 capsules daily is without untoward consequences, or unpleasant symptoms.

When the change is being made from some other medication to epanutin, this should be gradual, one of the daily doses of bromide or of phenobarbitone being substituted in the first week, a second one in the following week, and complete substitution being achieved in the third week. It is perhaps too soon to estimate the value of this drug in comparison with its many predecessors, but in some instances it is certainly more effective in controlling fits. Its use is said to be contra-indicated in elderly persons with hypertension and in debilitated subjects.

Many other remedies have been advocated in epilepsy; a few only have stood the test of time and are still in use, both as alternatives and adjuvants to the treatment above given. These may be placed in order of merit as belladonna, digitalis and allied drugs, especially adonis vernalis, opium and borax.

Belladonna has a striking effect upon a few isolated cases. It makes some cases definitely worse. Digitalis and adonis vernalis are commonly used as adjuvants, and I think sometimes with benefit. Morphine given in careful doses is of great use in status epilepticus. Thyroid is often of value in the epilepsy associated with cerebral agenesia (cerebral diplegia), mental and bodily backwardness and infantilism. It probably acts by rendering bodily metabolism more normal and in enhancing development.

STATUS EPILEPTICUS.—The treatment of this condition, and that of rapidly repeated fits which not infrequently merges into status epilepticus, is quite different from that of epilepsy in general, for the remedies useful in the latter condition are useless and even do harm in this urgent and dangerous state. The first thing to be done is to check the convulsion, and this is best achieved by the hypodermic injection of $\frac{1}{6}$th of a grain of morphine. (Gowers preferred hyoscine.) Another remedy is paraldehyde, in large doses (360 minims), and this has recently been successful at the National Hospital. It has the obvious advantage that it is stimulating and not depressant. The remedies formerly used such as bromide and chloral by the rectum are worse than useless. The next measure is to secure that the patient shall be provided with adequate stimulants in the form of food, water and even alcohol. To which end a nutritious liquid meal of high stimulating value and containing sugar to combat acidosis should be given by means of the nasal tube at regular intervals. An action of the bowel should be obtained as soon as possible, with a rapidly acting aperient administered with the food, and by warm water enemata. The pyrexia should be controlled by sponging repeatedly, and if high by continuous immersion, and this alone will sometimes have a dramatic effect in checking convulsion when pyrexia exists. When consciousness returns, feeding and stimulation must be carefully continued, with a gradual resumption of the routine treatment of epilepsy.

NARCOLEPSY.—In this remarkable and, as Adie has shown, by no means rare condition, two quite different kinds of attack occur. The one is the sudden onset of apparently normal sleep, which comes usually at a moment of inattention, several times a day. The sleep lasts from a few seconds to a few minutes; it is rousable, and the patient is wide awake at once and knows that he has slept, and sometimes that he has dreamed and can describe the dream. Many of the patients have a warning in the way of a feeling of intense fatigue and, thereafter, can so far repel the onset of the attack by an effort of will as to be able to get out of harm's way; but the attack is inevitable, and it is always the more severe the longer it is resisted. The second variety of attack is called the "cataplectic" attack, and this is produced mostly from a sudden emotion, which may be of any kind, but is usually an emotion which provokes laughter. There is a sudden feeling of intense weakness in the limbs, which become flaccid. The patient drops anything that he may be holding and crumbles to the ground, but often only into the sitting position. The eyelids drop and the head falls forward with the jaw dropped, and there is sometimes twitching of the muscles of the face, tongue and neck. There is complete inability to move the limbs and generally inability to speak, but consciousness is completely retained, so that the patient is afterwards able to recount every event and repeat every word spoken during the attack. In one typical case a cataplectic access was habitually induced by feelings of amusement or of anger, but

surprise was equally effective. Thus, when fly-fishing, a suddenly rising fish caused the patient's rod to droop in his suddenly weakened arm, and when shooting his gun drooped helplessly if a bird broke unexpectedly into view near him.

Usually an idiopathic malady, narcolepsy has been recorded in a few instances as a sequel of encephalitis lethargica. The malady appears never to be familial, and it does not occur before the age of puberty. Once developed, it usually continues throughout life, with variable frequency of the attacks. In most cases (amphetamine) benzedrine sulphate is specific in its action on narcolepsy. An initial dose of 1 tablet (10 mgm.) after breakfast and another after luncheon. This may be cautiously increased to 2 or even 3 tablets after these two meals, with a smaller dose after tea. Symptoms of overdosage are sleeplessness, restlessness and tremulousness. Less efficacious, but yet of distinct value in some cases, is ephedrine sulphate of doses of ½ grain twice daily.

MIGRAINE

Synonym.—Paroxysmal headache.

Definition.—A common malady of which the only essential characteristic is recurring intense headaches, which usually develop on waking in the morning, and may be unilateral, frontal, occipital or general. The attacks usually date from childhood, but sometimes commence during later life. The headaches are often associated with vomiting, which has given rise to the designation "sick headaches" or "bilious attacks," with which is associated much vestibular disturbance as in sea sickness, and with peculiar disturbances of vision. Less common symptoms of the disease are peculiar slow sensory auræ, which occur in no other malady, attacks of hemiplegia or monoplegia or of aphasia, and attacks of ophthalmoplegia. Some of these phenomena may accompany the headaches, but others occur in attacks quite apart from the headaches, and may for that reason give rise to difficulty in diagnosis.

Ætiology.—The malady commonly makes its appearance at about the age of puberty, and tends to persist, with fluctuations in severity and frequency of attacks, until middle age, disappearing in women with the menopause. Its persistence in old age is exceptional. A history of familial incidence is common, and the subjects are commonly of an energetic and intelligent type.

Nothing is known with certainty of its essential nature of causation, and in consequence hypotheses are rife. Thus, digestive disorders, errors of refraction, of metabolism and of endocrine function have all been evoked as responsible factors, though without clear evidence in the case of any of them. Yet the correction of such errors when they obtain does not suffice to cure the malady, and it is probable that they are never more than precipitating factors in susceptible subjects. Spasm of cerebral arteries has also been suggested as a cause of the attacks, but again without adequate grounds.

The subjects of migraine are often bad sailors and bad train travellers, and mental and bodily fatigue and emotional disturbances are commonly

followed by an attack. It is important to remember that tumours of the occipital lobe and also intracranial aneurysms may be associated with attacks exactly resembling migraine.

Symptoms.—The subjects of migraine are usually otherwise quite healthy, and are often robust and strong. No peculiarities of blood pressure are noticeable. Premonitory signs of the attacks are present in some cases, and these may take the form of an unusual feeling of well-being and intellectual acuity, or, on the other hand, of lassitude and depression. The attack commences most commonly on waking in the morning, when on raising his head from the pillow the patient experiences a sense of vestibular disorientation with giddiness, ocular confusion and nausea, such as is commonly felt at the commencement of sea sickness. It is at this stage of the attack, and within a few moments of its commencement, that the visual phenomena occur when these are present. Often the patient vomits at once from the vestibular disturbance, but sometimes vomiting is delayed for hours, and the vomiting may be continued as long as the giddiness persists. The visual disturbances last but a short time (from 10 to 20 minutes), but leave, as a rule, some confusion of vision and discomfort throughout the attack. The headache follows shortly upon these initial symptoms. It is cumulative, and expansile in character, and often begins constantly in a localised spot in the temple, forehead or eyeball, as a sharp boring pain which gradually spreads, and may involve the neck and arm. The pain may be unilateral, frontal, occipital or quite general. As the headache increases the face becomes pale and grey, the patient becomes much prostrated and incapable of mental or physical effort, and is unable to take food. Light, noise and movement aggravate the pain. After remaining in this condition for many hours, he falls into a heavy sleep, and awakes next morning shaken by his illness, but otherwise well. The above description covers many attacks of migraine, but many variations occur. The attacks do not always occur on waking, they may come on at any time of night or day. They may be rapidly transient, lasting but a few hours only, or they may last for days and even as long as 3 weeks, and give much anxiety in the attempts to provide nourishment and sleep for the patient. In some cases of long standing, the attacks become less severe towards middle life, and a persistent aggravating headache may develop between the attacks. When such a persistent headache is complained of alone, it is very important to inquire about preceding migraine, for the same treatment is applicable to the two conditions. One of the most characteristic features of the headache is that when once it is in full swing, no remedies will relieve it except natural sleep.

Visual phenomena.—Considering how very common migraine is, it must be clearly understood that any visual phenomena except slight confusion of vision accompanying the attacks, are rare. These may take the form of general mistiness of vision, floating spots, scotomata, bright stars and colours, hemianopia, double hemianopia with complete blindness, or psychic hallucinations of vision. In connection with scotoma and with hemianopia, the phenomenon of teichopsia may occur as follows: Upon the dark background of the scotoma or hemianopic field, a ball of light appears, which grows larger and becomes dark in the centre. This ring of light breaks at one spot, opens out and takes the form of a series of entering and retreating

angles (castellation figure) which become gloriously coloured (fortification spectrum) and which later become fragmented and fade. These visual events usually occur at the very beginning of the attack, before the headache develops, and they are rapidly evanescent, but they may occur as isolated phenomena, when no headache occurs.

Aphasic attacks may take the form of confusion of speech, word-blindness, or even of loss of speech-acceptance and exteriorisation. They accompany the headaches and occur at the commencement of the attacks. They are not of common occurrence.

Hemiplegic and monoplegic attacks usually occur quite apart from the attacks of headache. They, too, occur on waking, and consist of a transient uselessness and weakness of limbs, which lasts a few hours only. They are characterised by their occurrence in young subjects who suffer from pronounced migraine; they are rapidly transient and are not accompanied by organic signs, and almost invariably other members of the family are migrainous, and suffer with similar attacks of paralysis. In Michell Clarke's cases, 11 members of one family in three generations were so affected.

Sensory aurœ.—These are somewhat rare events, but they are pathognomonic of migraine, and usually occur quite apart from the headaches. The aura commences upon the periphery of a limb and is likened to that which would be produced by a multitude of cold-footed insects creeping on the skin. It travels very slowly towards the proximity, taking half an hour or more to reach from the fingers to the head, and is very alarming to the patient. It disappears rapidly without further event. It is the only aura with an exceedingly slow spread.

Ophthalmoplegia.—This is a very rare but most important event. It occurs only at the height of the headache, in severe attacks. Indeed, the patients usually say that the headache, during which the ophthalmoplegia occurred, was the very worst they had ever experienced. It is a paralysis of the oculomotor nerve trunks, most commonly of the sixth nerve alone, but sometimes of the third or fourth nerves, or of a combination of these three. It is generally unilateral, but may occur simultaneously on both sides. Severe diplopia results. It passes off in from a few days to a few weeks. When once it has occurred, it is apt to recur with subsequent attacks. In one of my patients, paralysis of the sixth nerve persisted for 18 months, gradually lessening between the attacks, and becoming complete with each fresh attack of headache. It disappeared completely, with the cessation of the headaches, when adequate treatment was adopted.

Diagnosis.—This presents little difficulty, if it be borne in mind that long installed recurring headaches on waking in the morning are surely migraine. The condition of the urine should exclude those renal cases with migraine-like headaches. Each case should be carefully examined for signs of organic nervous disease, and especially for persistent hemianopia and papillœdema, which would indicate an organic lesion of the occipital lobe. Those who are not familiar with the full range of sensory symptoms that may precede the onset of the headache, and do not realise the severe disturbance of the speech function which in some cases accompany them, are apt to take an unduly grave and erroneous view of the history given by a subject who has experienced them. Thus, a diagnosis of petit mal, or of cerebral tumour is not rarely made. It should be remembered, therefore, that the disturb-

ances which occur in a minor epileptic attack are momentary in duration and never persist, as do the migrainous symptoms in question, for several minutes. Again, consciousness is neither lost nor blunted in migraine. Although, as has been pointed out, a rare case of migraine ultimately turns out to be one of cerebral tumour, the latter diagnosis cannot readily be made unless there are supporting signs of a structural lesion. It is probable that the so-called ophthalmoplegic migraine, in many instances at least, is a symptom-complex bearing no relation to true migraine but dependent upon a gross intracranial lesion, perhaps most often an unruptured aneurysm of the internal carotid artery.

Treatment.—There are but few cases of migraine that cannot be materially benefited by treatment. Some are completely cured, while in others the attacks become milder and occur at much longer intervals. Careful attention should be paid to improvement of nutrition and general health, should these be defective. The avoidance of undue fatigue and of worrying emotions, and of any factors which are known to produce the attacks, is important. Errors of refraction should be adjusted if they are important. Medicinal treatment is by far the most useful agent. A mixture containing min. 1 of liq. trinitrinæ, min. 5 of liq. strychninæ, min. 10 of tinct. gelsemii, and 10 grs. of sodium bromide, made acid to preserve the stability of the nitro-glycerine, and administered thrice daily for many weeks or months, was advocated by Gowers; and truly there are few cases of migraine which do not derive great benefit or complete cure from this treatment. Phenobarbitone, in doses of 1 grain given every night, is most valuable, and may be used in addition to the foregoing prescription. The individual attacks are difficult to relieve. Sometimes a full dose of phenazone, acetanilide, phenacetin or aspirin given at the very commencement of the attack will ward it off, but these are useless when the headache has fully developed. The use of ergotamine tartrate—by mouth or hypodermically—has recently been recommended as an effective method of cutting short an attack of migraine. In some subjects, though by no means in all, it is useful for this purpose. Sometimes a full dose of alcohol has the same effect. It remains to keep the patient as comfortable and quiet as possible till sleep occurs. Where the attacks last over the 24 hours, and especially when they last for days, the only remedies are to induce sleep and to keep the patient nourished, the latter object being difficult to attain in long-lasting attacks. To this end hypnotics, such as barbitone or carbromal (adalin) may be used.

JAMES COLLIER.
Revised by F. M. R. WALSHE.

CHOREA

Synonyms.—St. Vitus' Dance; Sydenham's Chorea; Rheumatic Chorea.

Definition.—Chorea is an affection of the nervous system caused by rheumatic infection, and characterised by the occurrence of spontaneous involuntary movements, irregular both in time and in place of occurrence and in nature; by inco-ordination of voluntary movements; by muscular weakness, and by a variable degree of psychic disturbance.

Ætiology.—Chorea is rare among negroes, Indians and coloured races, whilst it is especially common in Jewish races. It is much more common among the poorer classes than among the well-to-do. Its incidence is upon nervous highly-strung subjects rather than upon the phlegmatic, and this is probably to be explained by the fact that the rheumatic subject is likely to be nervous and highly strung. Chorea is practically unknown during the first three years of life, and is very rare before the fifth year has passed. Common between the ages of 5 to 10 years, it reaches its maximum incidence between 10 and 15 years. After the age of 20 it is rare, except in connection with pregnancy; but a few cases have been reported up to the age of 60 years which have certainly been examples of rheumatic chorea. Females are affected twice as frequently as are males. Heredity concerns the incidence of chorea in two ways: firstly, as regards the inheritance of the rheumatic tendency, which is the most important cause of chorea; and secondly, in respect of the inheritance of the neuropathic tendency, for it is when these two are coincident that chorea is most prone to occur. As early as 1802 rheumatism was regarded as the cause of chorea, and all subsequent investigations have upheld this theory. The family history of a choreic patient generally brings to light the occurrence of acute rheumatism, of cardiac disease and of other rheumatic manifestations among other members of the family. Often the patient has suffered with rheumatic erythema, purpura, rheumatic nodules, recurrent sore throat and growing pains before the appearance of the chorea; less often an attack of acute rheumatism or cardiac disease has occurred. A large percentage of those patients who have never shown any sign of the rheumatic state before or during the attack of chorea subsequently suffer with rheumatic symptoms. The British Medical Association Collective Investigation Committee found that rheumatism preceded the chorea in 26 per cent. of the cases, and that in 46 per cent. of the remainder rheumatic signs accompanied the chorea, or appeared subsequently. If to the total of choreic patients who present rheumatic signs at some time or other, one adds those with no personal history of rheumatism, but with a family history of rheumatism, it will be found that there are but few cases of chorea in which a personal or family history of rheumatism is absent.

Psychical disturbances.—Any emotional disturbance, such as fright, anxiety, depression or overpressure in school, may sometimes act as immediate determining factors, but much more often these events simply aggravate symptoms which are already present in slight degree.

Pregnancy.—The relationship of pregnancy to chorea is very definite. It is generally met with in first pregnancies, and before the age of 25 years, and in most cases the pregnancy appears to be the only obvious cause for the chorea. The onset of the chorea is usually between the first and third months of pregnancy. It is liable to recur with subsequent pregnancies.

Pathology.—The complex nature of the involuntary movements in chorea, and their association with psychical disorders of greater or lesser degree indicate the cerebral cortex as the seat of the pathological process. The essential lesion has proved very difficult of detection by microscopical investigation, but according to Greenfield and Wolfsohn it consists in a diffuse meningo-encephalitis affecting mainly the cerebral cortex, the basal ganglia and the pia-arachnoid.

Symptoms.—The onset is usually gradual, but it is sometimes abrupt,

when emotional disturbance has been the determining cause. The appearance of choreic movements is often preceded by alterations in the mental and physical condition of the child. She becomes nervous and more impressionable than before. She is increasingly unable to apply her attention. She becomes clumsy in her movements—and lets fall objects which she is holding. Anæmia, apathy and languor and irregularity of appetite are commonly present. At this time, careful observation will discover slight involuntary movements of the face and fingers which are often unilateral in distribution. From day to day the movements become more marked and spread to the limbs and trunk. The face is constantly grimacing, and the hands and arms scarcely cease from turning about, and affection of the legs makes the walking irregular and clumsy. The child can no longer keep still, the respiration movements become irregular and spasmodic, and the chorea is fully developed. The characteristic symptoms of a well-marked case of chorea are—(1) involuntary movements; (2) weakness of voluntary movements; (3) ataxy or loss of precision of voluntary movement; (4) emotional instability and other psychic disturbances.

1. THE INVOLUNTARY MOVEMENTS are always irregular as regards time and as regards the nature of the movement. Similar movements are never repeated successively in the same part. Each movement begins rapidly, and ends suddenly, and one frequently sees the involuntary movement complicated by the addition of a voluntary movement to cover the fault. The majority of the movements are complicated, involving several muscles and often more than one joint. In the face, the more simple movements take the form of asymmetrical twitches in the lips, and about the angles of the mouth and orbits. In more severe cases, the strangest grimaces may occur. The tongue is thrust into one cheek, then projected just in time to escape the sudden snap of the open mouth. When asked to show the tongue, the child puts it out rapidly and holds it there by closing the teeth upon it. Smacking of the tongue and palate may often be heard at a distance. Lateral movement of the jaw is common. According to the severity of the case, speech may be difficult, the words being articulated slowly in slurred monosyllables. For the same reason, swallowing may be difficult or impossible in severe cases, and may necessitate nasal feeding. That the ocular muscles participate in the involuntary movements only in very severe cases.

In the upper extremities the movements appear first in the hand. The thumb is more restless than the fingers, which are spread and pressed together, flexed and extended, alternately; the wrists twist about irregularly, the forearms are constantly agitated with movements of pronation and supination, flexion and extension; while all possible movements of the shoulder occur. When the upper extremities are outstretched, the hands assume the position of flexion at the wrist and over-extension at all the finger joints in so many of the cases as to make this a characteristic feature of chorea. The lower extremities are less severely affected than is the rest of the body, and here the movements are best seen when the child is lying down. The gait tends to be clumsy and insecure, and in severe cases walking becomes impossible. Alteration of the rhythm of the respiratory movements is conspicuous and is highly characteristic of chorea. The breath is often taken rapidly and held for some time, then let go with a loud sigh. The trunk is often involved, and movements of a writhing nature are characteristic.

So far as the limbs are concerned, the movements may be confined to one side, more commonly the left side, and the condition is then called hemichorea; but the involvement of the face and trunk is always bilateral and is generally equal upon the two sides. In hemichorea, the movements are always of slight severity. Severe chorea is never confined to one side. Choreic movements cease during sleep, and, except in severe cases, can be controlled more or less by voluntary effort; the attempt to write, for example, will generally cause cessation of the movements in the right arm for the time being. They are generally increased by observation, emotion and self-consciousness, but in a few cases it will be found they are worse when the child is alone and unobserved. The violence of the movements of the limbs may cause the skin over the prominences to ulcerate from friction against the clothing, and the head and limbs may be badly bruised from contact with adjacent objects, and unless the patient be properly protected, wounds may occur, which are liable to infection with such grave consequences as abscess, erysipelas and pyæmia.

2. Loss of power is shown in the mild cases by incapacity for exertion and undue fatigue. More severe degrees of paresis may accompany or succeed the appearance of the movements. It may be observed that in one limb, or upon one side of the body, the choreic movements are becoming less marked, and that the limbs are becoming progressively weaker. Soon the arm hangs loosely by the side, and the leg is dragged in walking. The degree of choreic paralysis bears no relation to the severity of the movements, for the former may be severe, when the latter are slight and vice versa. Choreic paresis is apt to return with successive attacks of chorea, but not always in the same region.

Limp Chorea (*chorea mollis*).—This is a more severe degree of choreic paralysis affecting the whole musculature. It may be preceded by the usual symptoms of chorea. More often the paralysis is the first noticeable symptoms, and this develops rapidly in from 24 to 48 hours. The paralysis is characterised by complete flaccidity of the limbs; the child lies upon its back and does not move, and if one of the limbs be raised from the bed and then released, it falls limp and lifeless. The head is no longer held in a natural position, but falls round on to the ear. Careful investigation, however, rarely fails to reveal some slight choreic movements, either in the face or in the fingers. Paretic chorea and chorea mollis run a benign course, and recovery is said to be almost invariable.

3. Inco-ordination of voluntary movement may be the first symptom of chorea to draw attention, and it may precede the appearance of the choreic movements. It may be very obvious when the movements are slight, and it is most noticeable in those of the hand and forearm, which lack precision, and in those of articulation, deglutition and respiration. The involuntary movements that have been described are superimposed upon voluntary movements which they render inco-ordinate, at times interrupting them abruptly and at other times tending to prolong them.

4. Psychical disturbances are common, some degree of emotional instability, failure of attention and depression being present in most cases, and, generally, in proportion to the severity of the affection. Delirium may occur in acute and grave cases. It is usually violent and loquacious, and resembles other forms of toxic delirium, and it is of serious prognostic import.

Mania is quite exceptional in children, but it is not an uncommon complication in adolescents and adults. The form of the aberration may be acute mania, melancholia or delusional insanity. The psychical disorders, slight or severe, usually disappear with the chorea, and in all cases the prognosis as regards permanent mental recovery is good.

Ocular Phenomena.—The pupils are frequently dilated and may be unequal and excentric, and hippus may be present.

Sensibility is not impaired. The sphincters are not affected. The skin reflexes are normal. The deep reflexes are also normal in a large proportion of cases, but often the knee-jerk shows an alteration which is peculiar to chorea. On tapping the patellar tendon, the resulting contraction of the quadriceps is unduly sustained, and the leg remains in a position of extension at the top of its excursion for several tenths of a second. This is not invariably present even in a series of knee-jerks taken successively from a single subject, and the occasional appearance of an apparently sustained jerk is due to the coincidence of reflex contraction and choreiform movement. In severe cases, the deep reflexes may be diminished and rarely may be absent for months.

Rheumatic Manifestations.—Cardio-vascular changes are common in chorea. In nearly all the cases, careful and repeated examination of the heart will reveal slight dilatation and reduplication of the second sound, often with reduplication of the first sound, and increased rapidity of the pulse. Doubtless these are signs of a slight myocardial weakness, resulting from the rheumatic infection. Irregularity of the pulse is probably dependent upon the altered rhythm of respiration. Systolic murmurs are common, and these may be hæmic in nature, or may be the expression of cardiac dilatation, but in the majority of cases they are indicative of endocarditis. Endocarditis is present in 90 per cent. of the fatal cases. At least one-half of all cases present cardiac murmurs, which are suggestive of the presence of endocarditis, while some cases with no cardiac murmur during life are found post mortem to have endocarditis. The mitral valve is commonly affected, lesions of the aortic valve being quite rare. Pericarditis is a frequent associate of endocarditis; only in rare instances does it occur alone. The valvular affections which are met with in chorea may be the result of antecedent rheumatism, or they may develop in the course of the chorea; or while no signs of endocarditis are present during the attack, the patient may shortly afterwards present the signs of organic valvular disease. Cutaneous affections which occur in rheumatism are met with also in chorea, namely, erythema, purpura and subcutaneous nodules. Acute articular rheumatism is comparatively rare, and when it occurs it is usually accompanied by a cessation of the choreic movements. When rheumatic phenomena are present and in the acute mania of chorea, pyrexia is usually present, but uncomplicated chorea is an apyrexial disease.

Recurrence.—One-third of the subjects of chorea have more than one attack. Females are more prone to a recurrence than males in about the same proportion as they are more liable to original attacks. The average interval between the attacks is one year. If, therefore, a patient has remained well for 2 years, it is improbable that a recurrence will take place. The greater the number of choreic attacks, the more likely is the heart to be found affected, and, therefore, cardiac complications are more often met with

in recurrences. In a recurrence of chorea the symptoms are usually less severe and their duration shorter than in the original attack.

Course and Prognosis.—The disease tends to a spontaneous termination after a variable time, which is usually from 6 weeks to 6 months. The duration rarely falls short of the earlier period. The average duration of cases treated in hospital has been found to be 10 weeks. Cases which last for more than 12 months are not rare, and slight cases with remissions may last several years. The course of the malady is that after a gradual development of symptoms, there is a stationary period during which symptoms are well marked, followed by a period of gradual diminution. In some of the more severe cases of chorea where deglutition is difficult the patient is likely to be insufficiently fed; and this constitutes a grave danger, since in the condition of semi-starvation so induced, the chorea develops apace. Articulation and swallowing become impossible, and the movements become ceaseless, so that both rest and sleep become impossible; the patient wastes rapidly, and is in danger of death from exhaustion unless prompt measures for restoring the depleted nutrition are taken. This is the condition known as "chorea gravis."

The proportion of fatal cases occurring in chorea is less than 2 per cent. Death is most often met with in first attacks, occurring about the age of puberty, and it is very uncommon in young children and in recurrences of chorea.

Diagnosis.—The nature of the involuntary movements of chorea is usually so characteristic as to make diagnosis easy, and to avoid any confusion with other maladies which present conspicuous involuntary movements. Nevertheless, occasionally a case of multiple tics in a child does present difficulties, for the movements are not—as is so commonly stated—invariably repetitive. In chorea the involuntary movements may lead to the dropping of objects from the hands. This does not happen in the case of tics. Again, when the choreic subject gives the observer a firm and sustained handclasp, the irregular waxing and waning of the muscular contraction may be felt throughout by the observer. In a case of tics, the contraction is steadily maintained as in the normal subject. In myoclonus, the movements are short and shock-like, while in athetosis they are slow and rhythmic.

Treatment.—It is all-important in the treatment of chorea, from the mildest to the most severe cases, that physical and mental tranquillity should be secured. It is well to commence treatment in every case with several days' absolute rest in bed, provided that such treatment can be carried out without entailing the fretting which enforced imprisonment may produce. A bright room, an interesting companion, and varied amusements during the period of rest, are desirable, and isolation from other children is advantageous. It is, however, better to abandon enforced rest than to allow it to become irksome to the patient, and result in mental depression and emotional upsets—conditions above all things to be avoided.

When absolute rest is considered inadvisable, or after it has been carried out, the ordinary periods of rest should be prolonged. The child should be well clad in woollen garments, especially at night, since the spasmodic movements are liable to leave her uncovered. Improvement in the condition of bodily nutrition is to be aimed at in all cases. Choreic children are mostly

ill-nourished and thin, and the effect of a liberal supply of food and nutritious food upon the course of the disease is striking. When swallowing is difficult, it is best to resort at once to nasal feeding, which rarely causes as much discomfort as the ineffectual and exhausting endeavours to take food with the spoon. A china feeding-cup must never be used, since the spout may be broken off; an enamelled metal cup is safe. It has been pointed out above that chorea gravis is dependent upon a condition of relative starvation, and here nasal feeding should be employed, and the meal should consist of strong beef-tea, Benger's food, lactose and milk; it should not measure more than three-quarters of a pint for a child of 8 years old. Severe cases, in which the movements are violent, call for skilled attention, and a trained nurse is required night and day. The patient should lie upon a water mattress, placed upon a large guarded bed, the sides of which are everywhere protected by pillows, which must be fixed. When a cot is used, it is easy to pad all the ironwork with cotton-wool, over which bandages are wound. If the limbs are injured, they should be wrapped in cotton-wool applied with a light bandage.

When the patient is improving, measures calculated to enhance control of the limbs, such as exercises under supervision and simple drill, are very useful in hastening the disappearance of the movements. Warm and tepid baths and douches applied regularly and in such a way as to be grateful to the patient, and to produce no fright, are very useful adjuncts. The compounds of salicylic acid are of great value, and of these aspirin is the most useful. It should be given thrice daily after meals in doses of 10 grains for a child between the ages of 6 and 14 years, and 15 grains for an adult, and it should be continued until convalescence is complete. It is well borne and has no deleterious effect, and even more frequent doses may be given. A larger dose given at night is the best remedy for sleeplessness. In very severe cases, the administration of hyoscine is sometimes very useful. It should be given in doses of $\frac{1}{100}$th grain thrice daily. The administration is followed immediately by wide dilatation of the pupil and slight flushing, and by peaceful sleep. The bromides have little or no value as sedatives. In addition to the above remedies, tonics such as iron, glycerophosphates, hypophosphites, strychnine, cod-liver oil and malt are often valuable, especially during convalescence.

Huntington's Chorea

Synonym.—Hereditary chorea of adults.

This is a somewhat rare disease, in which symptoms almost identical with those of rheumatic chorea, namely, involuntary spontaneous movements, ataxy, paresis and slow and slurring articulation, gradually appear in adult life, and usually about the age of 40 years, and are accompanied by progressive mental failure, with delusions and suicidal tendency. The choreic movements are never severe, but the inco-ordination may be well marked. Maniacal outbursts are not uncommon. The disease always progresses slowly to a fatal termination in from 5 to 30 years, and treatment is entirely unavailing. It is a familial disease, and the transmission is direct from parent to child; but if a generation escape the malady, it seems not to reappear subsequently. Sporadic cases, in which no heredity can be traced,

do, however, occur. The sexes are equally affected. Further than the heredity no causal factors are known. The morbid anatomy consists in a slow progressive degeneration of the nerve-cells of the cerebral cortex and basal ganglia, with consecutive atrophy of the convolution, neuroglial overgrowth and meningeal thickening.

Senile Chorea

A malady in which typical choreic movements constitute the chief feature is met with in elderly people, and is possibly due to a progressive neuronic degeneration in that region affected in the other forms of chorea. It differs from Huntington's chorea in the late onset, the absence of heredity, and in the absence of mental changes.

MYOCLONUS

Synonym.—Paramyoclonus multiplex.

The characteristic symptom of this condition is the occurrence of sudden shock-like contractions of the muscles, which may vary in intensity from simple fibrillary twitching to contraction which causes a violent movement of a limb. The movements are often symmetrical, and are especially incident in the proximal muscles of the limbs.

Ætiology.—The malady appears in children usually between the ages of 5 and 15 years, while in adults it commences between the ages of 25 and 40 years. Both sexes are liable to the affection. Many instances, in which several children of the same parents have been affected, have been recorded, and in a few the malady has been transmitted through several generations. Nothing further is known as to the causation.

It is probable that the seat of the morbid process is in the cells of the cerebral hemispheres, since myoclonus is further associated with epilepsy and with progressive mental failure.

Symptoms.—The movements of myoclonus are simple sudden movements, and may exactly resemble the movement resulting from a single faradic stimulus. Each movement commonly involves a single muscle only, and it may concern no more than a few fibres, resembling then the fibrillary twitching common in progressive muscular atrophy. In other cases, many muscles may be implicated in the shock-like spasms, which may be of so violent a nature as to throw the patient to the ground. The distribution of the contraction is never determined by that of the nerve supply, nor do the muscles contract according to their synergic association. Myoclonic movements are irregular as regards rhythm and range of successive movements. The upper limbs are more affected than the lower, and the proximal parts more than the distal, while the periphery, the hand and foot, often escape. Voluntary muscular effort usually checks the myoclonic movements, but in rare instances it excites or augments the spasm. The electrical excitability of the muscles is unaltered, and there is no muscular wasting, but the mechanical excitability of the muscles is increased, and percussion of a muscle may evoke the spasms. The sphincters are unaffected. The reflexes, both superficial and deep, are normal. Sensory phenomena are

absent. Speech may be seriously interfered with when the muscles of jaw, tongue, palate and larynx are implicated, and spontaneous laryngeal and pharyngeal noises may occur. The ocular muscles seem never to be the seat of the movements. Epileptiform convulsions are present in some cases, and for these the term " epileptic myoclonus " has been used.

Diagnosis.—This is not difficult since the simple shock-like movements in symmetrical muscles, without any resemblance to volitional movements and entirely destitute of rhythm, occur in this disease alone.

Course, Duration and Prognosis.—Myoclonus, as a rule, is a slowly progressive affection up to a certain stage, and when this is reached it may remain stationary for years, having little tendency to shorten life, death ultimately occurring from some other disease, without any period of freedom from the spasms. Rarely the disease has ended fatally within a few months of the onset, with progressive mental failure and coma.

Recovery may take place spontaneously, or as a result of treatment, but the affection is very prone to recur.

Treatment.—Every available measure should be used to improve the general bodily condition so as to bring about a more stable condition of the nervous elements, by improving their nutrition. The only drug which influences the disease is arsenic. It must be borne in mind that the malady is an intractable one in proportion to the time the symptoms have persisted, and that some cases recover spontaneously.

SPASMODIC TORTICOLLIS

Definition.—A disease of the nervous system, characterised by tonic and clonic contraction of the superficial and deep muscles of the neck, causing the head to assume either a position in which it is turned to one side and upwards, or a position of marked retraction (retrocollic spasm). It is more correctly to be regarded as a disturbance of movements than of muscles, and perhaps, physiologically considered, it may be spoken of as a disorder in the carriage of the head. This carriage is a more complex and highly co-ordinated function in the erect posture than in the quadrupedal posture; it is a function peculiar to man, and in this sense is of recent evolutionary development. We may perhaps see in this a factor determining its frequent derangement, as in spasmodic torticollis.

Ætiology.—The disease is most frequently met with in middle-aged adults, but it may occur at any age from puberty onwards. It is twice as frequent in females as in males. The causation is most obscure. Not infrequently neuropathic heredity, such as epilepsy and insanity, exists, and the patients are often of highly-strung, nervous, irritable dispositions. Nervous shock, prolonged anxiety, and general ill-health have frequently preceded the onset of symptoms. Less often local strain, or injury and exposure to cold, have been the presumably exciting causes. In a few cases it appears to develop from an occupation neurosis; it developed, for instance, in a tailor who in drawing each stitch had the habit of making a short jerking movement of the head to one side. It occasionally occurs as a symptom of hysteria; but such cases should be carefully separated from those in which there is no hysterical manifestation, as being more susceptible

to treatment and having no tendency to recur when once cured. A torticollic movement may occur as a variety of tic. In one case under our care typical torticollis was the end-result of lethargic encephalitis.

Pathology.—No morbid anatomical changes have been found. On account of the involvement of several muscles, effecting special movements, in this disease (as is well instanced by the over-action of the frontalis in retro collic spasm, for retraction of the head is always normally associated with raising of the eyebrows in the act of looking up), it is probable that torticollis is due to disorder of those centres which direct such associated movements of the affected muscles.

Symptoms.—The onset is usually insidious, but in rare cases may be quite sudden, as in the case of a man aged 40 years, who, when walking along a London street, suddenly turned his head at the sound of an accident which shocked him severely; he was unable to turn his head back without using his hands to do so, and he subsequently developed the most severe torticollis. The initial symptom is always spasm, which may be either tonic or clonic, and frequently both forms of spasm are combined in the same case. In the tonic form, the head is retracted and the face turned to one side, usually the left, and owing to the retraction of the head the face is turned upwards. The shoulder on the side to which the head is inclined is usually raised. In severe cases all the muscles of the upper extremity, the scaleni and the face muscles, may become involved. The spasm, except in the earliest stages, always involved muscles of both sides of the neck. Where the bilateral involvement is general and equal, the rotation of the head does not occur, but it becomes strongly retracted, and the condition is then known as retrocollic spasm. Such retrocollic spasm is always accompanied by marked over-action of the frontales, the skin of the forehead being thrown into transverse wrinkles. In the clonic variety there is jerking movement of the same muscles, usually associated with some degree of tonic spasm. The eyes do not follow the movements of the head in the jerkings. The muscle primarily involved is the sterno-mastoid, the action of which is to incline the head forwards and towards the shoulder of the same side, and rotate the face to the opposite side. The next muscle involved is the splenius of the opposite side, which inclines the head backwards and rotates the face towards its own side, its rotatory action thus coinciding with that of the opposite sterno-mastoid. When the splenii of both sides act together, the head is strongly retracted. Next to be affected are the upper part of the trapezii, the trachelo-mastoids and other deep neck muscles, and with further spread of the spasm, any neighbouring muscles of the shoulder and upper extremity may be affected. Sleep causes cessation of the clonic spasm, but not always of the tonic spasm when the case is severe. The spasm is always increased by fatigue and excitement. There is no wasting of the muscles involved, but on the other hand, they may be even hypertrophied if the spasm has existed for long, and their electrical excitability may be increased. The amount of pain associated with the spasm varies greatly. There may be a slight feeling of cramp only, but usually there is a great deal of aching pain, which may radiate down the arm and into the side of the head, and make life unbearable to the patient. More rarely, sharp neuralgic pains are present.

The course of the disease, which has no tendency to shorten life, is chronic

exacerbations and remissions under treatment being common, and recurrence, after temporary cure, frequent.

Diagnosis.—This is usually quite simple. Fixed positions of the head associated with spasm occur in disease of the cervical spine, especially in spinal caries, and are also associated with enlarged lymphatic glands in the neck. The local signs of these conditions, however, are characteristic.

Treatment.—Spasmodic torticollis is a most intractable condition, and in many cases temporary alleviation is all that can be secured. It is usually best to begin treatment by rest in bed, the patient lying supine with the head low and between sandbags or pillows. The regular administration of phenobarbitone, of chlorbutol, or of chloral and bromide may then be tried. Many years ago Bastian claimed good and permanent results from a continuous narcosis lasting 3 weeks and induced by chloral hydrate. Probably a combination of rest as above described, together with massage and resistance exercises is the most useful line of treatment. In some cases the application of a plaster mould, fixing head and shoulders, and worn for one or more months, or a more easily removed and lighter metal splint will give complete respite from muscular spasm while it is worn, and very occasionally permanent respite after removal. In severe and disabling cases this is well worth trial. Surgical measures (tenotomy, excision of the sternomastoid, posterior root section) have all proved disappointing and are not to be recommended.

There is a *congenital form of torticollis* which is of a very different nature. The disease is prenatal and analogous to congenital talipes, the sterno-mastoid alone is affected, and nearly always that of the right side. Such a muscle is frequently ruptured during birth, and this has given rise to the opinion that the birth injury and subsequent hæmatoma of the muscle were responsible for the torticollis. In many of these cases there is marked facial asymmetry, the face being smaller on the side of the affected sterno-mastoid. This association points strongly to some defect in the nerve centres of the medulla.

Treatment.—This consists in tenotomy of the contracted muscle.

THE TICS

Synonym.—Habit spasm.

Definition.—A group of maladies characterised by the occurrence of either—(1) sudden, rapid, twitch-like, involuntary co-ordinated movements, always of the same nature and in the same region; or of (2) sudden psychical phenomena, imperative ideas and explosive utterances; or (3) of a train of deliberate highly co-ordinated actions produced by an imperative idea. Any combination of these phenomena may occur.

The tics are both ætiologically and clinically related to spasmodic torticollis, into which some of the motor tics gradate. A torticollic movement may occur as a tic, and it may in rare cases pass over into an established torticollis.

The tics may be conveniently divided for clinical purposes into the following groups, between which any combinations may occur:

1. The clinical picture is made up by the occurrence of sudden twitch-like co-ordinated movements, which resemble reflex or defence movements. The

movement is always of the same nature and occurs in the same region, though several different tics may occur in the same patient. The usual region affected is the face, with the pharynx and larynx, the neck and upper extremity. This form occurs chiefly in children, and usually runs a favourable course—Simple Tic.

2. The spasms are more severe and complicated than in simple tic, and imperative ideas and explosive utterances are common and important symptoms. The condition is met with soon after puberty, and more commonly in males—Convulsive Tic.

3. There is no spasm or other motor manifestation, but the psychic tic is expressed by uncontrollable imperative ideas, explosive utterances, arithmomania, etc.—Psychical Tic.

4. Under conditions of mental stress and embarrassment, and in conditions of boredom, the patient performs some highly complicated and co-ordinated act which relieves his nervous tension and fascinates him—Co-ordinated Tic.

The tics are expressions of unrest and of physiological embarrassment in consciousness in a nervous system which is highly sensitive and not too stable. There is always the desire to relieve the embarrassment by the occurrence of the tic, and a feeling of relief when it has occurred, coupled often with disappointment at the failure of its suppression.

While the more simple forms of motor tic from their pattern suggest strongly that they are caused by some peripheral irritation from the conjunctiva in the case of a blinking tic, from the nose in a case of snuffling tic, and from the larynx in a case of laryngeal tic, and that constant irritation from these regions has set up a habit, yet it cannot be too strongly pointed out that no such peripheral irritation precedes the onset of tic, for the irritation and cause come from within the nervous system. Severe peripheral irritation does not cause tic, nor does the correction of errors of refraction, the removal of tonsils and adenoids and of teeth, or circumcision aid in the cure of the malady, though it is only too common to see cases in which these procedures have been inflicted upon the tiqueur one after the other, to the detriment of his tic and of his general health.

1. SIMPLE TIC

Synonym.—Habit spasm.

This is a common disorder of late childhood, the majority of the cases occurring between the fifth and the tenth year. Either sex is prone to the disease. The onset may be preceded by deterioration of health from any cause, and sometimes fright and emotion bring on the tic. Often the malady arises in perfectly healthy children without assignable cause. The children are usually highly strung and intelligent. It is a rare event to see a dull and backward child with a tic.

Symptoms.—The recurring tic appears somewhat suddenly, and may reach its height in a few days. The movements are of the nature of a simple act. They occur suddenly and without warning, and are executed rapidly. Usually the movement is of one kind only; but sometimes several movements coexist. The common site of the spasm is the head, face and neck. Blinking, winking, alternate elevation and depression of the eyebrows, side to

side movements of the mouth, tossing the chin in the air, sudden movements of the tongue, palate or larynx, accompanied by an unpleasant fidgeting sound, are of frequent occurrence, while any movement of the head upon the shoulder, torticollic movements, shrugging of the shoulder, and any movements of the arm may be met with. Respiratory movements are often associated with those occurring in the tongue and larynx. Tic affecting the legs is much less common. The movements cease during sleep. Generally a variable time of some length separates the individual movements, but in severe cases these may follow one another almost unceasingly. They are increased by excitement and by observation, and can usually be controlled by the will, but only for a limited time.

Diagnosis.—The movement of tic is so peculiar that it cannot be confused with any other spontaneous, involuntary movement. It is the same movement, repeated with very rapid execution, in the same place. It is short and sharp, like a twitch. In chorea the movements are slow compared with those of tic, and are irregular in nature, in time and in place.

Prognosis.—Most cases of simple tic recover, whether they are treated or not. They recover much more quickly under treatment, and two or three months suffices in most cases to see the end of them. The longer a tic lasts, the more difficult it is to cure. In the rarest cases only does a tic of this nature persist or merge into one of the more severe forms.

Treatment.—A scrutiny of the general health should be made, and any defects attended to. Matters of hygiene, diet, education, exercise and pleasure should be correct and normal. Observation and remarks upon the child's defects, and anything tending to increase self-consciousness should be avoided. The confidence of the child should be gained if possible, and any source of mental worry, or grief, or annoyance should be ascertained and comforted. Restraint and discipline should be kindly taught, and an orderly life followed in which the child is happy, and in which his time is fully and congenially employed. In severe cases only is it necessary to interdict all physical and mental exertion and excitement, and enjoin rest in bed, and these measures should only be employed for a short time. Aspirin in 10-grain doses 3 times a day is a most valuable remedy, hardly to be dispensed with in any case. Tonics are often useful.

2. CONVULSIVE TIC

In this malady, which was first described by Gilles de la Tourette, and which bears his name, the same movements as are met with in simple tic occur; but these are more severe and more widely spread, and they may involve the whole body in spasm at one time. In addition, there are psychic tics, which cause irresistible impulses, among which are explosive utterances, repetition of words, sounds and gestures, and also imperative ideas.

Ætiology.—The stigmata of physical and mental degeneracy are rarely absent, neuropathic and sometimes direct heredity is often present. The malady is said to be more common in males, and is met with more often in France than in England—where it is a rare disease. The symptoms appear usually between the ages of 10 and 15 years, and commonly follow physical or mental shocks or acute illness of any kind.

Symptoms.—The spasmodic movements resemble at first those of simple tic in their nature and rapidity, and favour the same sites; but they are not restricted to the repetition of the same movement, but successive movements may vary widely in position and extent and sometimes involve the whole musculature of the body. The great variety of facial grimaces, head jerking, grotesque attitudes and ridiculous pantomime which may occur in this affection lead commonly to the belief that the patient is shamming. The tic is not continual as in the simple form. It occurs in the form of bouts in which the same pantomime is reproduced. These are often excited by observation and emotion. They can often be controlled, but with much fatiguing effort on the part of the patient, who becomes so worn out with half successful efforts to control them that he ceases to make the attempt. Between the attacks the patient seems quite normal. The psychic phenomena are the same as in psychical tic, about to be described, and the treatment of the two conditions is identical.

3. PSYCHICAL TIC

In this condition there is no muscular spasm; but the sudden event takes the form of explosive utterances, imperative ideas and impulsive acts. This condition often occurs as a part of convulsive tic. The exclamatory tic consists of some sound or word or group of either, which is habitually uttered, with complete irrelevancy of time, place or sense. Sometimes the words are of an obscene nature and cause the greatest distress to the patient, who, often of innocent mind, is never safe from putting himself to shame. The utterances may be single, or may be repeated over and over in rapid succession. Echolalia, which is an uncontrollable impulse to repeat sounds heard, or to repeat words which the patient or others have just spoken, may be met with. The great characteristic of the condition is that though the patient desires above all other things to prevent their occurrence he cannot do so by any effort of will. Other symptoms that are commonly met with in this condition are imperative ideas and impulsive acts of all sorts, and in addition insanity of doubt, agoraphobia, acrophobia, mysophobia, etc., and arithmomania. In severe cases grave signs of mental deterioration slowly supervene, judgment and memory fail, will power and attention are lost, and the patient becomes incoherent and insane.

Diagnosis.—Both in the convulsive and psychical tics the diagnosis is placed beyond doubt, both by the nature of the movements and by the peculiarity of the psychic disturbance.

Prognosis.—Permanent recovery has occurred from both these conditions; but such an event is rare. Most of the cases follow a downward course despite treatment, and many end in suicide or insanity.

Treatment.—General tonic treatment, with change of circumstance and kindly moral and physical discipline, with healthy pursuits and congenial intellectual and physical occupation are the most likely to benefit. When fixed and imperative ideas are present the patient must be guarded, as one of unsound mind.

4. CO-ORDINATED TIC

In this condition complicated co-ordinated movements are habitually repeated without apparent cause or purpose—especially in conditions of

mental stress. It can be best illustrated by the account of an individual case under our care: A brilliant scholar at a public school was noticed to absent himself for no apparent reason, and when sought for, on the occasions on which he could be found, was always discovered in some secluded place rapidly revolving the two index fingers round the inside of a loop of string. He explained to me that this act had always given him relief from mental stress and anxiety, and that he was ashamed of it, and did his best to overcome it, and often succeeded, but that sometimes the desire for relief from stress overcame him. He was treated, and had no return of the tic for some years. He had become head boy of the school and captain of the football team, and on the occasion of the match of the year with another great school with much anxiety and responsibility upon his shoulders, at the moment of the commencement of the match the captain was not to be found. He was recovered from the act of revolving his index fingers round the inside of a loop of string in a secluded place, in time to perform brilliantly and win for his side.

CRAFT PALSY

Synonyms.—Occupation Palsy; Occupation Cramp.

Definition.—A peculiar malady determined by the habitual use of one set of muscles for the constant repetition of an act of short range, to the exclusion of acts of wider range and acts involving a different set of muscles. The symptoms are: (1) local pain in the muscles concerned; (2) local spasm of the muscles; (3) loss of volitional control of the range and nature of the movements; and (4) weakness of the movements. These symptoms may occur separately or together.

Ætiology.—This disease may be occasioned by any occupation which requires the constant repetition of movements of small range, and which necessitates the holding of the limb rigidly for the fine co-ordination, to the exclusion of free and wide range movements. Consequently it is almost confined to those employments involving finely co-ordinated movements of the fingers, hand and upper limb. As far as is known, a neuropathic inheritance is neither an essential nor a common factor in the production of this disability. Yet at the same time, the fact that young persons are apt to break down while in training, while others follow the occupation of scrivener or telegraphist for years with impunity, it has been suggested that some inherent weakness in the nervous system may underlie the development of the cramp. But, however, it is not necessary to invoke these obscure factors, when faulty motor habits are known to play an important rôle and are adequate to account for the disability.

In the case of writing there are two motor components, pen holding and pen moving. The former is of no importance in the production of writer's cramp, but defects in the latter are of primary importance. The pen may be moved solely by the muscles which hold it, the hand being fixed and the digits alone moving. Less faulty is the habit when writing is done largely by movement at the wrist. Best is the method in which writing is a free movement involving all the limb muscles. Of note in this connection is the fact that subjects of writer's cramp may be able when standing to write on a blackboard. It is those who confine the muscular action most rigidly to

the small hand muscles and the flexors of the index and middle fingers who are most likely to develop cramp. In the use of the Morse key such restriction of activity to small muscles groups is more or less inevitable, but the more modern machines which do not involve this, and have come into greater use, have not this fault and thus telegraphist's cramp is less common now than formerly.

It has been reported that focal lesions in the subthalamic region have resulted in a disability resembling writer's cramp, but the observation is not necessarily relevant to the ordinary example of this condition.

The following is a list of some of the occupations in order of frequency in which this malady occurs: writers with the pen, telegraphists, seamstresses, violinists, machinists, cigar and cigarette rollers, dairy milkers, pianists and typists. It has been said that shorthand writers never suffer from this complaint. In most instances the disability in the use of the hand is confined to the particular movement which first gave rise to it, but in some severe cases other movements may ultimately come to be difficult: *e.g.* shaving, sewing, knitting. It should be borne in mind, however, that when at an early stage of what seems to be writer's or telegraphist's cramp other movements become deranged the presence of some organic nervous affection should be suspected. This point is further dealt with under the heading of diagnosis. The very general use of the typewriting machine, with its free and multitudinous movements required for its manipulation, has made writer's cramp a very rare disease compared with years ago; but it must be borne in mind that when the malady is once installed it is likely to follow the sufferer from one occupation to another. As an example, a telegraphist developed cramp in manipulating the Baudot instrument. He was rested and transferred to lighter duties involving the use of the Morse instrument, where he after a time failed. He was then transferred to counter duties, involving the use of the pen, and became incapacitated with writer's cramp. He was then used to close envelopes, and developed cramp over that act, and ended his service as a messenger. Several of the occupations above mentioned are scheduled in an Act of Parliament as dangerous trades, owing to the liability to cramp, and the employer is bound to compensate for such disability arising in his employ.

Symptoms.—These are of two orders, namely: subjective, consisting of discomfort, pain and the sense of fatigue; and objective, comprising muscular spasm and the abnormalities of movement arising from it and from the effort to avoid both pain and spasm. In some subjects pain, in others spasm predominates.

The onset is gradual, the movements of the pen become inexplicably difficult and tend to be irregular, the strokes extending too high or too low. The subject then finds himself grasping the pen with excessive force, and the correct adjustment of the finger ends becomes hard and apt to fail, the index slipping off the penholder. This he tries to correct by a still firmer grasp. The hand then begins to ache, and feels heavy and tired. With the passage of time all these symptoms increase, and the writing becomes more irregular and the nib is driven more firmly into the paper which it penetrates, the ink spluttering over the sheet. Some tremor may develop in the limb. As the condition grows worse, the cramp appears more and more readily when writing is started, so that even taking the pen in the hand

may evoke cramp. At the same time, other fine and repetitive movements of the hand may be performed with normal ease and facility. The pain which in varying degree accompanies the cramp tends as the affection grows worse to spread from the small hand muscles up the limb until the whole arm and shoulder ache.

Telegraphist's Cramp

There are four instruments commonly used for sending. The Morse instrument is a hard contact key provided with a spring and knob, and the manipulation is performed by making the contact against the spring pressure with the knob held loosely in the palm of the hand. The movements involved are flexion and extension of the wrist only. The arm is supported from the shoulder only. This is a bad cramp-producing instrument, but it has the advantage that it can be manipulated with either hand. If telegraphists are taught to be ambidextrous from the first the incidence of cramp falls to a very low level.

The Baudot instrument consists of a piano-board with five keys, which are manipulated by three fingers of one hand and two fingers of the other, and with the permutations and combinations of these five keys all the signals are made. The movements have to be synchronised to the beats of the commutator. The forearms and wrists rest upon the table. This is the worst cramp-producing instrument that ingenuity could devise, for the movement is of the fingers only, and it is utterly restricted both in space and in time. The Hughes instrument is a piano keyboard with many more keys, and its use is not often productive of cramp. The Gell instrument is a typewriter keyboard, and the movements are free. It is the best instrument in so far as it is not a producer of cramp. Two points of interest stand out, especially in connection with cramp in telegraphy. The one is that, notwithstanding the discomfort, spasm and obvious disability, the subject is rarely reported for faulty sending, so great is his aptitude for dodging his disability. The second point is that so many subjects will work for years, and often to the end of their service, with very obvious cramp, which never proceeds to incapacity. On the whole, the incidence of telegraphist's cramp is now small.

Diagnosis.—From what has been said of the character of the symptoms in these forms of cramp, of the mode of their production by a particular movement-complex, and of their occurrence in the absence of signs of organic nervous disease, it seems reasonable to state that errors of diagnosis should not occur.

Nevertheless, errors are not infrequent and consist in the diagnosing of writer's or of telegraphist's cramp when in fact some organic affection is present. Paralysis agitans, with little or no tremor, and post-encephalitic Parkinsonism provide fruitful sources of error. In the clinical picture thus presented, the initial symptoms may involve the right arm and hand, and at first consist in a difficulty in the normally rapid and free performance of fine movements. Not unnaturally the handwriting may be affected early. It becomes slow in performance, spidery and progressively smaller, and the effort to continue writing may be irksome and even painful. The total clinical picture in such a case is made up of such small deviations from the normal that the inexperienced or careless observer may miss them and may note no more than the patient himself has noted; namely, that it has become

difficult and uncomfortable to write. Amongst other organic conditions which may be encountered under the erroneous diagnosis of writer's or telegraphist's cramp may be included cervical rib, any organic nervous affection which impairs find hand movements, arthritis, and painful affections of muscles. The general principle which underlies accuracy of diagnosis here as elsewhere is careful and systematic clinical examination.

Course and Prognosis.—In a young subject, who shows signs of the malady during training or soon thereafter, the outlook is hopeless with regard to continuance of the occupation, and the progress is from bad to worse. In older subjects the course varies greatly. Some cases recover completely and permanently, even though they continue with the occupation. In others—and this class is much larger than is usually supposed—the condition of cramp becomes stationary, and persists though not in disabling fashion. In a third and numerous group it progresses to incapacity, and tends to reappear with every change of occupation. In a few cases the patients become incapacitated for all the finer movements of both hands. The prognosis is usually serious; but a correct forecast can only be made from the history and progress of each individual case.

Treatment.—The responsibility and costliness which the Compensation Act entails upon employers are slowly enough but surely leading to the abandonment of those instruments, the manipulation of which may produce cramp. Good teaching of unconstrained methods of manipulation and encouragement of ambidexterity in all the occupations concerned are important prophylactic measures. Long hours and the speeding-up of work should be avoided. After long absence from work, the work should be gradually resumed and not recommenced at full pressure. When the malady appears, rest and change of work afterwards are absolutely essential. Long-continued rest, be it remembered, cuts both ways for, as has been pointed out above, resumption after long rest is actually a cause of cramp, for long unemployment decreases the stability and the aptitude of the mechanism. General hygienic and tonic treatment are important. It is doubtful whether local treatment, in the way of massage, electricity, etc., can do any good, except to satisfy the patient. Sporting exercise of any and every kind is most useful. The Post Office authorities adopt the very admirable plan of retraining cramp subjects by daily practice with the instruments for a few minutes, the time of practice being gradually lengthened as capacity increases.

Craft Atrophies

Under this title are described a medley of conditions in which local atrophy of muscles, pain, numbness and sensory loss occur in connection with regions which are habitually over-exerted. These conditions have been met with in platers, filers, file-makers, locksmiths, rowers, glassworkers, etc., and seem to be really examples of local traumatic fibrositis, involving the nerves, and produced in some cases by the continued pressure of the tools.

Many of the cases recover with rest and treatment appropriate for a local interstitial neuritis.

James Collier.
W. J. Adie.
Revised by F. M. R. Walshe.

COMPRESSION OF THE SPINAL CORD

In compression the lumen of the spinal canal is reduced in a small part of its vertical extent, and the spinal cord is injured at this point, either directly by pressure, or indirectly by interference with its vascular supply. With the exception of acute inflammation of the membranes, all the extramedullary lesions of the spinal cord come under this heading. The characteristic clinical feature of compression is the combination of two sets of phenomena: local or root symptoms in those regions supplied by the roots arising from the cord at the level of the lesion, and remote or cord symptoms due to interruption of the conducting paths in the white matter. It is convenient to divide this subject into two parts—slow compression and compression of rapid onset.

1. SLOW COMPRESSION

The commonest causes are tuberculous spinal caries, vertebral tumours, meningeal tumours and cysts; rarer causes are aneurysm, gumma, leukæmia, Hodgkin's disease, Paget's disease, syphilitic caries, spondylitis deformans, and other chronic inflammations of the bones and joints of the spine.

Ætiology and Pathology.—1. *Tuberculous spinal caries (Pott's disease).*—Spinal caries is the most frequent cause of slow compression. It occurs most often in children, but is common in adults, and may begin late in life. Signs of injury to the cord develop in about 1 case in 20, and are usually preceded by obvious deformity of the spine; but in many cases they appear before disease of the bone is suspected. Rarely paralysis comes on for the first time in an adult who has had a curvature since childhood.

The cord may be damaged by direct pressure of displaced bone, or by an abscess beneath the periosteum of the diseased vertebræ; but in almost all cases the injury is indirect, and results from œdema of the cord, arising from interference with its blood supply by tuberculous granulation tissue, which forms on the outer surface of the dura mater and fills the epidural space (pachymeningitis externa). The functions of the cord may be temporarily deranged for long periods by this œdema, without permanent damage to the nervous tissues; hence, when the disease is cured, the œdema subsides and the cord recovers. In cases of greater severity necrosis of the nervous structures follow thrombosis of the vessels, or prolonged pressure causes atrophy of nerve roots, and complete recovery is impossible.

2. *Tumours of the vertebral column.*—Vertebral tumours are about twice as common as all the other forms of extramedullary tumours together, and almost all of them are malignant. Carcinoma is always secondary, and is a frequent and distressing complication of cancer elsewhere. A very small primary carcinoma, *e.g.* of the breast, thyroid or prostate, may produce extensive disease of the vertebræ, and signs of compression may appear before the existence of the primary growth is suspected. On the other hand, they may appear several years after complete removal of the primary growth, and may be the first evidence of a recurrence. Sarcoma, the commonest form of primary growth, begins in the bone or periosteum of the bodies or laminæ, often in several at once, or simultaneously at different levels. Secondary

sarcoma arises by metastasis from sarcoma elsewhere, or by direct extension from a growth in neighbouring soft parts, *e.g.* of tumours in the mediastinal and retro-peritoneal spaces.

The growth of vertebral tumours is usually rapid, and extensive portions of the spinal column may be completely destroyed. The cord is compressed by the growth itself, by displaced bone, or by a process of the growth which invades the spinal canal through an intervertebral foramen. As a rule, the dura mater sets bounds to its inward extension. Benign tumours of the spine are rare. They usually grow forwards, but occasionally an osteoma, a chondroma, or an exostosis produces signs of compression.

3. *Meningeal tumours.*—These are divided into two groups—intradural and extradural. The first are twice as common as the latter, and more than half of them are simple, encapsuled, and easily removable. Myxoma, fibroma, sarcoma, endothelioma, and psammoma are common. Other forms are rare. In most cases they lie posterior or postero-lateral to the cord, and are seen when the cord is exposed by laminectomy; but in a few cases they lie in front and may escape detection.

Sarcoma is the commonest extradural tumour. It is sometimes encapsuled, but more often it is a diffuse growth difficult to remove.

These tumours usually grow very slowly, and several years may elapse between the onset of the first symptom and the time when an accurate diagnosis can be made. They do not invade the substance of the cord, nor penetrate the dura, nor give rise to metastases.

4. *Cysts.*—Cysts, parasitic and non-parasitic, may compress the cord and produce symptoms indistinguishable from those of solid tumours. In some countries hydatid cysts form a high proportion of all spinal tumours. They may invade the spinal canal from adjacent soft parts or from the vertebræ, or arise primarily in the membranes. They are often multiple, and are nearly always extradural. Cysticercus cysts, which are very rare, are usually single and intradural. Non-parasitic cysts are collections of fluid contained within slightly thickened adherent membranes. They are among the most frequent of spinal tumours. They are most likely a result of circumscribed inflammation of the pia-arachnoid, and have been known to follow an injury; but their ætiology is obscure. The cyst is often opened inadvertently during operation, and the only evidence of its former presence is flattening of the cord and atrophy of the nerve roots at the point where a solid tumour was expected. Sometimes the position of the cyst can be inferred at operation, from the absence of normal pulsation below it. On puncturing the membranes in this position fluid escapes under pressure, and the pulsations reappear. The name *meningitis serosa circumscripta* is applied to this condition.

5. *Aneurysm of the aorta* is a rare but well-known cause of spinal compression. The dorsal region is most often affected, three or four vertebral bodies being slowly eroded until the dura mater is exposed. Rupture into the spinal canal has been observed. Berry aneurysms upon the surface vessels of the cord occurring in connection with occult coarctation of the aorta have been many times recorded. The pathognomonic sign of this cause of compression paraplegia is the high arterial blood pressure in the arm as contrasted with the low pressure in the leg.

6. *Syphilitic caries.*—Gummata and caseous masses of syphilitic origin

in the bones of the spine may cause a condition not unlike that of tuberculous caries. It is very rare, and usually occurs in the cervical region where the cord may be compressed.

Extradural Compression

Symptoms.—*Local or root symptoms.*—Pain in parts supplied by the sensory roots arising from the cord at the level of the lesion is often the first symptom. It may be a dull ache, a feeling of constriction, a sharp cutting pain, or pain so severe as to be almost unbearable. It is often brought on or greatly increased by movement of the spine or by coughing. The skin in the painful area is sometimes hypersensitive at first, but very soon its sensibility is diminished, while the pains persist (anæsthesia dolorosa). The nerve trunks are not tender as in ordinary neuralgia. Severe pains are rarely absent in cases of vertebral tumour. In spinal caries they are usually absent or slight. Injury to the motor cells or anterior roots leads to weakness, wasting and loss of tone in the corresponding muscles. In some cases root symptoms are absent throughout the course of the disease, and the first effects of compression are referable to interruption of the conducting paths in the cord.

Remote or cord symptoms.—Although all the tracts are submitted to the same degree of compression, their functions are not impaired at the same time. While variations are common, the symptoms usually arise in the following order: first weakness and spasticity in the lower limbs, then impairment of sensation, position and passive movement, temperature, pain and touch being affected in this order. Defective sphincter control often precedes and sometimes follows sensory loss.

Motor symptoms.—Interruption of the pyramidal tracts produces spastic paraplegia in parts below the lesion. The clinical features are—(1) diminution of voluntary power; (2) alterations in the amount and distribution of muscle tone and in the attitude of the limbs; (3) changes in the tendon and skin reflexes; (4) the occurrence of certain involuntary and reflex movements.

The phenomena of spastic paraplegia have been analysed by Walshe as follows:—It is essential to remember that the muscles of the lower limb are divided into two distinct groups—the flexors and the extensors—and that the muscles which dorsiflex the foot and toes are physiologically flexors, while the corresponding plantar flexors are extensors. In all that follows these important muscles will be grouped according to this nomenclature.

1. Loss of voluntary power varies from slight weakness of one group of muscles to complete paralysis of both limbs, and depends on the degree of damage to the pyramidal tracts. It usually begins in the distal segments of the limb, and is greater in the flexors than in the extensors. Dorsiflexion is the earliest and remains the most severely impaired movement.

2. The tone in all the muscles increases early, and is greatest in the extensors. Hence an early symptom is generally stiffness of the limbs, especially a difficulty in flexing them. If the limbs are handled passively, the resistance to flexion is found to be greater than to extension. As power diminishes spasticity increases, until at length the limbs are held constantly in an attitude of complete extension. This combination of weakness and spasticity with extended lower limbs is known as "paraplegia in extension."

3. Exaggeration of the tendon reflexes is a constant early sign. The abdominal reflexes below the level of the lesion and the cremasteric reflexes are lost early. The normal plantar reflex is also lost, and is replaced by a different kind of reflex—Babinski's sign, the " extensor " plantar response.

As the damage to the cord increases, and when certain extra-pyramidal motor tracts are affected, the extensor muscles gradually lose their tone, for which connections with the brain-stem through these extra-pyramidal tracts are essential, while the tone in the flexor muscles, which depends on a reflex arc which is purely spinal, is retained. The result is that the knee- and ankle-jerks, which indicate tone in extensor muscles, are lost while the reflexes from flexor muscles (hamstring-jerks) persist. At the same time, in some cases, the limbs are gradually drawn up by the unopposed action of the flexors. This combination of weakness and spasticity with flexed lower limbs is known as " paraplegia in flexion." At first the flexed position is occasional—flexor spasms—later it becomes constant, but is still due entirely to excess of tone in the flexors. Finally, contractures occur in the muscles, and the deformity becomes permanent. In many cases of compression the stage of paraplegia in extension gradually merges into one of complete flaccidity of all the muscles, without the occurrence of paraplegia in flexion, and all the tendon reflexes are lost.

4. While the limbs are still rigid in extension, the commonest involuntary movement is a spontaneous clonus of the extensor muscles, in which the whole limb trembles as it does when ankle clonus is elicited in a case with marked spasticity. In the later stages, where the extensor muscles are beginning to lose their tone, a new kind of movement appears, in which the limbs are drawn up suddenly from time to time by an involuntary contraction of the flexor muscles—flexor spasms. Further, by appropriate stimulation may reflex movements can be produced in the paralysed limbs. The most important of these is the " flexor reflex of the lower limb." It is elicited most easily by stimulating the outer border of the sole by firm pressure or a pin-prick, and in its complete form consists in flexion of the hip and knee, dorsiflexion of the foot, and an upward movement—so-called extension but physiological flexion—of the great toe. When the damage to the motor tracts is slight, when the limbs are rigid in extension and the movement of flexion is prevented by the hypertonus of the extensors, or when almost all reflex activity has disappeared, the reflex appears in its minimal form. A part of this minimal response is an " extension " of the great toe. The normal plantar response is obtained from the sole alone. The pathological reflex, of which the " extensor " response is a part, may be obtained not only from the sole, but when well developed by stimulating the skin and deeper structures on any part of the lower limb. In the light of this the nature of many reflexes which have been described as isolated signs of pyramidal tract disease, *e.g.* the " extensor " plantar response, Oppenheim's and Gordon's signs, and many others, becomes clear. In all of them a stimulus is applied to some part of the lower limb, and the response is a flexion reflex, whose most obvious component is " extension " of the great toe. It is unfortunate that the term " extensor response " is commonly used to describe a movement which is physiologically one of flexion.

Sensory symptoms.—Sensory loss may appear first in the area supplied by the roots arising from the cord at the level of the lesion, or in parts below.

As a rule motor disturbance is severe before any remote sensory loss is found. In some cases, especially of spinal caries, the limbs are completely paralysed before sensation is affected. The reverse condition, severe sensory loss with slight motor disturbance, does not occur in compression. Remote sensory loss appears first in one of two positions. In most cases the soles first become less sensitive, then the legs, and later the thighs. In a smaller number the loss appears first over the lower sacral segments, and extends upwards in segmental progression. When both sides are equally compressed all forms of sensation may suffer equally; but in most cases position and passive movement, temperature, pain and touch are impaired in this order.

If one side of the cord is more affected than the other the signs are those of a modified Brown-Séquard syndrome with the superficial sensory loss greatest in the limb in which most power is retained, and loss of position and passive movement greatest in the weaker limb. Ultimately, whatever the order of loss at the beginning, as the compression increases, sensation of all kinds is diminished or lost in all parts below the lesion. In exceptional cases the skin in the distribution of the lowest sacral segments retains its sensibility when the loss in all other parts below the lesion is severe. Such a distribution of sensory loss suggests a lesion damaging the more mesial fibres of the sensory path. Occasionally the onset of symptoms in extra-medullary compression is rapid, and severe paraplegia develops in a few days. This is seen most often in cases of sarcoma of the mediastinal or retro-peritoneal spaces where the growth, which has infiltrated one or more vertebral bodies, surrounds the dura and produces œdema of the cord. In cases of rapid onset the limbs are flaccid from the beginning, and the tendon jerks are diminished or lost.

Intradural Compression

When the pressure is equal on both sides of the cord, the symptoms are the same as in extradural compression. If one side is affected before the other, as by tumours growing from a nerve root, the symptoms are at first unilateral, and in many cases spasticity and weakness are confined for a long time to the lower limb on the same side as the tumour. Occasionally alterations in subjective sensation (paræsthesiæ) in the limb of the opposite side precede motor symptoms by a considerable interval, and form the grounds for the patient's first complaint.

At a later stage the following characteristic syndrome appears:

1. A band of sensory loss, on the side of the tumour in an area corresponding to the distribution of the sensory roots arising from the cord at the level of the lesion, often with root pains in the same area.
2. Weakness and spasticity confined to or greatest in the limb on the same side (pressure on the pyramidal tract).
3. Diminished sensibility to temperature, pain, and touch on the opposite side (pressure on the crossed sensory tracts).
4. Impairment of the sense of position and passive movement in the weaker limb (pressure on uncrossed sensory tracts in the posterior columns).

As the compression increases both limbs become weak, spastic, and insensitive, and the symptoms progress as in extradural compression. Examination of the cerebro-spinal fluid often reveals a condition which is practically

pathognomonic of compression—*the loculation syndrome* of Froin. This consists, in its complete form, in an increase in the amount of albumin with absence of or slight increase in the number of cells, and a yellow colour (xanthochromia) in the fluid. The normal amount of albumin is about 0·025 per cent. In compression it is often increased a hundredfold or more, and readings above 1 per cent. are very common. A low cell count and 0·1 per cent. of albumin are very strong evidences of compression, and as the amount increases the diagnosis becomes more certain. Xanthochromia is common; but it occurs in other conditions, and its value as a sign is slight. These changes are found in the fluid only below the site of compression.

Diagnosis.—A complete diagnosis establishes: (1) the existence of compression; (2) its situation; (3) its pathological nature.

1. When signs of injury to the cord or nerve roots are found associated with disease of the spine at a compatible level the diagnosis is obvious. What root pains are the only symptom the diagnosis is difficult. They are often falsely interpreted as referred pains, or as indications of disease in the painful part itself. Thus angina pectoris, gall-stones, pleurisy, renal colic, hip-joint disease and other painful conditions have been diagnosed, and unnecessary operations have been performed. Pain of root distribution should always arouse suspicion, and provoke a careful examination of the spine and of the nervous system.

If the signs are those of spastic paraplegia, spinal syphilis, disseminated sclerosis, syringomyelia and amyotrophic lateral sclerosis must be excluded. *In many cases this can be done by examination of the cerebro-spinal fluid.* Patients with removable spinal tumours are still allowed to develop incurable paralysis because this examination is not made. Such an omission in a case of paraplegia of doubtful origin amounts to neglect. The loculation syndrome in the fluid is almost pathognomonic. It is never absent in chronic cases, and is never found in any of the focal or system diseases, for which compression might be mistaken.

Spinal syphilis is detected by examination of the blood and cerebro-spinal fluid. Valuable time may be lost, however, or an irretrievable error made, when the blood of a patient with a removable tumour happens to react positively to Wassermann's test. In a series of cases operated upon by Sargent at the National Hospital, the reaction was positive in four patients from whom a non-syphilitic tumour was removed.

Disseminated sclerosis may present the picture of progressive spastic paraplegia with considerable sensory loss, and confusion between it and compression by slowly growing tumours is common, each disease being mistaken for the other. The more serious error is to mistake the curable for the incurable disease. It is advisable to feel dissatisfied with the diagnosis of disseminated sclerosis, so long as the symptoms are purely spinal, and to re-examine the patient at intervals in the hope of finding evidence of a simple tumour. The transient nature of the early symptoms and the presence of signs of cranial nerve troubles serve to distinguish disseminated sclerosis in most cases. Slight nystagmus must not be accepted as decisive evidence against tumour, as it may be present in compression, especially of the cervical region.

Amyotrophic lateral sclerosis simulates compression in the cervical region, in that wasting in the muscles of the hands and arms is associated with

signs of spastic paraplegia in the lower limbs; but is distinguished by exaggeration of the tendon reflexes in the wasted arms, by fibrillary tremors in the muscles, and by the absence of objective sensory disturbances.

Syringomyelia is easily recognised by the characteristic sensory changes. Dissociation of sensation to the degree which is common in this disease is never seen in extra-medullary lesions.

2. SEGMENTAL DIAGNOSIS.—As the motor sensory and reflex functions of each segment of the cord are known, the level of the lesion can be deduced by noting the highest point at which these functions are impaired.

Motor localisation.—Each segment of the cord contains nuclei for several muscles, and most muscles receive nerve fibres from more than one root; but as each muscle seems to have one main root of supply, the weakness, wasting and loss of tone vary in distribution with the segment affected. The muscles which suffer most when the corresponding segment is damaged are named hereunder:

C_4. Supraspinatus, infraspinatus. C_5. Biceps, deltoid, brachialis anticus, supinator longus. C_6. Pronators of forearm. C_7. Triceps, extensors of wrist and fingers. C_8. Flexors of wrist and fingers. D_1. Small muscles of the hand. $D_{2\text{-}10}$. Intercostal muscles. $D_{7\text{-}12}$. Muscles of abdominal wall. D_{12}-L_4. Ilio-psoas (mainly L_2). L_2. Adductors of thigh. L_4. Abductors of thigh, extensors of knee. L_5. Hamstrings. S_1. Glutei—calf muscles. S_2. Anterior tibial muscles—peronei—small muscles of foot.

Wasting of the muscles in an intercostal space is a valuable guide, as the muscles of each space are innervated from one segment alone. If the lesion is at the level of the ninth dorsal segment the rectus abdominis is paralysed below a point about an inch above the umbilicus. In such a case, when an attenpt is made to raise the head against the resistance of a hand placed on the forehead when in the supine position, the upper part contracts and the umbilicus is drawn upwards (excursion of the umbilicus). If the lesion is at the twelfth dorsal segment the entire rectus contracts, but the iliac regions bulge, owing to paralysis of the lower part of the oblique muscles.

Localisation by changes in the reflexes.—Above the lesion the reflexes are normal, at its level they are diminished or lost, below it the skin reflexes are diminished or lost, and the tendon reflexes are exaggerated. The segments on which important reflexes depend are:

C_5. Biceps- and supinator-jerks. C_6. Pronator-jerks. C_7. Triceps-jerks. $D_{7\text{-}12}$. Abdominal reflexes. L_1. Cremaster reflexes. L_3. Knee-jerks. S_1. Ankle-jerks. S_1. Plantar reflexes.

In lesions involving the fifth cervical segment of the cord, such as may be found in syringomyelia and in injuries associated with dislocation of the cervical spine, Babinski has recorded that the supinator jerk may be abolished and replaced by finger flexion when the lower end of the radius is tapped. This is known as "inversion of the radial reflex," and is a useful localising sign in lesions of the segment in question.

Sensory localisation.—The sensory areas supplied by each segment of the cord are shown in the diagram on the opposite page. Root pains in the distribution of one or more of these areas form a sure guide to the affected segment. When they are absent, the level of the lesion is determined by ascertaining the highest point at which sensation is impaired. Very often when

the two sides of the cord are compressed unequally the anæsthesia is confined to one side, or extends higher on one side than on the other. In these cases, when the segmental diagnosis is made from the sensory signs alone, the lesion, a tumour for example, is found several segments higher than the point indicated by the signs. The uppermost limit of sensory loss in these circumstances is a result of interruption of the sensory paths in the cord, and the discrepancy in the signs is due to the oblique course taken by the sensory fibres in crossing the cord. In the mid-dorsal region the decussation for pain and temperature is complete one segment above the point of entry of the root conveying these impressions to the cord, that for touch in two segments. At higher levels, crossing takes place more slowly, until in the upper cervical region impulses which enter together in one root ascend on the same side of the cord for five or six segments before all of them reach the opposite side. At all levels pain crosses soonest, then cold, then heat, and touch slowest of all.

It follows that in unilateral lesions the upper level of the anæsthesia on the opposite side of the body, caused by injury to sensory paths in the cord, is below the segmental level of the injury. Also that the level is higher for one form than another. The fibres which cross slowly escape by ascending beyond the lesion on the uninjured side before they cross, while those which cross quickly are caught after crossing. Hence the level of sensory loss is highest for pain and lowest for touch, with temperature intermediate. Occasionally the tumour is found below the level predicted. In these cases the functions of the segments above the lesion are impaired by œdema.

Surface anatomy.—If the cord is to be exposed at the level of the affected segments their relation to the spinous processes of the vertebræ must be known. This is obtained as follows: In the cervical region to the number of the spine add 1—the fifth cervical spine lies over the sixth cervical segment; to the number of the upper five dorsal spines add 2—the fourth dorsal spine lies over the sixth dorsal segment; down to the tenth dorsal spine add 3—the tenth dorsal spine covers the first lumbar segment. The eleventh dorsal spine corresponds to the third lumbar segment, and the twelfth to the first sacral. The cord terminates just above the level of the first lumbar spine.

Intrathecal injection of lipiodol.—The upper level of a lesion which narrows or obliterates the lumen of the spinal canal, or simply blocks the spinal subarachnoid space, can be ascertained by injecting lipiodol through the occipito-atlantoid ligament into the subarachnoid space, the lipiodol falls rapidly to the point of constriction, where it is arrested and can be seen clearly by X-rays. If there is no constriction it falls to the bottom of the thecal space, where it remains indefinitely and does no harm. This procedure is of great practical value when the existence of a compressive lesion or its exact site is in doubt.

3. Diagnosis of the Cause of Compression.—When spastic paraplegia develops in a patient who is known to suffer from *spinal caries*, the cause is obvious; but when it precedes the appearance of signs of bone disease the diagnosis is difficult. In all cases of compression the spine must be examined repeatedly for deformity, tenderness and limitation of movement. If tenderness is found constantly in the same place, and the nervous symptoms are compatible with disease of the underlying segments, disease of the bones is

almost certain. In young persons disease of the spine is usually caries, and in adults caries is also the commonest cause; but tumours of the spine and aneurysm must be excluded. Severe root pains are rare in caries but are the rule in vertebral new-growths. An aneurysm would present other signs.

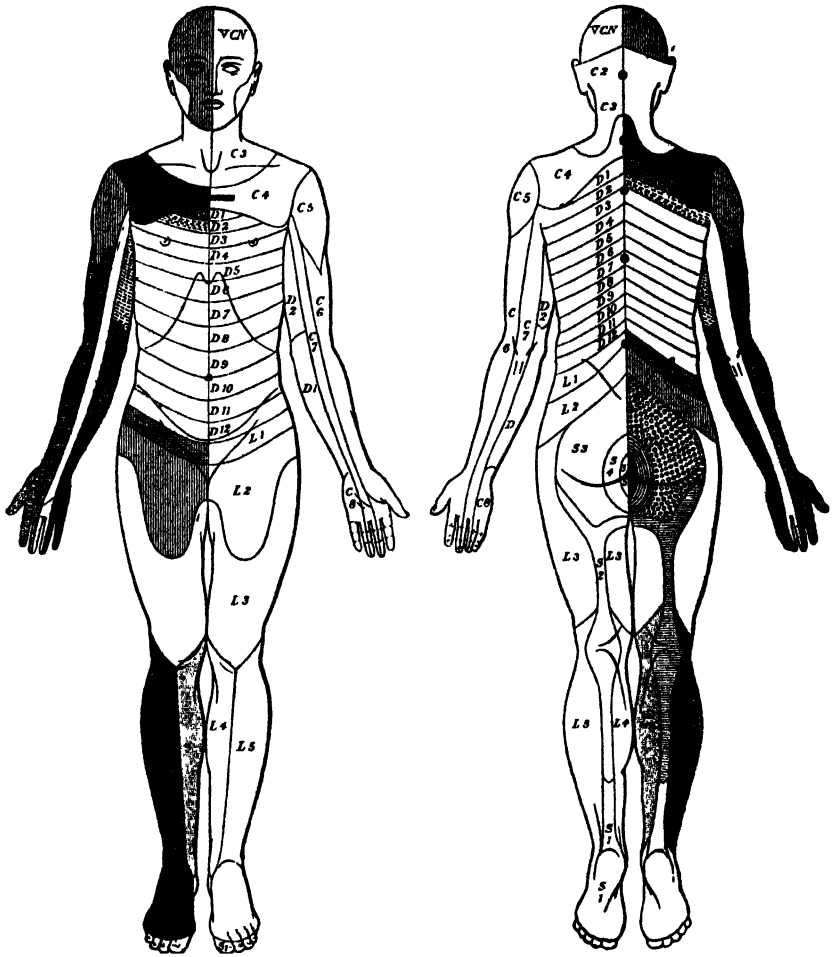


FIG. 99.—Diagram of cutaneous areas of posterior nerve roots (after Collier and Purves Stewart).

An X-ray picture will usually demonstrate the presence and nature of the bone disease.

Vertebral tumours.—When root pains occur in a patient with malignant disease, or from whom a malignant growth has been removed, the diagnosis is clear. Mistakes are easily made when pains are the first symptom, as their

root origin is not recognised. Diminished sensibility in the painful area indicates the nature of the pain, and this directs attention to the spine, where tenderness or deformity is discovered. As most vertebral tumours are secondary, the next step is to examine the parts where carcinoma is common, remembering that a small primary growth, *e.g.* in the breast, thyroid or prostate, may give rise to widespread metastases in the bones. In the absence of a history or signs of new-growth in other parts, the diagnosis is founded on the combination of local tenderness or deformity and rigidity of the spine with root or cord symptoms. The severity of the root pains, and their great aggravation by movement, are characteristic.

Meningeal tumours.—Severe pain of root distribution is present in many cases, and when this is followed after some time by spastic paralysis of slow onset and steady uninterrupted progress, affecting first one leg and then the other, the combination and especially the course of the symptoms are almost pathognomonic. In caries the root pains are rarely severe, signs of bone disease are rarely absent, the paralysis is usually bilateral from the beginning, and is severe before any sensory loss is found. The distinction from vertebral new-growth may be impossible when the latter occurs without bone symptoms or X-ray signs. Practically the diagnosis between meningeal and intramedullary tumours is impossible. If the signs and symptoms in any case are those of compression, and an approximate indication of the level of the lesion can be given to guide the surgeon, then, if other obvious causes such as caries, aneurysm and vertebral tumour have been excluded, an operation must be performed. Until the lesion can be seen the diagnosis is in doubt.

Course and Prognosis.—*Spinal caries.*—The course of the bone disease does not always run parallel with the paralysis, and either may alter in severity independently; but if the caries undergoes cure the paralysis usually diminishes. Considering the severity of the paralysis, the prognosis is favourable and astonishing recoveries occur. The outlook is best in young people with disease in the dorsal region. Many recover completely, but more often, especially in adults, recovery, though considerable, is partial. So long as the lower limbs remain spastic in the extended position with exaggerated tendon reflexes the prognosis for complete recovery of power is good; but if the limbs become flexed, if they become flaccid, if the knee- and ankle-jerks are lost, if sensory loss is severe, or if there is wasting in the limbs following damage to lower motor neurones, the outlook is very bad. Many patients live for years with severe paralysis; but life is constantly endangered by sepsis from bed-sores, ascending infections of the urinary tract, chest complications, and tuberculous disease in other parts.

Vertebral tumours.—When sarcoma or carcinoma spreads to the vertebræ from surrounding parts the duration of the disease is measured in weeks or months, and death is due to the primary condition. In primary sarcoma, and in some cases of carcinoma of the vertebræ, life may be prolonged for a year or two, and death is due rather to complications of the cord disease—bedsores, cystitis, etc.

The course of *tumours of the meninges* is often extremely slow. Root symptoms may precede paralysis by months or even years, and the weakness may increase gradually for several years before walking becomes impossible. Malignant growths are fatal, and simple growths equally so, if not removed. Most patients with simple tumours come to operation during the second

year after the onset of the first symptom. The mortality after operation for the removal of simple tumours is very low in skilled hands. The prognosis for recovery of power depends in part on the duration of the weakness in the lower limbs. Complete recovery may be expected if it has not lasted more than a year, and if sphincter control has not been lost. When the paralysis is of longer duration recovery, though gratifying, is rarely complete. Nevertheless, full return of power has been seen after three years of severe paralysis.

Treatment.—*Spinal caries.*—This is to be directed to curing the bone disease in the hope that cure of the paralysis will follow. Complete rest on the back and fixation of the spine for many months is the routine treatment. The general condition of the patient is to be improved by fresh air, a liberal diet and cod-liver oil, iron and arsenic, and great care is to be taken to prevent bedsores, cystitis and deformities of the limbs. For adults, especially if they are bread-winners, a more rapid cure is desirable. This is provided by surgery in Albee's operation, or a modification thereof, in which a bone graft from the tibia is wired into a cleft made in the spines of the affected region. In this way fixation is effected, further deformity is prevented, and the time lost is reduced from a year or more to a few months. Adults sometimes recover after a short rest in bed, if a suitable jacket is worn to immobilise the spine.

Operation must be considered—(1) when a sudden increase of deformity or severe root pains and great increase of paralysis come on together, and suggest pressure by displaced bone; (2) when an abscess forms; (3) when paralysis persists long after the bone disease is cured, or when in an adult there is no improvement after 6 months' rest; (4) when life is endangered by respiratory paralysis.

Vertebral tumours.—In slowly growing primary growths of the vertebræ laminectomy is indicated to relieve pressure, or to prevent pain by cutting sensory roots or dividing the antero-lateral columns of the cord. The operation is merely palliative, but is often followed by considerable temporary recovery.

Meningeal tumours.—If the symptoms suggest an intraspinal tumour, and a segmental diagnosis has been made, an exploratory laminectomy should be done in the hope of finding a removable tumour.

2. COMPRESSION OF RAPID ONSET

Ætiology.—The commonest causes of rapid compression are fracture or dislocation of the spine.

Dislocations occur most often between the atlas and axis, or between the fifth and sixth cervical vertebræ. They are sometimes incomplete, and thus may cause compression of slow onset. More often they are complete, and the cord is compressed between the laminæ of the dislocated vertebra, which is displaced forwards, and the body of the underlying vertebra. Fractures are commonest in the lower dorsal and upper lumbar regions, and follow most often a fall from a height on to the feet or buttocks. They also occur apparently spontaneously in spinal caries and in vertebral tumours. A blow on the back may fracture the vertebral arches, and cause compression of the cord. The degree of damage to the cord varies greatly.

Symptoms.—Sudden severe compression produces a complete interruption of conduction through the damaged segments; that is, a physiological transection of the cord. There is total flaccid paralysis, total sensory loss, abolition of tendon reflexes, and retention of urine. For a few days there may be no plantar response, but a Babinski response then makes its appearance. Bedsores often develop with great rapidity, and many patients succumb within a few weeks. But in those that survive, retention of urine gives place to overflow incontinence, the tendon jerks may return, and the condition described above (p. 1718) as "paraplegia-in-flexion" may ensue. In this case, any stimulus applied below the level of the lesion produces violent flexion spasms in the legs, contraction of the abdominal wall, and the expulsion from the bladder of some—but not of all—its contents. Head and Riddoch have applied the term "mass reflex" to this phenomena.

Dislocations between the fifth and sixth cervical vertebræ may produce severe damage to the cord as described above, with the addition that the arms are paralysed also, the sympathetic pathways in the cord are interrupted, and there is narrowing of the palpebral fissures, and sometimes priapism. Less well-recognized are the various clinical pictures of minor injury to the cord as the result of vertebral injury. These include slight weakness, with ensuing wasting of the hands and forearms, slight spastic paresis of the legs, with the corresponding changes in the reflexes, narrowing of one or both palpebral fissures, and inversion of the radial reflex on one or both sides. There may be no sensory loss after the first two or three weeks. The slow progress of the wasting in the arms for some time after the injury may lead to a diagnosis of amyotrophic lateral sclerosis, but care in examination and history-taking should prevent this error.

Prognosis.—The prognosis is always extremely grave in severe cases, death resulting in high cervical lesions from paralysis of all the muscles of respiration, in lesions at lower levels from sepsis following bedsores, or from infection of the urinary tract.

Treatment.—When the signs are those of complete division of the cord, treatment by operation is directly contra-indicated. If some voluntary power is retained, or if sensory loss is not absolute, operation may be considered, especially if the compression is caused by fracture of the vertebral arches. The cord should be exposed in every case where the level of the fracture points to injury of the cauda equina. These roots being peripheral nerves have a chance of regenerating, and this may be enhanced by freeing them from compression by displaced fragments of bone. With skilled nursing, patients with complete division of the cord may survive and live for many years.

General Management of Paraplegia.—In all cases of severe paraplegia from spinal cord lesion where sensory and sphincter functions are also impaired or lost, whatever the nature of the lesion, there are certain general principles of treatment. The patient should be nursed on a fracture bed with an air, water, or rubber mattress. The back should be attended to four hourly, first washed with soap and water, then carefully dried, rubbed with surgical spirit or eau-de-Cologne, and powdered. These measures harden the skin and make it less likely to break down under the constant pressure of the body weight. The patient's position should be changed from time to time to prevent the development of sacral bedsore. As far as possible

care should be taken to prevent the skin from becoming wet and sodden when there is incontinence of urine, and the toilet of the anus after defæcation should be careful and thorough. There are various remedies for the sacral or trochanter bedsore when it develops. Separation may be hastened by wet dressings of eusol, sometimes by fomentations—though the latter should be used with caution. The ulcer is packed with eusol gauze, or with an ointment of zinc oxide and castor oil. When it is clean and healing begins, it may sometimes be hastened by dressings of gauze soaked in red lotion. The heels should also be carefully watched for the appearance of the hæmorrhagic blisters which herald the development of a sore. Rings for the heels may avert them, and air rings for the sacrum may also be needed.

SYRINGOMYELIA

Synonym.—Slatus Dysraphicus.

Definition.—Syringomyelia is a very chronic and irregularly progressive disease of the spinal cord and brain stem, dependent upon a peculiar lesion of the grey matter, glial increase and the formation of irregular cavities being the most conspicuous features of this lesion. Clinically, the malady is characterised by a deep loss of sensibility to pain and to temperature, other forms of sensibility remaining relatively unaltered, and by muscular atrophy and weakness of varying distribution in the upper extremities, and further by spastic weakness of the lower extremities, owing to involvement of the pyramidal tracts at the level of the lesion.

Ætiology.—Both sexes may be affected, and males are more prone to suffer than females. Heredity plays no part in its causation. Age is most important, in that this disease appears either to be congenitally installed, or to commence during the period of growth. It has been diagnosed with accuracy as early as the sixth year of childhood, and rarely if ever do the symptoms commence later than the age of 30 years.

Pathology.—The primary lesions of syringomyelia are always found in that region of the spinal cord which was originally occupied by the central canal, or in close connection with the ventricular system of the brain stem; and it is certain, therefore, that syringomyelia is referable to a pathological process affecting the central canal and its surrounding glia, and that this pathological process, in many cases at least, is installed before the completion of the development of the central canal of the nervous system. Two essential lesions and four other commonly occurring lesions make up the morbid process of this disease:

Essential lesions.—(1) Cavitation of the posterior part of the grey matter; (2) gliosis, with liquefactive degeneration of the abundant glia—*other lesions commonly but not invariably present*; (3) degeneration of lower motor and vasomotor neurones; (4) degeneration of lower sensory neurones; (5) distension of cavities producing pressure effects; (6) secondary ascending and descending degenerations.

The seat of commencement of the disease is invariably in the dorsal grey matter of the lower half of the brain stem and upper half of the spinal cord, and most commonly of all, in the lower three cervical and upper three dorsal segments. The cavitation occurs primarily always in that part of the grey

matter which held the original central canal, namely, the region of the posterior commissure, posterior median septum and posterior horns.

Degeneration of the lower motor neurones occurs in at least half the cases. It is most marked in the cervical and upper dorsal regions of the cord, and may be very local or extensive. It is commonly explained as caused by the extension of the gliosis and cavitation into the anterior horns of the grey matter, and by the distension of the cavities exerting pressure upon these regions, and causing atrophy of the cells. To the pressure exerted by such distended cavities are also attributed the ascending and descending degenerations which are commonly found in the pyramidal tracts below the level of the lesion, and in the posterior columns above.

Tumour formation is not uncommon in cases of syringomyelia. Massive growth may be found in the pons and in the spinal cord.

Symptoms.—*Disturbances of sensibility.*—By far the most constant and characteristic feature of syringomyelia is a sensory loss of a peculiar kind which was named by Charcot "the dissociated sensory loss." This is a loss of sensibility to painful impressions and to thermal stimuli, while sensibility to touch, to vibration, to position, to passive movement and to the appreciation of location upon the skin, remain relatively or entirely intact. In other words, those forms of sensibility which travel by a path crossing in the commissures of the spinal cord are lost, because the lesion of syringomyelia destroys especially the region of the commissures, while these forms of sensibility which travel by paths which are uncrossed in the spinal cord and do not traverse the region especially affected by syringomyelia, but are conducted by the posterior columns, are not affected. Further, the lateral region of the dorsal reticular formation of the medulla, mesial to the restiform body and ascending root of the fifth nerve, and a little ventral to these structures, is especially prone to the lesion of syringomyelia, and it is this region which contains the whole path for pain and temperature sensibility from the opposite half of the body, and a lesion in this situation will produce hemianalgesia and hemithermanæsthesia, while the paths for other forms of sensibility, situated mesially on either side of the raphé of the medulla, escape. Again, the lesion excavating the ventral horn in any part of the cervical region may extend so as to interrupt the spinothalamic tract which lies immediately dorso-lateral to the ventral horn, and so cause loss of pain and temperature sense on the opposite side everywhere below the level of the lesion.

The destruction of the commissures in the lower cervical and upper dorsal regions produces the dissociated sensory loss symmetrically over the thorax, upper extremities, neck and face, the distribution varying with the extent of the lesion. The sensory loss over the face is explained in that the sensory root of the trigeminal nerve has its ending in the upper three segments of the cervical spinal cord, and the pain and temperature sensibility of the face is interfered with if the posterior grey commissure in the region of these segments is damaged. Only rarely does the symmetrical sensory loss extend below the thorax, for the reason that the spinal lesion does not often extend below the mid-dorsal region. The sensory loss will vary in depth, extent and symmetry of distribution according to the completeness, extent and symmetry of the lesion. Thus, in early and slight cases, the sensory disturbance may not amount to more than a relative loss of pain and temperature confined to the

hands and ulnar borders of the forearms, while in an advanced case there is usually complete inability to appreciate painful and thermal stimuli over an area which would be covered by a sleeved jacket, and this area often extends over the neck and the face. Combinations of the "sleeved jacket" sensory loss with hemianalgesia and hemithermanæsthesia often occur in cases where both the spinal lesion and the medullary lesion are present. The dissociated sensory loss makes its advent insidiously, and is often unnoticed by the patient and discovered for the first time on medical examination. Or it may appeal to the patient, who on bathing finds that he appreciates heat and cold upon some parts of the skin and not on others. Not infrequently he finds that he injures himself or burns himself without noticing it at the time.

Subjective sensibility is not often affected, and for the most syringomyelia may be described as a painless disease; but there are very notable exceptions. Sensations of heat and cold, dull fixed pains, lasting neuralgic pains, and lightning pains in no way differing from those of tabes, may occur. These pains are confined to the regions which are the seat of the other symptoms. Especially important in this connection are those cases in which the distension of the cervical spinal cord is so great as to cause that structure to press upon the bones of the spinal canal. Here constant and often intolerable aching pain in the neck, upper extremities and thorax may result, with rigidity of the neck, and this may render life so insupportable as to necessitate surgical interference for the relief of the pressure.

Muscular atrophy.—This common clinical feature of syringomyelia is met with in considerably more than half the cases. As may be gathered from the nature of the lesions, though usually bilateral, it is often not symmetrical, and may be entirely confined to one side. The intrinsic muscles of the hands and the muscles of the ulnar side of the forearms are first and most affected in the ordinary run of cases. The atrophy is often here confined, but it may extend up the arm; but it is unusual for the whole upper limb to be affected. Sometimes the shoulder muscles are first affected, and again the scapulo-thoracic and humero-thoracic muscles may be early involved. The upper intercostals, and that section of the muscles which supports the spine, supplied from the upper six dorsal segments suffer, but the scalenes seem generally to escape. The muscular atrophy is strictly limited, and is apt to become complete in the muscles affected. The lesions of the medulla may involve the motor nuclei of the cranial nerves. Atrophic paralysis of the muscles supplied by the vago-accessory nerve is far from uncommon, and the discovery of this paralysis in a young subject should always arouse suspicions of the presence of syringomyelia. The paralysis is unilateral and involves palate, pharynx and all the muscles of the larynx upon the affected side. Similarly but in much rarer cases, atrophic paralysis of the face, of the trigeminal muscles, of the sternomastoid and trapezius or of the hypoglossal muscles may occur from a unilateral involvement of the corresponding motor nuclei. Fibrillation in the affected muscles is said by most writers to be of common occurrence. It has been conspicuous by its absence in most of the large number of cases which have come under our observation. One would expect it to be confined in syringomyelia to such times as the muscular atrophy is progressing.

Contractures resulting from the muscular atrophy are commonly seen in the hands, and the deformity resulting tends towards the "griffin's paw"

type, but hardly reaches the degree seen in ulnar nerve paralysis, and is often much modified by trophic and vasomotor changes, and by the results of injuries and whitlows.

The lower extremities escape so far as atrophy of muscles is concerned. Spinal curvature is present in many cases. It consists essentially in a kyphosis or kypho-scoliosis of the upper dorsal region, with a compensatory lordosis and lateral curve in the lumbar region. The upper convexity is to the left from the major use of the right hand. It is dependent upon paralysis of the trunk muscles, from involvement of the anterior horns in the upper dorsal region, and, in addition, dystrophic changes in the bones may be factors in its production. It is more marked the earlier it commences during the period of growth, and where heavy manual occupation has been followed.

Trophic and vasomotor disturbances.—Thickening of the bones or a condition of osteoporosis and brittleness may be met with. More often Charcot's arthropathy occurs. It differs in no way from the similar condition in tabes dorsalis, and is confined to the joints of the analgesic region, and affects the joints of the lower extremity only when there is a hemianalgesia from a lesion of the spinothalamic tract either in the cord or in the medulla. In syringomyelia Charcot's joints are seen chiefly in workmen who are engaged in occupations which constantly expose the analgesic joints to jarring and bruising.

The most characteristic of the trophic changes consists in thickening of the subcutaneous tissue and of the skin itself, which is seen in the hands. The fingers become thick and swollen and lose their natural outline, the tips become blunted, and the knuckle-folds thick and coarse, and some vasomotor paralysis renders them unduly red, or even blue. They have been termed " sausage-like " fingers, and often stand out in contrast to the wasting of the intrinsic muscles of the hand. A similar condition affecting the whole hand is common, and was termed by Charcot the " fleshy hand " or " main succulente." The analgesic condition of the hands and the thermanæsthesia present expose them unduly to injuries and, since these injuries are likely to be unnoticed or disregarded, septic infection arises easily, and the results of injuries, burns and whitlows are frequently seen, giving rise to further deformity from scars, loss of the terminal phalanges, from whitlows and contractures, and from sepsis extending to the tendons.

The lower extremities usually present a slight spasticity, with the signs of involvement of the crossed pyramidal tracts. This does not often produce much disability in the use of the lower limbs. In cases, however, where the lesions involve the lateral regions of the cord, either by direct extension or by the pressure of distended cavities, severe spastic paraplegia may result. And again, in very rare cases, such pressure may lead to total evascularisation and total transverse lesion of the spinal cord with the appearance of a complete flaccid paraplegia with incontinence, total sensory loss and absent deep reflexes.

Sphincter trouble is usually absent, or slight and occasional; but in cases where paraplegia is severe any degree may occur.

The skin reflexes of the trunk are diminished or absent, and the plantar reflexes are of the extensor type, according to the degree of pyramidal involvement. Some degree of pes cavus is often present. The knee-jerks and ankle-jerks are increased, and foot-clonus, etc., is present.

Considering that the efferent neurones of the cervical sympathetic system have their origin in the brain stem, and their exit from the spinal cord in the lower cervical and upper dorsal segments, thus traversing the whole of the region usually affected by the lesion of syringomyelia, the frequency with which paralysis of the cervical sympathetic occurs is easily understood. It may be complete or incomplete, unilateral or bilateral, and is recognised by smallness of the pupil, narrowing of the palpebral aperture (sympathetic ptosis), and a peculiar flatness of expression on the side of the face affected, with decrease or loss of sweating. These signs are much more obvious when unilateral than when bilateral, for, in the absence of the contrast which a normal side of the face gives, they are often overlooked when bilateral.

Ophthalmoplegia is very rare, but it may occur, since the syringomyelia lesion may be found as high as the region of the third nucleus. Nystagmus is an almost constant feature of syringomyelia, as it is also of most lesions of the cervical spinal cord.

Morvan's Disease.—This variety of syringomyelia is so peculiar in its clinical aspect as to need especial description. In addition to the lesion of the spinal cord characteristic of syringomyelia, there are intense changes in the periphery of the nerve trunks of the limbs. Instead of the usual loss of pain and temperature sensibility, distributed in jacket form upon the upper limbs and trunk, there is absolute loss of all forms of sensibility in the hands, wrist high, and in many cases also in the feet, ankle high. Progressive atrophy of the intrinsic muscles of the hands and feet occurs. Severe vasomotor paralysis brings about permanent cyanosis of the hands and feet, with much thickening of the skin and subcutaneous tissues, to which are added the effects of injury and septic processes in insentient regions, in the form of whitlows, necrosis and loss of digits. Another peculiarity of this malady is that the extremities are exceedingly painful in the early stages and until the sensory loss becomes deep. Morvan's disease resembles Raynaud's disease in the cyanosis and tendency to necrosis of the fingers and toes, but it is easily distinguished by the complete absence of intermitting vascular spasm and by the peculiar loss of sensibility. Anæsthetic leprosy may be distinguished from Morvan's disease by the characteristic skin lesions in other parts of the body, by the palpable thickening of the nerve trunks, and by the less definitely limited areas of sensory loss. Every transition between typical syringomyelia and Morvan's disease has been described.

Course and Duration.—The malady, commencing insidiously, progresses very slowly, and often ceases to progress for periods which may amount to many years. The tendency to the destruction of life is not great; but when rapid extension of the physical signs, and especially of paralysis and muscular atrophy of the upper extremities and respiratory muscles, occurs, the end is likely to come quickly. Signs of great distension of the cavities, such as pain and rigidity of the neck, and also severe and increasing paraplegia, with sensory loss of all forms of sensibility below the level of the lesion, point to a rapidly fatal termination.

It is not unusual to meet with well-marked cases in which the signs develop and increase during late childhood and early adult life, and then remain more or less in a stationary condition, allowing an occupation to be followed until well after middle life has been reached; but with the advent of the degenerative period of life, from the age of 45 years onwards, there is

always a slow increase of the disability which puts an end to useful capacity. Many of the cases become incapacitated in early life, after which the disease becomes arrested, and the patients live on for many years, sometimes in a bedridden condition. Few reach the age of 60 years. Rapid extension of the physical signs leads to death from involvement of respiratory muscles. Otherwise the patients succumb to intercurrent disease. Sudden and unexpected death sometimes occurs, and it is especially to be remembered that this is likely to occur after the administration of anæsthetics, and as a result of surgical procedures.

Diagnosis.—Syringomyelia has to be differentiated, in its early stages, from those diseases which cause slowly progressive muscular atrophy in the upper extremities, and, in its later stages, from other lesions of the central region of the spinal cord. Those cases in which the lesions are chiefly in the ponto-medullary region must be distinguished from other slowly oncoming lesions of the brain stem.

The age of onset, during the later years of childhood and the earlier years of adult life, is important, and during this period slowly developing paralysis, with or without muscular atrophy and with sensory loss, should always suggest the possibility of syringomyelia. Other causes, which may produce this symptom group, and which may be confused with syringomyelia, are local lesions of the peripheral nerves, local lesions of the brachial plexus, and, especially, the lesion produced by the presence of cervical ribs, root lesions, lesions of the central grey matter of the spinal cord, especially central tumours of the spinal cord, hæmatomyelia, and lastly certain general diseases of the nervous system, progressive muscular atrophy, peroneal atrophy and myotonia atrophica. That the sensory changes of syringomyelia of peculiar nature are usually the first signs of that disease is important; but unfortunately is not without many exceptions, both as to the nature of the sensory changes and as to their time of appearance.

Local lesions of the peripheral nerves produce signs which are confined to the distribution of the nerve involved; the sensory loss is to all forms of sensibility, and the condition is commonly unilateral. In syringomyelia, however, the lesion in the early stages may be confined to one side of the cord, and to one posterior horn so far as the production of sensory loss is concerned, and the muscular atrophy may be so narrowly confined to the distribution of the ulnar nerve as to cause close resemblance between the two conditions. Any sensory loss over the trunk, or signs outside the distribution of the peripheral nerve, will, if present, clearly divide the two conditions.

Cervical ribs may produce slowly progressive atrophy of muscles, pains and sensory loss, very difficult to distinguish from those resulting from syringomyelia. The diagnosis in these cases is beset with peculiar difficulties, for so frequently do cervical ribs produce no nervous symptoms at all that their presence, when demonstrated, does not argue that they are the cause of the symptoms. Again, cervical ribs are among the commonest of the developmental peculiarities which are so frequently seen in the subjects of syringomyelia. Slow muscular atrophy and slowly oncoming sensory loss and perhaps pain characterise both syringomyelia and cervical rib paralysis, and the distribution may be unilateral or bilateral in either condition; but it is only when the signs and symptoms are strictly confined to the upper

extremities and neck that difficulty arises. The slightest definite physical sign outside of this region at once turns the diagnosis in favour of syringomyelia, and of these signs cervical sympathetic paralysis, sensory loss on the trunk, and alteration of the abdominal and plantar reflexes are most important. A very careful search must be made for any such signs, and the patient observed over a considerable time before a certain diagnosis is made.

Lesions of the nerve roots, either from inflammatory conditions, bone disease, pachymeningitis or neoplasms give rise to more severe pain than does syringomyelia, and the development of the symptoms is much more rapid. Lesions of the central grey matter of the spinal cord may produce a symptom complex, closely resembling that of syringomyelia. Central tumours of the spinal cord, when of slow growth, are hardly distinguishable, inasmuch as the lesion of syringomyelia is in reality a central tumour of the cord. The majority of central tumours, however, are of more rapid development, and speedily produce severe paraplegia. The presence of Froin's syndrome (hyperalbuminosis in the cerebro-spinal fluid) is much in favour of tumour.

Progressive muscular atrophy in its early stages may cause difficulty in diagnosis, since the muscular atrophy in syringomyelia may in rare cases precede the appearance of any sensory loss or may be well marked when the sensory loss is slight. In this connection widely distributed fibrillation is of great importance in indicating a diagnosis of progressive muscular atrophy, particularly if it be seen in muscles not conspicuously wasted. In peroneal atrophy the atrophy of the intrinsic hand muscles is always preceded by a more extensive atrophy of the muscles below the knee, which are never atrophied in syringomyelia.

Syringomyelia of the brain stem may be distinguished from other lesions of this region by its insidious onset and the special tendency to the involvement of the lateral region of the medulla containing the vago-accessory nucleus and the central pain and temperature path, so giving rise to a unilateral paralysis of palate, pharynx and larynx with hemianalgesia and hemithermanæsthesia on the opposite half of the body. Often some signs of cervical syringomyelia coexist; but the medullary lesion may exist alone, and it cannot be too prominently borne in mind that any very slowly progressive lesion of the brain stem of insidious onset may be of the nature of syringomyelia.

Prognosis.—Recovery never occurs; but arrest of the disease for long periods is frequent. Those disabilities, which are the result of pressure or distension, may abate spontaneously or as the result of treatment, and in arrested cases training may bring about lessening of the disability. Increasing symptoms, especially if the increase be rapid, are always a cause for anxiety, and increasing involvement of the respiratory muscles is the gravest of events.

Treatment.—Some authorities believe that mercury and iodide of potassium have a definite effect in benefiting the disease when the symptoms are progressing. Application of deep X-rays to the cervical and upper dorsal regions of the spinal cord has been followed by arrest of the progress of the disease and, rarely, improvement of symptoms. Pains are to be relieved with the common analgesics. Massage, exercises and training are all likely to make some improvement in the disability in arrested cases.

HÆMATOMYELIA

Ætiology and Pathology.—Hæmatomyelia, or hæmorrhage into the spinal cord, has in the past figured in neurological literature to a much greater extent than its frequency warrants. It has been commonly supposed, for example, to be an almost invariable consequence of serious local injuries of the cord, whereas in fact in these circumstances hæmorrhage plays a very minor rôle. G. Jefferson has in fact expressed the view that it is doubtful whether such a state as hæmatomyelia actually exists. It is true that small punctate hæmorrhages may be seen in the damaged areas, but as Holmes, from his study of the spinal injuries of warfare, has pointed out, the essential lesion in these circumstances is œdema, followed by degenerative changes in the cells of the grey matter, and in severe cases by central necrosis. Large central hæmorrhages are not found. Similarly, certain inflammatory affections of the cord, such for example as acute poliomyelitis, may show minute hæmorrhages, but here again nothing occurs to which the term hæmatomyelia can reasonably be applied. In short, hæmatomyelia is an exceedingly rare form of spinal cord lesion.

A recent study by C. Richardson made on material at the National Hospital, Queen Square, has lent a necessary sense of proportion to our views on this matter. By the term hæmatomyelia is now usually meant a large central hæmorrhage, with a tendency to spread longitudinally over several segments. The central region of the cord and the dorsal horns are the situations in which this hæmorrhage is commonly observed in the rare instances in which it is to be found. If we agree that traumatic hæmatomyelia is an extremely rare condition, we are left with what has been called "spontaneous hæmatomyelia" and with secondary hæmatomyelia.

Spontaneous Hæmatomyelia.—This rare condition appears to arise only when there is some abnormality of the spinal vessels. Such abnormalities are angioma and other malformations, and—excessively rarely—syphilitic and arterio-sclerotic disease of spinal arteries; in other words, the so-called spontaneous hæmatomyelia is really secondary hæmatomyelia.

Symptoms.—From what has been said it is apparent that the clinical picture usually given of hæmatomyelia is that of local trauma of the cord, and since such local crushing is commonly associated with fracture, fracture-dislocation, or transient dislocation of the cervical spine between the fifth and sixth vertebræ, this picture is that of a quadriplegia of sudden onset with slow recovery of variable degree. True hæmatomyelia may indeed occur in the cervical region of the cord, when it is apt to prove fatal. Richardson's analysis indicates that the characteristic clinical picture is that of a sudden paraplegia, accompanied by pain and sensory changes, subjective and objective. It appears that all forms of sensation are lost at first.

In the non-fatal cases a variable degree of recovery is possible. In a few reported cases, it appears that a syringomyelic type of dissociation of sensation may ensue.

Diagnosis.—The diagnosis of primary hæmatomyelia rests upon the sudden onset, the rapid development of symptoms which soon come to a standstill, and the physical signs of a central lesion of the spinal cord. The

distinction has to be made from acute myelitis. Acute myelitis, though rapid in onset, does not show the sudden development of symptoms seen in hæmatomyelia. Prodromata often precede the onset.

Treatment.—The general treatment is that of any severe spinal cord lesion with paraplegia. When there is evidence that a syphilitic lesion of the spinal arteries is in question, the treatment is that of spinal syphilis. Angioma and other malformations of the spinal vessels are not amenable to surgical intervention.

MYELOMALACIA

Synonym.—Softening of the Spinal Cord.

The term "myelomalacia," which implies softening of the Spinal Cord, has been applied by some authors to those conditions of local destruction of the spinal cord consequent upon the cessation of blood supply, and especially upon thrombosis of its blood vessels, as apart from the extensive local destructions which may result from inflammatory conditions. Such a distinction does not rest upon any logical, pathological or clinical basis, for thrombosis and ischæmia make up a part of the pathological process of all traumatic, inflammatory and pressure lesions of the spinal cord, and may occur as terminal events in certain diseases of the spinal cord where vascular lesions are otherwise conspicuous by their absence. Therefore, since softening of the spinal cord may be the result of widely different pathological processes, and since it does not constitute a definite clinical entity, it will suffice here to refer to those maladies in which it is chiefly observed.

Traumatic Conditions.—As a result of high explosives bursting in the neighbourhood of the spinal column, even without signs of external injury or signs of damage to the bones, the spinal cord may be found to be completely diffluent over several segments. The same result may be met with from the passage of a high velocity bullet through the spinal canal, whether the spinal cord be touched by the bullet or not; and again, the same condition occurs from the vibration of an impact when a missile hits and lodges in the surrounding bone, without directly involving the spinal canal or cord. A slighter degree of the same condition may be seen in fracture dislocation. When, as the result of injury to the spinal column, the spinal cord is torn across, the distal segment may soften completely.

Pressure Lesions.—Pressure upon the spinal cord abrogates function chiefly by producing ischæmia and, if the pressure be prolonged or severe, necrotic softening occurs, and the more readily, if there be strangling of the segmental vessels which supply the cord and accompany each nerve root.

Inflammatory Conditions. —In acute spreading myelitis, in which the spinal cord is infected with micro-organisms secondarily to a general blood infection, as may occur in small-pox, gonorrhœa, dysentery, etc., the cord softens and may become diffluent. In acute transverse myelitis, softening depends upon the severity of the initial œdema and its duration, the degree of obliterative arteritis, and the consequent thrombosis that may occur. It may be largely avoided by the energetic and early application of anti-syphilitic treatment.

Senile Paraplegia.—This condition, which is not very rare, and in which

spasticity of the lower extremities with weakness comes on gradually in later life, and does not, as a rule, reach a severe degree, has been attributed to ischæmia and even to softening of the spinal cord from arterial disease and the failing circulation of old age, by Moxon, who first described it. The pathology of these cases seems by no means certain, and there are few records of the anatomy. It seems certain that no appreciable softening can occur, on account of the slightness of the paraplegia and the absence of any sensory loss. Gowers doubted whether they were spinal in origin at all, and attributed some to the occurrence of cortical changes in the brain, while others he placed in the category of paralysis agitans. From the occurrence of definite mental failure in some of the cases, a cerebral site for the lesion is likely. Dr. Greenfield has recently examined for us a very typical case and found no changes in the spinal cord, but extensive degeneration of the pyramidal cells of the motor cortex.

SUBACUTE COMBINED DEGENERATION

Synonym.—The Anæmic Spinal Disease.

Definition.—Subacute combined degeneration is a disease most common in the second half of adult life, of which the onset is usually insidious and the course progressive. The lesions in the nervous system consist of a primary demyelination, commencing in the centre of the white columns and affecting the long fibres first and most, and the short intersegmental fibres which lie close to the grey matter last and least. Neuroglial condensation follows very slowly upon the demyelination. The posterior and lateral columns of the spinal cord are early affected, and it is to the affection of both these columns that the term "combined degeneration" alludes. The clinical features are usually strikingly distinct, in that subjective sensations, such as tingling, numbness and burning, occurring usually at the periphery of the limbs, are early, obtrusive and persistent, and are accompanied or followed by the development of a paraplegia which may be of a spastic, or a flaccid and ataxic, or of a mixed type, according to the degree of affection of the lateral and of the posterior columns in each case, and the degree of involvement of the peripheral nerves. We owe to Risien Russell, Batten and Collier the first complete pathological and clinical account of this disease.

In the late stages of the malady, the paraplegia tends to become complete and of the flaccid type, with loss of the deep reflexes. Anæmia accompanied by a peculiar "buscuit-like" discoloration of the skin is present in all cases at some period of the disease, with the exception of some few of the cases of short duration. This anæmia tends in every case, if life is prolonged, to develop into a pernicious anæmia which is typical, both clinically and pathologically.

Ætiology.—First met with in the third decade of life, the malady becomes increasingly frequent until a maximum incidence occurs in the sixth decade, while cases commencing in the seventh decade are not uncommon. The sexes are equally affected. Familial incidence in this disease, as also in pernicious anæmia, has been recorded by Hurst, Piney and others.

Pathology.—The essential lesion is demyelination of the axis cylinders, and subsequent degeneration of the latter, in the posterior and lateral columns of the cord. It has also long been known that some degeneration of peri-

pheral nerves occurs in this disease, and recently Carmichael and Greenfield have confirmed that the same process of demyelination seen in the cord is to be found in the peripheral nerves. At first the myelin sheath swells and later disintegrates. This change first occurs in the lower dorsal region of the cord, and is first seen in the centre of both posterior columns, and soon afterwards in the centre of either lateral column, as small areas of a darker and more translucent appearance than the normal white matter. It is only at an early stage of the disease that the anatomical picture is strictly one of postero-lateral degenerations, for soon after, spots of degeneration appear on either side of the anterior median fissure and in other parts of the antero-lateral columns. The degenerated areas increase in size centrifugally, coalesce with one another, reach the surface of the cord and eventually involve the whole of the white matter of the cord as seen in transverse section, with the exception of the narrow zone of short internuncial fibres which everywhere clothe the grey matter. This "annular or ferrule-like" degeneration in the lower dorsal region is highly characteristic, and occurs in no other disease.

From its starting-point in the lower dorsal region the degeneration spreads upwards and downwards in the white columns of the spinal cord, and for this reason the term "funicular myelitis" was applied to it by Henneberg. This extension depends upon the occurrence of small isolated spots of degeneration in the posterior, lateral and antero-lateral columns, which increase in size and thus join the area previously degenerated. The degeneration tends to extend upwards indefinitely, and in severe and advanced cases has been found as high as the internal capsule in the pyramidal tract.

The lesions of the white columns entail the usual secondary degenerations, both ascending and descending; but these occur late, and are often much less obvious than might be expected from the severity of the local lesions. The destruction of the axons by the local lesions also causes a series of retrograde changes in the corresponding nerve-cells, and tigrolysis, vacuolation, shrinking and neurophagy may be conspicuous, especially in the cells of Clarke's column and in the cells of Betz, which gave origin to the pyramidal fibres. Occasionally the disease is entirely confined to the posterior columns of the spinal cord. The muscles are conspicuously wasted in the later stages, and the muscle fibres show great diminution in size and poor striation. There is not any considerable increase of the muscle nuclei, and little or no fibrosis occurs.

Blood.—In a few instances, anæmia has been absent throughout, the hæmoglobin content and the cytology being normal; this has occurred chiefly in cases which have run an acute and fatal course in a few months. Usually the blood shows an anæmia of varying severity; the hæmoglobin ranges from 35 to 75 per cent., the lower of these figures being common; the colour index is usually above the normal, and may be as high as 1·6. Macrocytosis is present. Anisocytosis, poikilocytosis and polychromatophilia are common. Normoblasts are often numerous and megaloblasts may be found in numbers. A relative lymphocytosis is almost always present, and may reach as much as 55 per cent. This change occurs early, and is helpful in the confirmation of the diagnosis of the nervous disease.

A careful investigation of the blood-changes at various stages of the disease and of the post-mortem findings in a large series of cases has proved beyond any possible doubt that the blood-changes in every case are identical with

those met with in the various stages of pernicious anæmia, and that a typical post-mortem picture of pernicious anæmia occurs frequently in subacute combined degeneration. The cerebro-spinal fluid presents no abnormalities either as regards albumin, sugar or cells.

The early writers believed that the anæmia was the essential part of the disease, and that the degenerations in the nervous system were the result of vascular changes consequent upon the anæmia. This view is negatived by the facts that some cases progress to a fatal issue without any evidence of anæmia, and that in others the nervous manifestations may become severe long before any anæmia is evident; and, most importantly, no case has been recorded in the literature, nor has one occurred in the very large series examined by the writers, in which the nervous manifestations developed in a patient already under observation for anæmia.

The experimental evidence and the clinical and pathological features of the disease suggest, therefore, that the anæmia and cachexia and the degeneration of the nervous system are not dependent the one upon the other, but that they are the concomitant but not necessarily synchronous results of one and the same cause, which is deprivation from a product of gastric digestion in the presence of hydrochloric acid which is subsequently stored in the liver, and which is essential to the normal formation of the erythrocytes. Hurst and others have shown that achlorhydria is present in nearly all the cases.

Symptoms.—In a large majority of instances the symptoms appear insidiously and without any exciting cause. Sometimes the onset is more rapid, and may be preceded by severe gastro-intestinal symptoms such as vomiting, diarrhœa, jaundice, malaise and pyrexia In a few cases the onset has been so rapid as to suggest the diagnosis of acute myelitis, and in one of these which was under our observation and pathologically verified, two attacks of temporary paraplegia has preceded the onset by 8 and by 4 months respectively.

The cardinal signs may be summarised as follows: peripheral subjective sensations, which occur early and are remarkably obtrusive, are complained of in the periphery of the limbs in most cases, but may occur in the perineum, neck and back of the head and in the tongue. Sensory loss is found, which commences upon the limbs with peripheral "stocking and glove" distribution, and reaching on to the trunk ascends in segmental distribution. Astereognosis occurs in the upper extremities. Paraplegia may be (*a*) flaccid from the first, with loss of deep reflexes; (*b*) spastic, remaining spastic throughout (rare); (*c*) spastic, changing to flaccid paralysis with loss of the deep reflexes. The first of these three clinical types is the commonest, and it provides almost all—if not all—the cases which respond favourably to treatment. Both forms of paraplegia are accompanied by marked ataxia. Girdle sensations, lightning pains, fixed pains, gastric crises, exaggeration of superficial reflexes, are all encountered. Sphincter paralysis is late. Loss of sexual power is early. There are muscular wasting and lowering of electrical excitability of general distribution in the paraplegia region. Anæmia, which may be absent throughout or may become apparent at any period in the course of the disease, is conspicuous at the time of the onset of the nervous symptoms in about one-half of all cases.

Peripheral subjective sensations are so constantly the earliest symptom, so discomforting to the patient and so persistent, as to form a most distinctive

feature of the disease. These sensations are variously described, but tingling and numbness are the most common. Creeping sensations, smarting, burning, icy coldness, tightness and pain are all common. They are usually felt first upon the tips of the fingers and toes, and subsequently spread up the limbs. A girdle sensation is the rule, and it is sometimes painful.

Sensory loss first appears at the periphery, and spreads up the limbs like the sensory changes of a polyneuritis, waning in severity as the base of the limb is approached. In time it reaches the abdominal wall, but rarely extends as high as the thorax. Earliest to diminish, and first to disappear, are the postural modes of sensibility and vibration sense; tactile sensibility may also be severely affected; but thermal and cutaneous pain sense are usually least affected. A marked and almost constant feature of the disease is the tenderness of the calf and plantar muscles to pressure. Such tenderness is not usually found in association with a spinal cord lesion, and its presence is one of the reasons for regarding the peripheral nerve changes already referred to as of importance in determining the symptomatology.

In the common *flaccid type* of paraplegia, weakness and unsteadiness of gait are commonly preceded by the paræsthesiæ and sensory changes described above. There is at first a ready fatigue on exertion, a dragging of the feet and an ataxy of gait when tired, and also aching pains in the muscles of the legs. Examination reveals some weakness, especially of flexion and dorsiflexion in the legs, the tenderness already mentioned, and diminution or loss of the knee-jerks, and loss of the ankle-jerks. Sooner or later an extensor plantar response betrays the development of lesions in the lateral columns of the cord; but at first the plantar response may be of the flexor type, and when this is the case, the nervous clinical picture is not readily distinguishable from that of polyneuritis. In some cases it is doubtful if the distinction could be made were it not for the accompanying abnormalities in the blood and gastric secretions.

In this clinical type, of course, some of the signs may be the expression of a posterior column lesion, and it is known that in a few cases the spinal cord lesion is confined to this column. In the less frequently seen *spastic type*, the clinical picture is one of a predominating lateral column lesion in the cord. The case may pass through the stage of paraplegia-in-extension to the final one of paraplegia-in-flexion, with extremely painful flexion spasms, loss of sphincter control, and the development of bedsores. In some such cases, the limbs may become flaccid, and the tendon-jerks disappear before contracture ensues. But whether this change from spasticity to flaccidity occur or not the clinical type is one which progresses ruthlessly and does not respond to treatment.

Sudden exacerbations of the symptoms may occur at any time, and these are commonly associated with malaise, pyrexia, vomiting or other signs of gastro-intestinal disturbance and by an increase in the anæmia, as if there had been a sudden increase in the condition, which is responsible both for the anæmia and for the spinal degeneration. As the disease advances, the paraplegia involves more and more of the trunk, progressing upwards. In some cases the upper extremities are affected early, and may even be the first regions to show signs of the disease. In the course of time the paraplegia becomes complete, with great wasting of the muscles and reduction of their faradic excitability.

The paraplegia does not, as a rule, reach the upper limits of the region supplied by the cervical enlargement of the spinal cord, and even in the most severe cases the condition of the upper extremities is one of partial paralysis, most marked in the periphery and associated with considerable wasting of the muscles of the hands and forearms. In addition to the muscular wasting, there is usually conspicuous wasting of the subcutaneous fat. In late stages of the disease the general bodily wasting becomes extreme.

Dysuria generally appears when the paraplegia becomes pronounced. It does not often occur in the early stages of the malady, and sometimes its appearance is delayed until remarkably late. When once established, it does not show any tendency to improve with treatment. Finally, the control of the rectum and bladder becomes completely lost.

Soft translucent œdema of the extremities and trunk is frequent, especially when the anæmia is severe, and is dependent upon the anæmia and upon the impaired innervation of the paraplegic region.

General mental deterioration, mild delirium, drowsiness and torpor frequently occur at any stage of the disease, and are referable to the anæmia and the metabolic disturbance, and possibly also to widely spread cell changes in the cerebrum. General convulsions have been reported in a few cases.

Dimness of vision is common when anæmia and debility are severe. Papill-œdema of slight degree is sometimes met with, and doubtless in relation to the anæmia. Optic atrophy has been reported in a good many cases. Small retinal hæmorrhages are not uncommon. A minor degree of nystagmus is the rule, and may depend upon the involvement of the cervical spinal cord, all lesions of which seem to be regularly associated with nystagmus, or this may be attributed to affection of the cerebellum, for changes in the Purkinje cells of this organ have been repeatedly found. Herpes is not infrequent. It may occur anywhere, and has several times affected the distribution of the trigeminal nerve. A hæmorrhagic lesion of the sensory ganglion has been found.

Although anæmia is one of the most characteristic features of subacute combined degeneration, since it occurs in every case of long duration at some time or other, and since it is sufficiently striking as at once to suggest the diagnosis in at least two-thirds of all the patients when they first come under observation for nervous symptoms, yet it may be absent throughout the course of the disease in a rapid case, and its appearance may be delayed until several years after the disease of the nervous system is manifest. The anæmia in almost every case is identical in every respect with pernicious anæmia. Of those cases in which the blood picture is not typical, nearly all show megalocytosis, with a relative lymphocytosis and a high hæmoglobin index, as do early cases of pernicious anæmia, and it may be said with certainty that the longer the patient survives, the greater the likelihood of typical pernicious anæmia developing. The spleen has been enlarged in many cases, and the marrow of the bones is typical of pernicious anæmia, as may be also the iron reaction in the liver and the changes in the myocardium and other muscles. As in pernicious anæmia, the tongue is clean, and this occurs so regularly that any appearance of furring of the tongue may justly be said to exclude the diagnosis of this disease. Fractional test meals show an absolute achlorhydria, or a relative achlorhydria, in the same proportions

as do cases of pernicious anæmia. The colour of the skin is often peculiar and striking, even when anæmia is not severe, and is best described as "biscuit-coloured." A bright malar flush upon this yellowish biscuit-coloured background gives a characteristic and vivid facial aspect in the earlier stages of many of the cases. The symptoms and signs common to all anæmic states, breathlessness, headache, cardiac and venous murmurs and œdema, are commonly present, but hæmorrhages are uncommon. Syncopal attacks may occur. Irregular pyrexia is almost invariably present at some period in the course of the disease, and this quite apart from fever-producing complications, such as cystitis and bedsores. In the later stages progressive emaciation is constant, and if life be prolonged it becomes extreme.

Diagnosis.—In the earliest stage, and before the appearance of any definite sign of organic spinal disease, there may be such disability as to suggest the diagnosis of functional paraplegia. When organic signs appear, it is especially from disseminated sclerosis, spinal tumour and tabes dorsalis that the diagnosis has to be made. The preponderance of the peripheral subjective sensations, and the presence of a florid complexion with anæmia, should always suggest the diagnosis. Slight spastic ataxy is the common clinical picture of subacute combined degeneration, of disseminated sclerosis and of spinal tumour. Peripheral sensations and peripheral numbness are not features of disseminated sclerosis, and the presence of peripheral sensory loss should always challenge that diagnosis, whereas diplopia, nystagmus, transient amblyopia and intention tremor are not early symptoms of subacute combined degeneration. Spinal tumour is especially distinguished by a sharp line of sensory loss, transverse to the axis of the body, which does not spread up from below in slow fashion.

When subacute combined degeneration commences with flaccid ataxy and loss of the deep reflexes, the distinction must be made from tabes dorsalis. The extensor plantar reflex, which is almost always present in the former disease and which is rare in early tabes, the entirely different distribution of the sensory loss in the two diseases, the loss of power in subacute combined degeneration, and the results of the examination of the blood and cerebro-spinal fluid for syphilitic reactions and of the latter fluid for lymphocytosis, are important aids in the differential diagnosis.

In the well-developed stages of the disease, its recognition presents no great difficulty. Attention is quickly attracted by the conspicuous anæmia and biscuit-coloured skin. Following a period of slight paraplegia, often lengthy, the steadily increasing paralysis of the lower extremities, with perhaps sudden exacerbations, producing complete and lasting helplessness, the characteristic distribution of the sensory loss which spreads upwards towards the cervical region, the severe lightning pains, the irregular pyrexia, the anæmia and the relatively late onset of sphincter trouble serve to separate this disease from other forms of paraplegia. The change from the spastic to the flaccid type of paraplegia with loss of the deep reflexes and persistence of the extensor response, which occurs in some of the cases in the late stages, is highly characteristic.

It is also necessary to bear in mind the strikingly close resemblance which the disease we are considering may bear to polyneuritis. The differentiation may in the early stages depend chiefly, if not wholly, upon the examination

of the blood and the result of a fractional test meal. But, sooner or later, the appearance of an extensor plantar response will indicate the presence of a cord lesion. On the other hand, in the spastic type, the presence of muscular tenderness in the legs is a strong indication in favour of subacute combined degeneration.

Course and Prognosis.—The duration of the disease varies within wide limits, but the rapid downhill progress, ending in death within a few weeks or months which was formerly common, is now exceptional. Conflicting claims are made as to the possibility of cure, and it is probable that some at least of the difference of opinion depends upon a failure to appreciate that in the common flaccid type of the disease some at least of the signs and disability may be due to a peripheral nerve lesion and not to degeneration within the cord. This is certainly the clinical type which responds most favourably to liver, stomach, iron and thyroid therapy; while all but the very slightest cases of the spastic type—in which the important lesion is plainly in the lateral columns of the cord—fail to respond to the most intensive therapy.

In the flaccid type, appropriate treatment—if given early enough—will effect considerable restoration of muscular power, of co-ordination and of sensation. Usually, however, paræsthesiæ in the legs and feet, and sometimes in the fingers, remain. The restoration of lost knee-jerks is rare, and that of lost ankle-jerks still rarer. Vibration sense may be partially restored, and very occasionally an extensor plantar response may disappear. It is yet too early to say how enduring these improvements may be. It is clear that for most sufferers, the prognosis of subacute combined degeneration is far better now than it was formerly, but the enthusiasm that would speak of cure as within reach, or prevention of nervous lesions in cases of pernicious anæmia when treated sufficiently early, as certainly possible, has still to justify itself. It is not shared by the neurologist.

Treatment.—Whatever the degree of anæmia present, intensive liver treatment is essential. Daily parenteral injections of the chosen preparation is necessary until the red cell count reaches the five million figure, or as near it as possible. Even this may be insufficient to secure improvement in the nervous symptoms. Indeed these require more and longer continued liver treatment than does the anæmia. The spastic type of case responds badly, but the more numerous flaccid cases may make remarkable recoveries if taken in hand before the malady is too advanced. Previous to the introduction of liver feeding we found that thyroid extract had a remarkable effect in removing the anæmia, and that it could be tolerated by patients suffering from subacute combined degeneration in very large doses, even as much as sixty grains a day. The more advanced the stage of the disease is, the less result may be expected from any form of treatment. Any suppurative condition of the body should be energetically treated. Every care should be taken to delay the advent of bedsores and cystitis. When present, these are often amenable to treatment in the early stages of the disease and in less acute cases, but in the more acute cases and in the later stages they are inevitable and the bodily vitality is too low for any reparative process to take place. Lightning pains and other pains are relieved by such analgesics as aspirin, acetanilide, amidopyrine, phenazone, etc. Reflexor spasms are among the most troublesome of the symptoms, since their frequent occurrence

denies sleep to the patient, and they are most important factors in the occurrence of bedsores. The remedy which seems to have most effect in checking these spasms is barbitone.

MOTOR NEURONE DISEASE

Synonyms.—Progressive Muscular Atrophy; Amyotrophic Lateral Sclerosis; Chronic Bulbar Palsy.

Definition.—A disease of gradual onset which may develop at any age from puberty onwards, and in which the anatomical findings consist invariably, whatever be the clinical picture, of three orders—(1) a progressive degeneration, shrinkage and disappearance, cell by cell, of the upper motor neurones or cells of Betz in the ascending frontal convolution, with consequent degeneration of the corresponding fibres in the pyramidal tracts; (2) a similar atrophy, cell by cell, in the lower motor neurones with corresponding degeneration of motor fibres in the peripheral nerves and atrophic degeneration of the muscles innervated by the affected cells; (3) a diffuse atrophy of the white matter of the spinal cord, the posterior columns conspicuously excepted.

A most mysterious feature of the disease is the non-correspondence between the anatomical findings and the symptomatology. In the first place, though the upper motor neurone lesion is constant, many cases run their course without the slightest external evidence that the pyramidal system is involved.

The clinical picture is one of gradually oncoming weakness and disability, due either to atrophy of the muscles from the lower motor neurone lesion, in which case the paralysis is flaccid and atrophic, or to spastic paralysis of the muscles from the upper motor neurone lesion, in which case the paralysis is spastic without atrophy, or to the combined lesion of both upper and lower motor neurones, in which case the paralysis is both spastic and atrophic, and the muscular atrophy never becomes complete. Fibrillary twitchings of the muscles are always present, and form an important diagnostic feature. Any of the skeletal muscles may be affected from the ocular muscles to those of the feet.

The clinical aspect varies greatly according as the incidence of the palsy is upon the muscles supplied by the brain stem, or upon the muscles of the trunk and limbs, and again, according as the atrophic element or the spastic element is present alone, or as both coexist in the same region or in different regions of the body.

The following are the usual clinical types, but it must be borne in mind that every transition between these types may be met with:

(A) With incidence upon the muscles supplied from the brain stem; Progressive bulbar paralysis: 1. Pure atrophic bulbar paralysis. 2. Spastic atrophic bulbar paralysis. 3. Pure spastic bulbar paralysis.

(B) With incidence upon the muscles of trunk and limbs: 1. Pure atrophic type—(*a*) local and slowly progressive; (*b*) general and rapidly progressive. 2. Spastic atrophic type; amyotrophic lateral sclerosis—(*a*) the spasticity and atrophy are coincident in the same muscles; (*b*) the atrophy affects the upper limb and the spasticity the lower limb. 3. Pure spastic type. This is more commonly seen as an early stage of amyotrophic

lateral sclerosis, where the spasticity of the lower extremities precedes the atrophy of the upper extremities by some months or years.

(C) Mixed bulbar and spinal forms.

Ætiology.—The earliest age incidence has been at 12 years, and several cases have been recorded which developed the disease at that age. As age advances the incidence of the malady becomes more frequent, until it attains a maximum between the ages of 30 and 40 years, after which there is a slow decline. It does not commonly commence in advanced age, but one case has come under the writers' observation which commenced at the age of 77 years. Males are affected three times as frequently as females, but in the cases occurring before the age of 25 years, the females predominate. Heredity only rarely influences the disease. The question of the relation of trauma to the causation of this disease admits of no decisive answer. In any given case it is impossible to establish a relationship, but some observers have recorded examples of a close sequence of injury and onset of the disease, and they regard the two as in the relation of cause and effect. We know of no pathological process by which a peripheral injury may set up within the central nervous system a selective neurone degeneration. If such there be, it has yet to be discovered. A series of cases of injury to the cervical spine associated with the signs of relatively minor injury to the fourth and fifth segments of the cervical cord which have been recorded by Walshe and Ross, raise the possibility that some cases of so-called progressive muscular atrophy are traumatic in origin, but are not at the outset or in their subsequent development genuine cases of motor neurone disease (cf. p. 1725, Section on Compression of Rapid Onset). Syphilis seems to be in definite causal relation with some of the cases. A positive Wassermann reaction, both in the blood and in the cerebro-spinal fluid, is found in a much larger proportion of the cases than give any history of syphilitic infection. Further, quite a number of instances of the supervention of a typical progressive muscular atrophy in cases of tabes has been observed and recorded at the National Hospital, London. It has been freely stated that progressive muscular atrophy of syphilitic origin differs from the non-syphilitic forms in its lack of symmetry and in its course; but this certainly does not hold good for very many of the cases which show a positive Wassermann reaction. In a large majority of all cases of progessive muscular atrophy, no causal factors whatever can be discovered.

Pathology.—To the naked eye, a cross-section of the spinal cord may show some diminution in size of the ventral horns. The essential lesion is a primary degeneration of the cells of the ventral horns of the spinal cord and in the homologous motor nuclei of the brain stem, namely, the hypoglossal, facial, trigeminal and oculo-motor nuclei. Coupled with the degeneration of the lower motor neurone, is a degeneration of the upper motor neurones of the pyramidal system. In the ventral horn cells the degeneration is evidenced by a gradual shrinking in size of the cells, which lose their dendrites and become oval or spherical in shape. The Nissl bodies slowly disappear, and only in rare and rapid cases is definite chromatolysis seen. The nuclei dwindle and become irregular and distorted.

The dorsal and lateral horns are almost invariably intact, but degenerative changes are sometimes seen in the cells of Clarke's column. The affection of the motor nuclei of the brain stem in the bulbar cases is in every way similar

to that of the ventral horns. The degeneration of the motor nerves which take origin from the degenerate ventral horn cells, often proceeds *pari passu* with the degeneration of the cells. But in some cases this is conspicuously and very mysteriously not the case.

The affected muscles are soft and toneless, and the muscle fibres are found irregularly degenerated, bundles of normal and of degenerating fibres, until the atrophy is complete, being found side by side. The characteristic change is shrinkage of the affected fibre to a calibre much less than normal. As is usual in all slow tissue degenerations, fibrosis and local arterial disease accompany the atrophy of the muscle fibres.

The pyramidal neurones (cells of Betz), which characterise the precentral cortex, undergo a degeneration very similar to that of the ventral horn cells, but with this difference, that the earliest structural changes are found in the most distal part of the pyramidal fibres, and that subsequently these fibres die back towards their cells of origin in the cerebral cortex. The degeneration of the upper motor neurones never proceeds to the complete destruction of anything like all the pyramidal fibres.

The pathological nature, therefore, of progressive muscular atrophy is a widely scattered degeneration of nervous elements not even confined to the motor systems, though these are in the main affected, since the afferent spino-cerebellar tracts are constantly found degenerated, from some unknown cause.

Symptoms.—The following description of the clinical features is based upon an analysis of 500 cases which have come under observation at the National Hospital, London. The onset is in most cases very gradual, but it may be more rapid, and severe incapacity may result in the course of a few months. In rarer cases, a severe degree of paralysis may develop in the course of a few days, and in such cases it is not uncommon to see the most remarkable temporary improvement. The nature of the onset, as a rule, indicates the course which the malady will pursue. A very slow onset is followed by a very slowly-advancing disease, often interrupted by long stationary periods, whereas the more rapid the commencement, the quicker will be the advance and the sooner will a fatal issue occur. Accompanying and sometimes preceding the onset, and not infrequently conspicuous during the early states of the disease, are certain sensory symptoms which, from the confusion in diagnosis they may cause and from the scant attention which has been paid them in descriptions of the malady hitherto, deserve emphasis. These symptoms are confined to the regions where the wasting first appears, and consist in a subjective feeling of stiffness and uselessness, much increased when the limb or the body is cold. Or there may be dull aching pains, intermittent neuralgic pains which may be severe, or a sensation of coldness or numbness which may be intense. Painful cramp in the muscles which are about to be affected is comparatively common.

The *muscular wasting*, which constitutes the most characteristic feature of the disease, may commence in any group of the skeletal muscles whatsoever. It may be first manifest in such rare situations as the facial muscles, intercostal muscles, muscles of the back and abdominal muscles. The commonest situation is in the muscles of the upper limb, where the distal (intrinsic muscles of the hand) or the proximal muscles (deltoids, spinati, etc.) are first affected in about an equal number of cases. In the hand, the muscles

of the thenar eminence are the first to waste, and this is followed by atrophy of the hypothenars, of the lumbricals and of the interossei with the usual flattening of the palm, exposure of the flexor tendons in the palm from loss of the bulk of the lumbricals, hollowing of the interosseal spaces and a tendency to the "griffin's paw" attitude of the hand. The *main en griffe* is never so marked in this disease as in paralysis of the ulnar nerve, syringomyelia, etc., because the wasting soon affects the long flexors of the fingers, and further contractures of the affected muscles are not well marked in progressive muscular atrophy. As the wasting spreads to the muscles of the forearm, the flexors are usually affected before the extensors.

When the upper arm is primarily affected the wasting is first seen most often in the deltoids, whence it spreads upwards, involving the spinati and the muscles attaching arm to scapula, and arm and scapula to trunk. Among these muscles some tend to escape the atrophy relatively, or to be affected much later than others, and these are the triceps, the latissimus dorsi, the lower half of the pectoralis major, the levator anguli scapulæ and especially the upper half of the trapezius, which for this reason was called "ultimum moriens" by Duchenne. In the limbs the wasting always commences in one limb, but soon spreads to the corresponding limb of the opposite side and tends ultimately to become symmetrical. The attention of the patient may be first drawn to his malady by the altered appearance produced by the atrophy, and this is more common when the commencement is in the hands, where the subcutaneous tissue is thin and the region constantly in view. Or the disability consequent upon the weakness may be noticed first, and this is always the case where the commencement is in the bulbar muscles, and usually also where the muscles of the legs, proximal muscles of the arms and trunk muscles are first involved. Lastly, the fibrillation may be so marked as first to attract notice.

The *loss of power*, which accompanies the muscular wasting, is, as a rule, commensurate with the wasting, and does not become absolute until the atrophy is complete. To this rule, however, there are two very important exceptions. In the first place, when the affected muscles are both tonic from the upper motor neurone lesion and atrophic from the ventral horn-cell lesion—the tonic atrophy of Gowers—the loss of power is always much greater than can be accounted for by the degree of wasting present. It is a remarkable and entirely unexplained fact that when this tonic atrophy is present the muscles never completely waste, whereas in flaccid atrophy they waste completely, if the patient survives sufficiently long. When the disease commences with initial flaccid paralysis without wasting, it is usually rapid in its course, any temporary improvements notwithstanding. This initial flaccid paralysis without wasting, especially if it improves temporarily, may give rise to great difficulty in diagnosis, for it generally occurs in one limb only, and its rapid development, and in some cases a conspicuous improvement, may give rise to the impression of a gross organic lesion of the ventral horn or ventral roots, and to hopes of recovery which are falsified later.

The disability which progressive muscular atrophy produces in the limbs is always much more marked when the limbs are cold, and conversely. There may be an appearance of vasomotor paralysis, redness, blueness and some swelling of the periphery, but this seems to occur much more as the result of the continual pendent position of the hands, when the muscles, which

flex the elbow and which raise the shoulder, are affected, than as the result of any definite vasomotor palsy. In the regions where the muscular atrophy is apparent, the fat and subcutaneous tissues also waste slowly and progressively, and in all but the rapidly progressive cases this wasting is conspicuous.

Next in order of frequency to initial wasting in the upper extremities comes the incidence of the disease upon the muscles concerned in facial expression, articulation, mastication and deglutition, and in lesser degree upon the muscles of phonation; and the disease may be confined to these muscles throughout the whole of its course. From the widely different clinical picture resulting, and from the fact that all these muscles are supplied from the brain stem and upper two segments of the spinal cord, this form of the disease has borne the name of "progressive bulbar paralysis," or "labio-glosso-pharyngeal paralysis." Here the wasting commences in the intrinsic muscles of the tongue and spreads thence to the orbicularis oris, to the extrinsic mucles of the tongue, pharynx and larynx, to the muscles of mastication and, eventually, but in less degree, to the facial muscles generally; but only in rare cases are the oculo-motor muscles affected.

The intrinsic muscles of the palate, the constrictors of the pharynx, the intrinsic muscles of the larynx, and the muscle of the œsophagus are little affected. This seems at first an anomalous and astonishing fact, considering how great and important are the troubles with deglutition in bulbar paralysis. But the anomaly disappears at once when one considers that the muscles which are concerned with buccal deglutition are the muscles of the tongue, those forming the floor of the mouth, including the mylohyoid and the digastric, the muscles which raise and lower the jaw, and those of the lips. Further, the muscles which are most important in pharyngeal deglutition are those which raise and lower the hyoid bone and larynx as a whole, and these are the stylohyoid and stylopharyngeus, the palatoglossus and palatopharyngeus, the geniohyoid, thyrohyoid, sternohyoid, sternothyroid and omohyoid. All these muscles are early and severely affected in bulbar paralysis; and when they fail, the intrinsic muscles of the palate are unable to shut off the naso-pharynx, the constrictors of the pharynx are entirely unable to perform the act of delutition, and the intrinsic muscles of the larynx—though phonation is never lost—are unable, since the larynx is unfixed by the extrinsic muscles, to modulate the tone of the voice. The very active pharyngeal reflex and the well-known great difficulty in using the laryngoscope on account of spasm of the pharynx in the subjects of this disease, are very good clinical evidence that the pharyngeal constrictors are not affected.

The earliest physical sign of bulbar paralysis is the loss of the finer movements which are essential for correct articulation, and consequently a slurring dysarthria develops and increases, and the consonants become less and less distinct until they are inaudible. The failure of the palate to close upon the posterior pharyngeal wall begets a nasal element in the voice. Later, the patient becomes unable to interrupt his blast at any of the stop positions, and his utterance becomes a long, moaning, monotonous, inarticulate sound. His phonation remains, but he cannot alter its pitch nor divide it into parts of speech, except by taking a fresh breath. The orbicularis oris is early affected, and the lips lose their firmness and become thin,

and as they weaken, the unopposed retractors of the angles produce a wide, straight mouth, both at rest and in emotional action. Whistling and pursing up the lips become impossible, and ultimately there is much dribbling of saliva, for this can neither be retained by the lips nor swallowed. The tongue shows fine fibrillation, and as it wastes it loses its point, becomes rounded, and is protruded with difficulty. Its surface becomes dimpled and faceted, and in the end consists solely of the covering mucous membrane, the glands and the fibrous tissue, and lies motionless in the floor of the mouth, resembling a crinkled mushroom. The muscles of mastication all become affected. The bite becomes feeble and the mouth cannot be opened against resistance. In the late stages the jaw drops and the mouth is constantly open. The combined weakness of tongue and buccinators makes it very difficult for the patient to keep his food between his teeth in mastication, and often he aids his disability by digital pressure upon the cheeks. Nasal regurgitation is not uncommon. The difficulty in swallowing is greatest with fluids, for these require quick action, and is next greatest with lumpy solids, for these necessitate powerful action. It is least with food of a porridge-like consistency, and this should be carefully borne in mind in feeding the patients.

The other muscles of the face are affected later and to a much less severe degree than is the orbicularis oris. It is as if there were a physiological selection on the part of the disease for the nervous mechanism subserving mastication and deglutition. Still in the majority of cases there are bilateral general facial weakness and wasting which, with the peculiar mouth and dropping jaw, produce a characteristic facies which can be instantly recognised. If the upper facial muscles are tested by raising the eyelid with the finger against resistance, invariably they will be found to be weak. Only in very rare cases does the atrophy extend to the oculo-motor muscles. As in the paralysis of the limbs, so also in bulbar paralysis, concomitant signs of both upper motor neurone and of lower motor neurone lesion may exist. When such tonic atrophy of the bulbar muscles is present, the symptomatology and clinical appearance are the same as have been above described for the simple atrophic form, with the exception that the jaw-jerk and the other muscle-jerks of the bulbar region, which are absent in the latter condition, are brisk in the tonic-atrophic form. And, further, it must be remembered that the additional element of spastic paralysis adds greatly to the degree of the paralysis as a whole.

In less common cases of progressive bulbar paralysis the upper motor neurone lesion alone is in evidence, and the bulbar paralysis is purely spastic. Here the symptomatology as regards articulation, deglutition, etc., is the same, and the facial aspect identical with that of the simple atrophic and tonic-atrophic forms. The muscle-jerks are brisk. The appearance of the tongue, however, is quite different; it is smooth, narrow, stiff and drawn into a narrow compass by the spasm of the muscles composing it. It appears too small for so large a mouth. There is no fibrillation, and the muscles are nowhere wasted.

The muscles of the back of the neck, the splenius, complexus, etc., are not uncommonly the first muscles to be affected with the wasting of progressive muscular atrophy. There is increasing difficulty in extending the head, which drops forward, causing a characteristic attitude, which is associ-

ated with a constant overaction of the frontales which raise the brows to clear the line of vision when the head is dropped forward, so giving rise to a permanently furrowed brow. The loss of substance in the muscles of the back of the neck, together with the dropping forward of the head, causes the lower cervical and upper dorsal spines to stand out in undue prominence, and to give an appearance approximating to that of an angular curvature.

Primary affection of the lower extremities is much less common than that of the upper extremities, bulbar region or neck muscles. The anterior tibial and peroneal muscles are usually attacked first, and less commonly the quadriceps. The clinical type is that of flaccid atrophy in most of the cases. Tonic atrophy, which is so common in the upper limbs and in the bulbar region, is rare in the legs. Spasticity without atrophy from the upper motor neurone lesion alone is very common in the lower extremities. It forms a characteristic part of the frequently occurring clinical type of amyotrophic lateral sclerosis, in which the upper extremities or bulbar region are affected with atrophic paralysis, and the legs with spastic paralysis. In this common combination the atrophic paralysis is usually of the tonic and much less frequently of the simple flaccid type. Spasticity from the upper motor neurone lesion may develop in the lower extremities long before there are any signs of atrophic paralysis elsewhere from the lower motor neurone lesion, and such cases present the physical signs of a primary lateral sclerosis. Therefore, it cannot be too strongly borne in mind that any case presenting the features of a primary lateral sclerosis in an adult may eventually prove to be one of progressive muscular atrophy.

Wherever the site of commencement of progressive muscular atrophy may be, it invariably spreads to other regions, sometimes slowly and with periods of arrest which may last for years, sometimes with remarkable rapidity. The manner of spread is usually in terms of the contiguity of the affected elements in the nervous system; but it is sometimes in terms of the physiological association of the muscles, as is commonly seen in the bulbar forms of the malady. When the disease is definitely installed the appearance of fibrillation, in any muscles otherwise unaffected, is a sure sign that atrophy will shortly commence in those muscles.

According to the method of advance shown by the disease, cases of progressive muscular atrophy fall into two groups which it is important to distinguish. In the first group, the atrophy spreads locally and slowly and remains confined to one region of the anatomy during most of the course of the malady. These cases are always of the simple atrophic type, and they usually survive a long time. Such cases, however, tend to become general just before the end. In contrast with the local type of the affection is the group in which the manifestations, commencing locally, spread within a comparatively short time to many parts of the anatomy, or even become universal. The spread may be very rapid, and the end may occur in a few months, or it may be slower; but it is unusual for any of the cases forming this group to survive for more than eighteen months. This group comprises (1) the generalised cases of simple flaccid atrophy; (2) all the cases of amyotrophic lateral sclerosis; and (3) most of the bulbar cases.

Fibrillation is a most important symptom of the disease, and is an associate of the muscular atrophy. It precedes the wasting of the fibres, and is a sure

herald of the advent of wasting in this disease. It ceases to occur when the muscle is completely wasted, and is not seen when the atrophy is not progressing. On account of the importance of fibrillation as a diagnostic sign of progressive muscular atrophy it is important here to consider those other conditions in which it is met with clinically. It occurs in syringomyelia and in peroneal atrophy, but only when the muscular atrophy is progressing, and, therefore, it is only an occasional symptom in either disease. It is often very marked in cases of interstitial neuritis (sciatica, etc.). It occurs in a most magnified and conspicuous form in certain conditions of gastro-enteritis, and is presumably due to an intoxication, and to this form of fibrillation the term "myokimia" has been applied. It is not met with in polyneuritis, poliomyelitis, myopathy, nor in the common gross lesions of nerve trunks, nerve roots or spinal cord.

The *electrical reactions* of the affected muscles vary according to the degree of degeneration. Since normal and degenerate fibres are stimulated side by side in the affected muscle, there will be some lowering of the response to faradism with a tendency to a polar change. This is known as the "mixed reaction," and it is common to all diseases in which muscle degenerates fibre by fibre. Faradic excitability lessens as more of the muscle fibres degenerate, and when degeneration is complete all electrical excitability is lost. The excitability of the affected muscles to direct mechanical stimuli, such as percussion, is increased so long as any living muscle remains.

Contractures are conspicuous by their absence in this disease, which is thus strongly contrasted with peroneal atrophy and some other muscular atrophies. If the atrophy becomes complete in a whole limb the end-result is that the limb is flail-like and without contracture.

Mental alterations are constantly present in the cases in which the bulbar region is affected. Emotional instability and hyperexcitability are the usual change. The patient is easily excited to tears or to laughter by trivial causes, and when so excited cannot control his expression of emotion. He himself feels little joy or grief during the paroxysms of laughing or crying.

Sphincters.—In the majority of the cases these are not affected, but every now and then dysuria in any of its forms occurs, and it may occur early in the course of the malady, and it may be severe. Loss of sexual power is very common.

Reflexes.—The superficial reflexes are modified in this disease, on the one hand by spasticity, when this is present, and, on the other, by the muscular atrophy which may prevent response in the affected muscles. The pharyngeal reflex in bulbar cases is usually brisk, notwithstanding the statement to the contrary, which most antecedent writers upon this subject have recorded; but the response is not the normal response, involving all the muscles concerned in deglutition, for these are atrophied and paralysed; it is confined to the constrictors of the pharynx and the muscles of the palate, with the feeble co-operation of such of the somatic bulbar muscles as are still able to act. The plantar reflexes are usually of the extensor type when the legs are spastic; but this does not always obtain, for there may be definite rigidity of the legs with brisk knee-jerks and foot-clonus with a persistent flexor response. Similarly, the abdominal reflexes do not disappear so constantly or so early as is the case in disseminated sclerosis, for example, and they may persist when the legs are markedly spastic and extensor plantar

responses have appeared. The muscle-jerks disappear from the affected region in simple atrophic cases *pari passu* with the wasting of the muscles. In cases of tonic atrophy they are everywhere increased, even in regions where the atrophy is severe, and in this type of the malady they never disappear. The same increase of the muscle-jerks occurs in the purely spastic cases.

Diagnosis.—The malady has to be distinguished from the many conditions in which progressive weakness and wasting of the muscles occur, from those in which muscular wasting and spasticity are conspicuous clinical features, and lastly from other diseases, in which bulbar symptoms are early evidenced. Peroneal muscular atrophy very closely resembles progressive muscular atrophy, in that slow wasting and fibrillation of the muscles are the chief clinical features. The points which distinguish the two conditions are that peroneal atrophy is often a familial disease, and is apt to commence in childhood, when it is unusual for progressive muscular atrophy to begin. The location of the atrophy is peculiar, and when well marked in the periphery of all four limbs, as is common in this disease, cannot be confused with progressive muscular atrophy since the latter disease never has this distribution. Syringomyelia is easily distinguishable by the early and striking loss of pain and temperature sensibility. Cervical rib not uncommonly produces atrophy of the intrinsic muscles of the hand, and, though this is usually confined to one hand, it may be bilateral. Further, it is exceptional for the atrophy to involve all the small hand muscles simultaneously, or equally. It picks out the opponens pollicis first and most severely, and is not uniform for all the hand muscles, as in progressive muscular atrophy. Pain in the distribution of the eighth cervical and first dorsal roots, and some loss of sensibility, may be present. The atrophy remains local, and is never accompanied by fibrillation. The abnormal rib is easily discoverable on radiographic examination. It must be borne in mind that cervical ribs are not uncommon, and that their presence does not necessarily prove the cause of atrophy of the hand muscles, for cervical ribs may be present in progressive muscular atrophy, in syringomyelia, and in any other disease.

Arthritic muscular atrophy occurs in the regions of joints which show easily recognisable disease. Fibrillation does not occur, nor are there alterations in the electrical excitability of the wasted muscles. Dystrophia myotonica is at once separated from progressive muscular atrophy by the myotonus, when this latter symptom is present. When myotonus is absent, the characteristic wasting of the sternomastoids, and of the muscles of the thighs, the age of the subject, and sometimes the presence of cataract should suggest the diagnosis.

Lesions of peripheral nerve trunks may be diagnosed by the history of a local cause, by the discovery of a palpable local lesion upon the course of the nerve, and by the confinement of the atrophy to the distribution of one particular nerve, while open pain and sensory loss occur in that same distribution.

Lesions of the nerve roots, and especially those produced by pachymeningitis and by neoplasm in the vertebræ may cause signs and symptoms so closely resembling those of the more rapid forms of progressive muscular atrophy, as to render correct diagnosis very difficult. Such a lesion in the cervical region, for example, may give rise to wasting of the hand and fore-

arm muscles, and a spastic condition of the legs, resembling exactly a condition of amyotrophic lateral sclerosis, without deformity or rigidity of the spine, and without pain or sensory loss. In such cases of difficulty the course of a little time will bring the advent of the conclusive symptoms of a local pressure lesion. It is important in this connection to remember that pressure upon the spinal cord results in hyperalbuminosis of the cerebro-spinal fluid, and if the lesion causing the pressure is syphilitic, there is likely also to be lymphocytosis in that fluid, neither of which conditions is found in progressive muscular atrophy.

Diagnosis is most difficult in those cases where spasticity in the limbs is the first sign of progressive muscular atrophy to appear, and where such spasticity precedes the appearance of any muscular atrophy by a long time. If it be clearly borne in mind that spastic paralysis may be the earliest, and for a time the only sign of progressive muscular atrophy, and that among the many diseases of the nervous system, which commence with the same clinical picture of spastic paralysis, a certain diagnosis cannot be made until further distinguishing signs appear, error will be avoided. The importance of the examination of the cerebro-spinal fluid in doubtful cases cannot be too strongly

Course and Prognosis.—The nature of the disease is to progress, and to extend its area of invasion until a fatal issue is reached. The progress may be rapid, and the end may be reached in a few months, or it may be slow, and many years may elapse before death occurs. The local types of slow onset are the most gradual in their development, and these are often characterised by periods of arrest in the progress of the disease. The generalised simple atrophic type of the disease is the most rapid, especially when it commences with severe initial flaccid paralysis without atrophy.

In the bulbar types of the disease, and in amyotrophic lateral sclerosis, the course is for the most steadily progressive. Every type will show, however, upon occasion, exacerbations and remissions, and the exacerbations are the most important, and in the bulbar types may bring about the end in a few hours. Of particular interest are rapid extensions of a flaccid paralysis, which may occur in a few hours, and which resemble, and indeed are identical with, onset of the disease with initial flaccid paralysis without atrophy, which has been already described. Whatever type of the disease be present, it tends in the end to spread and to become general.

Involvement of the respiratory muscles or severe bulbar symptoms, and the pulmonary complications which may accompany either condition, may bring about the fatal issue. It is usual, however, for death to occur in a manner which is common to so many degenerative nervous diseases, a rapid increase of the paralysis is associated with an increasing lethargy, which soon deepens into a rapidly fatal coma. It is uncommon for death to occur from intercurrent maladies. The average tenure of existence after definite signs are present is under 1 year in the generalised flaccid type, and it may be as short as 2 months. Bulbar symptoms are not generally survived for more than 12 months. Localised cases of simple atrophy may live for many years. Some of the patients in whom a positive Wassermann reaction is found improve, and the disease is sometimes arrested by antisyphilitic treatment.

The progressive character of the disease renders the prognosis grave in

every case. There are some cases occurring in middle life, which are presumably cases of progressive muscular atrophy of local distribution and slow onset and course, which become finally arrested or even improve; but in the absence of pathological verification the true nature of such cases is open to doubt.

In amyotrophic lateral sclerosis the average duration of life is not more than 2 years from the onset. When bulbar symptoms are present the average duration is under 2 years. In the generalised cases the average duration is under 1 year. Widely spread fibrillation in muscles, which are neither weak nor wasted, is the constant herald of generalisation, and renders the immediate prognosis serious. In cases where syphilis is present the prognosis is more favourable, and there is even a possibility of arrest and improvement if energetic treatment of the associated condition is provided. Rapid extension of the weakness, the advent of bulbar symptoms, involvement of all the respiratory muscles, and especially general asthenia and drowsiness are the signs which usher in the fatal result.

Complications.—By far the most common complication which is met with in cases of progressive muscular atrophy is the presence of some syphilitic lesion of the nervous system, and this may be of any nature, both local or general. Tabes dorsalis, associated with progressive muscular atrophy, is not uncommon. General paralysis of the insane has been noted in a few cases, as has also paralysis agitans.

Treatment.—For the most this malady seems to be entirely uninfluenced by any treatment that has hitherto been adopted. Even where syphilis is a factor in the causation, although appropriate treatment for these conditions has been applied, and improvement and even arrest may result, it is no rare thing to see no amelioration, and in some cases such treatment seems actually to hasten the progress of the disease. Recently, dramatic claims have been made in respect of vitamin E (tocopherol acetate), given in doses of 3 mgs. thrice daily. This is said to arrest wasting and weakness and in early cases to effect rapid improvement. In a brief experience since this claim was made the present writer has been wholly unable to confirm it, and it must be accepted with the greatest reserve. It remains, therefore, to secure favourable conditions of life for the patient, and to maintain the general health in as perfect a state as possible. Massage and passive movements are useful as giving bodily comfort to the patient, and satisfying him that something is being done for him. In bulbar cases, the dysphagia must be aided by avoiding liquids and solids, and by serving all the articles of diet in pultaceous form. Salivation, which is so troublesome in this condition, may be greatly helped by the administration of hyoscine by the mouth.

PERONEAL MUSCULAR ATROPHY

Synonym.—Charcot-Marie-Tooth Type of Muscular Atrophy, Neuritic Type of Muscular Atrophy.

This is an absolutely distinct and peculiar form of muscular atrophy, with a frequent tendency to occur in several members of the same family. It usually commences in mid-childhood, and after progressing for some twenty years or less, comes to a final arrest. The atrophy always commences

in the intrinsic muscles of the feet, and is throughout strictly distal in distribution. The muscles of the face and trunk and the proximal muscles of the limbs are never affected. The atrophy leaves a peculiar elastic fibrosis in the affected muscles, so that the incapacity caused by this disease is much less than in any other form of muscular atrophy of like degree. Sensibility is often slightly affected, and there may be deep sensory loss. The essential morbid anatomy is a primary neurone atrophy of the anterior horn cells and of some of the afferent neurones in certain regions of the spinal cord.

Ætiology.—The disease usually commences between the fifth and tenth years of childhood, but it may appear as late as the fourth decade of life. Males and females are both affected. Heredity plays an important part in the incidence, although isolated sporadic cases are not uncommon. It may exhibit every type of inheritance. The malady often occurs in families, and has been traced through five generations; it may skip a generation and then reappear.

Pathology.—The anterior horn cells of the affected regions show a slowly progressive atrophy and disappearance, with corresponding atrophy of fibres in the peripheral nerves. The cells of Clarke's column show signs of degeneration, as do also some of the fibres of the posterior columns of the spinal cord, and especially those of the postero-lateral column. Slight degeneration in some of the fibres of the pyramidal tracts is usually found. The affected muscles show a simple atrophy of the muscle fibres, indistinguishable from that seen when a motor nerve is divided. There is a simple shrinking of the fibres, which stain progressively and more and more deeply with hæmatoxylin, lose their striation, and finally disappear. Secondary fibrotic changes accompany the atrophy, together with sclerosis of the arteries of the muscle.

Symptoms.—Muscular atrophy dominates the clinical picture of this malady. It is strictly distal in distribution, and this feature will serve to distinguish peroneal atrophy from any other form of muscular atrophy. This is to say it does not affect one particular muscle, but the distal ends of all the muscles below a certain level on the limb, leaving the proximal ends of the muscles normal, and it advances up the limb inch by inch, the separation of the wasted portion of the muscle from the normal portion being always transverse to its length. In other words, the muscle fibres seem to waste in terms of the length of the spinal axons which supply them. The wasting commences always in the intrinsic muscles of the feet, and hollowness of the instep and thinness of the feet, together with retraction of the toes and the difficulty which the pes cavus so produced entails in fitting boots, first draws attention to the disease. As the process advances, the lower segments of the anterior tibial, peroneal and calf muscles become affected, and the limb is subsequently involved until the lower third of the thigh is reached, at which stage the disease is invariably arrested. This slow spread of the atrophy from the distal towards the proximal portion of the limb, gives rise to a most unique and characteristic feature in the appearance of the legs at the several stages of the disease. As an example, the complete atrophy of all the muscles below the middle and a well-developed musculature in the upper half of the leg, give rise to the inverted "fat bottle" calf. When the atrophy has involved the lower third of the thigh, the lower end of the femur, bare of muscle and covered only by skin and tendons,

contrasts strongly with the well-developed muscles of the upper thigh, and causes the thigh to resemble an inverted champagne bottle.

Some years after the atrophy has become marked in the lower extremities, and in the usual run of cases just before the age of puberty, the intrinsic muscles of the hands and first those of the thenar and hypothenar group begin to waste, and this wasting may extend as high as the middle of the forearm. It must be borne in mind that the disease may become arrested at any period of its spread, and especially that the upper extremities often escape altogether. With the exception of the lower part of the thighs, the proximal segments of the limbs do not become involved, and the muscles of the head, neck and trunk remain unaffected.

The affected regions of the muscles waste absolutely, and leave a very elastic fibrous tissue. The electrical excitability in the wasted regions becomes first lowered and then lost, and, in the earlier stages, may show a mixed reaction, in which there is lowering of excitability to faradism, with a tendency to an inverted polar reaction. Fibrillation of the muscles is an important sign. It is seen only when the disease is progressing, and in the muscles which are obviously wasting. It is never general, as in some cases of progressive muscular atrophy. And since peroneal atrophy is at times advancing and at other times stationary, fibrillation may be in one case conspicuous and in another never seen. It disappears entirely when the progress of the malady becomes finally arrested, and is, therefore, useful as a clinical indication of active advance of the disease. Contractures always occur, and from the nature of the distribution of the atrophy are necessarily confined to the feet and the hands. In the feet, pes cavus with retracted toes is the rule; but sometimes, and in some stages of the disease, the feet and toes may be dropped and the feet inverted. The sphincters are unaffected. The ankle-jerks are diminished or lost in proportion to the wasting of the calf muscles. In the final arrested stage they are usually lost. The knee-jerk is always retained and is usually brisk. The plantar reflexes are usually lost early so far as any response in the foot is concerned, but some response in the upper thigh muscles, upon stimulating the plantar region, often remains. Pain, tenderness and cramp are entirely absent. Conspicuous loss of sensibility is uncommon, but slight loss of deep sensibility, loss of the vibration sense and relative tactile loss, may often be detected upon careful examination: but in rarer cases all forms of sensibility may be severely affected, or even entirely lost. Perforating ulcers may be met with upon the soles of the feet, and are explained by the thinness of the feet and their deformity, which, coupled with the clumsiness of the use of the feet, lead to the formation of severe corns which break down into perforating ulcers. Loss of sensibility also is a factor in their production.

The most striking of all the clinical features of peroneal atrophy is the comparatively slight disability which the wasting of the muscles and consequent paralysis, and even the sensory loss, when present, cause.

Course.—The course is irregularly progressive for a number of years only, and the advance of the disease ceases usually in the third decade of life. Exacerbations of the weakness are likely to be followed in every case by considerable improvement, owing to the secondary fibrosis in the muscles.

Diagnosis.—Peroneal atrophy in the early stages is easily confused with progressive muscular atrophy, in that wasting of muscles and fibrillation

are the conspicuous features. The onset usually in childhood and the fact that the feet are affected first, the peculiar distal distribution and the presence of any familial incidence, are important. But the only distinction which is absolute is the distribution, for progressive muscular atrophy may begin in childhood and peroneal atrophy may not appear till after middle life, and often familial relations are absent in the latter malady. In the course of time the diagnosis always becomes clear, for progressive muscular atrophy never keeps to the classic distribution, nor is it followed by the peculiar fibrosis which characterises peroneal atrophy.

Dystrophia myotonica when commencing in the peroneal muscles may for a time closely simulate peroneal atrophy. The presence of the least sign of myotonia, the involvement of the face and the atrophy of the sterno-mastoids, will establish the diagnosis.

The usual forms of myopathy are at once separated from peroneal atrophy by the distribution of the muscular weakness and wasting, which in the former group of maladies is conspicuously upon the face, trunk and proximal muscles of the limbs, and in the latter upon the distal muscles. Peripheral neuritis is more rapid in its onset, and is apt to be associated with marked sensory disturbances, both objective and subjective, and the paralysis is in terms of individual muscles, which is not the case in peroneal atrophy.

Treatment. —The general health should be carefully maintained, and the nutrition of the affected muscles aided by the application of massage. Care must be taken, on the one hand, to avoid over-fatigue of the affected muscles, and, on the other, to ensure such regular exercise as is compatible with their capacity. Bicycling, for example, since it employs chiefly the thigh muscles, is a better form of exercise for these patients than is walking. In no circumstances should tenotomies be performed for the deformity of the feet, for such measures tend to destroy the effect of the conservative fibrosis, so essential to the production of a useful limb. The use of heavy mechanical supports is to be avoided above all things. Light, well-fitting boots, so as to interfere as little as possible with the exercise of the damaged muscles, are essential.

PROGRESSIVE SPINAL MUSCULAR ATROPHY OF CHILDREN

Synonym.—The Werdnig-Hoffmann Disease.

This is a malady of the first year of infancy, often incident upon several children of the same parents, and characterised by the gradual development of progressive muscular weakness and atrophy, which affects the proximal muscles first and most, increases to a complete paralysis of trunk and limbs, and finally affects the bulbar muscles. The disease is invariably fatal in from a few weeks to several months. The most striking pathological changes are a progressive degeneration and disappearance of the ventral horn cells of the spinal cord, and of their analogues in the brain stem.

Ætiology.—In some of the cases the paralysis is noticeable at the time of birth, and the disease is obviously of pre-natal development. In others the children are quite healthy at birth, and the disease develops some time during the first year of life, and most frequently within 8 weeks of birth. Though sporadic cases may be met with, yet in the majority of instances

several children of the same mother are affected. Both the pre-natal cases and the post-natal cases may be met with among the children of the same mother. The sexes seem to be equally affected. No maternal ill-health during pregnancy has been noticed, and nothing is known about any other ætiological factor.

Pathology.—The most extensive changes are found in the ventral horn cells throughout the spinal cord and brain stem, and at many levels no normal cells whatever are to be seen. Tigrolysis, swelling and glassiness of the cells, extrusion of the nuclei, disappearance of the dendrites, shrinking of the cells and final disappearance is the sequence of the changes. Degeneration of the anterior roots and of the peripheral motor nerve fibres consequently occurs. These changes are not confined to the lower motor neurones, for in our cases examination by the Marchi method showed extensive degeneration throughout the posterior columns of the cord, indicating that lower sensory neurones were also considerably affected.

The muscles show intense degeneration with hypertrophy of some fibres and atrophy of most of the fibres, waving, moniliform shape, hypernucleation of the spindles, general nuclear increase and fibrosis.

Symptoms.—In the cases which are pre-natal, the malady is noticed at the time of birth on account of the tonelessness, flaccidity and the poorness of movement in the trunk and proximal muscles of the limbs. In the post-natal cases there is a gradual onset of similar weakness and flaccidity in the trunk first, and in the limbs afterwards, which usually commences within six weeks of birth, but which may not appear until towards the end of the first year of life. The weakness seems always to be least marked in the periphery of the limbs, where curious, slow, involuntary movements of the fingers and toes have been noted in a good many of the cases. The paralysis is followed by a rapid and extensive wasting of the muscles, accompanied by occasional fibrillary twitchings. Since these children are not only well nourished, but often put on much fat during the illness, wasting of the muscles may not be apparent on inspection or palpation. It can, however, immediately be detected by radiography, which distinguishes sharply between fat and muscle.

As the malady progresses the trunk muscles become completely paralysed, the intercostal muscles being always paralysed before the diaphragm. The limbs become progressively weaker, and, lastly, bulbar paralysis supervenes in those cases where death has not already occurred from respiratory paralysis. The reaction of degeneration is present in the affected muscles. Sensibility may be unimpaired; but in several of my cases there has been conspicuous loss of pain sensibility over the limbs and trunk. The sphincters are unimpaired until the very last stages of the disease. The superficial and deep reflexes are lost. The ocular muscles have not been affected, and intelligence is preserved throughout.

Diagnosis.—The peculiar and striking features of the disease make the diagnosis easy, if the symptomatology be known. Amyotonia congenita presents the same helplessness and flaccidity of trunk and limbs as does the Werdnig-Hoffmann disease, and further resembles it in being sometimes congenital, and sometimes having an onset very early in life. In amyotonia congenita, however, the paralysis is not complete, and it tends to improvement and not to progressive increase. Contractures also occur, which are

not found in the Werdnig-Hoffmann disease, and, lastly, the definite spinal cord changes of the latter malady are not found in the former.

Course and Prognosis—The course is invariably progressive, and is more rapid the earlier in life the disease commences, and it is most rapid of all in the pre-natal cases, which are usually fatal within a few weeks. With an onset some weeks after birth, life is usually continued for several months, and a few cases have been reported with an onset towards the end of the first year, in which death has been delayed until the third or fourth year.

Treatment.—No treatment is known to influence the course of the malady.

LESIONS OF THE PERIPHERAL NERVES

LOCAL LESIONS OF NERVE ROOTS AND NERVE TRUNKS

PHRENIC NERVE.—This nerve supplies the diaphragm. Paralysis results most often from disease of the spinal cord, but the roots may be implicated in disease of the spine, and the trunk may be injured, in its course through the neck and thorax, by wounds or tumours. Bilateral paralysis occurs in lesions of the cord and spine, and in alcoholic, diphtheritic, saturnine and other forms of peripheral neuritis. Other causes usually affect one side only. When the diaphragm is completely paralysed, the normal inspiratory protrusion of the upper part of the abdomen disappears, or is replaced by retraction of this part with each inspiration. During rest, so long as the lungs are healthy, the respiratory rate does not increase, but if bronchitis or pneumonia arises as a complication, or if the patient exerts himself, the diminished reserve of respiratory power is seriously felt. When one nerve only is affected the diaphragm does not descend on that side. This is rarely detected by observation of the abdominal movements, but is easily seen on the X-ray screen. It produces no discomfort.

THE LONG THORACIC NERVE.—This nerve supplies the serratus magnus muscle. When all the fibres of this muscle contract, the scapula moves upwards, forwards and outwards. It contracts with the pectoralis major in the action of pushing forward the point of the shoulder and in the rapier-thrust movement. It also assists the deltoid in raising the arm. When it is paralysed alone, the position of the scapula at rest is unaltered, but if the trapezius and the rhomboids are paralysed as well the scapula drops, and its lower angle is displaced inwards. Paralysis of the serratus magnus is best demonstrated by causing the patient to hold the arms outstretched before him. The arm is not raised so high on the affected as on the normal side, because the scapula is not fixed and the deltoid works at a disadvantage. Viewed from behind the deformity is characteristic. The vertebral border of the scapula stands out prominently and the hand can be pushed between this bone and the thorax—"winged scapula." On raising the arm from the side, there is difficulty in attaining the horizontal position, but the winging of the scapula is less apparent.

The nerve may be damaged by carrying heavy weights on the shoulder, by falls or blows on the shoulder, and by continued muscular effort with the

raised arm. The nerve may be injured alone in gunshot wounds, but as a rule it is associated with lesion of the brachial plexus. In addition, a serratus magnus palsy may develop suddenly in an otherwise healthy person after exposure to cold, or as part of a rare reaction to the administration of serum or antitoxin. In the cases caused by compression, severe neuralgic pains in the neck precede the onset of paralysis. Recovery is always very slow and the defect may be permanent.

BRACHIAL PLEXUS.—The brachial plexus may be injured by stabs in the neck, by penetrating missiles, by dislocation of the shoulder or fracture of the clavicle, or by pressure of a tumour, aneurysm or cervical rib. Further, the nerves may be torn by forcible dragging on the arm in accidents or during delivery. In most cases the lesion is partial and the symptoms conform in the main to one of the following types.

Upper plexus paralysis (*Erb's palsy*).—This results from an injury to the fifth and sixth cervical roots. The muscles paralysed are: biceps, deltoid, brachialis anticus, supinator longus, supraspinatus, infraspinatus, rhomboideus, subscapularis, clavicular portion of pectoralis major, serratus magnus, latissimus dorsi, teres major. The arm cannot be flexed at the elbow (flexors of forearm), nor raised and abducted (deltoid). The movements of the wrist and fingers are not impaired. Adduction of the arm is weak (pectoralis major), and rotation is feeble or absent (spinati). On attempting to oppose the shoulders, the scapula on the affected side passes farther from the middle line (rhomboideus). The hand of the affected side cannot be placed on the buttock of the sound side (latissimus dorsi).

The reaction of degeneration is often complete in the deltoid and flexors of the forearm and nearly so in the spinati. It is usually incomplete in the other muscles. Sensation is diminished or lost along the outer border of the whole limb immediately after the injury, but improvement sets in rapidly. For some time the patient experiences pins and needles and burning sensations in the affected area, which last longest in the thumb and index finger. The biceps reflex is lost. In this form the tendency to complete recovery is great. As a rule all the symptoms disappear completely in from 6 months to 2 or 3 years. Weakness persists longest in the deltoid and supinator longus.

Lower plexus paralysis (*Klumpke's palsy*).—This results from a lesion of the eighth cervical and first dorsal roots, or of the common trunk of the median and ulnar nerves. The intrinsic muscles of the hand and the flexors of the wrist and fingers are paralysed, and the inner border of the forearm and hand is anæsthetic. When the roots are damaged, sympathetic fibres may be implicated with the production of myosis, narrowing of the palpebral aperture, enophthalmos and alterations in sweating on the face, neck, arm and upper part of the chest, on the affected side.

Middle plexus paralysis.—This form of paralysis is a common result of gunshot injuries of the plexus. It affects the muscles supplied by the musculospiral and circumflex nerves—posterior cord. As the nerve to the latissimus dorsi arises from the same trunk, this muscle is often paralysed as well. In addition to these simple types, more complicated paralyses occur, in which various parts of the plexus are injured together.

In *paralysis of the inner cord of the plexus*, atrophy is confined to the intrinsic hand muscles, and the sensory loss is confined to the hand.

Lesions of the brachial plexus show a remarkable tendency to spon-

taneous recovery. In many cases recovery is complete in 6 months to 2 years, in others it is partial, and some muscles remain paralysed.

THE MUSCULO-SPIRAL NERVE.—Owing to its long course, its position in relation to the humerus, and its peculiar vulnerability to compression, paralysis of the musculo-spiral nerve is one of the commonest peripheral palsies; although it is a mixed nerve, containing sensory, motor and vaso-motor fibres, the symptoms of an injury are almost entirely motor. In the upper arm the nerve supplies the triceps and the anconeus, in the forearm the supinators, the extensors of the wrist and fingers, and the extensors and long abductor of the thumb.

Symptoms.—Injury to the nerve is followed by dropping of the wrist and fingers. The wrist and the first phalanges are flexed. The flexion is limp and easily reducible.

When the lesion is in the axilla the whole of the *triceps* is paralysed, and extension at the elbow is lost. Occasionally in wounds of the posterior aspect of the arm the nerves to the triceps are injured, whilst the main trunk escapes. The patient is then able to extend the arm powerfully by means of the anconeus, but if he is made to raise the elbow as high as possible with his fingers on the point of the shoulder, extension of the bent forearm is impossible.

In most cases the nerve is injured in the middle third of the arm and the triceps escapes, but the supinator longus and *all* the extensor muscles in the forearm are paralysed. Partial paralyses, such as are seen in lesions of the median and ulnar nerves, are very rare. The *supinator longus*, so-called, is not a supinator. Its action is to flex the forearm, whilst the hand is in a position intermediate between pronation and supination. Paralysis of this muscle is detected by the absence of contraction when the pronated forearm is flexed against resistance. Owing to paralysis of the *supinator brevis* supination is abolished. During the movement of flexion of the forearm the biceps acts as a supinator, during extension the external rotators of the shoulder, but feebly.

Paralysis of the *extensors of the carpus* abolishes both extension and lateral movement at the wrist. The flexors of the carpus play no part in lateral movements. The *extensors of the fingers* extend the first phalanges *only*. Extension at the distal joints is carried out by the lumbricals and interossei. Paralysis of the *extensors and long abductor of the thumb* renders abduction of the thumb and extension of the phalanges impossible. On attempting to abduct the thumb, it passes no farther than the radial border of the hand. In some cases, the second phalanx of the thumb can be feebly extended by the muscles of the thenar eminence.

Many muscles not supplied by the musculo-spiral work at a disadvantage when the extensors are paralysed. These defects must not be mistaken for signs of injury to other nerves. Owing to the flexed position of the hand the grasp is feeble, but if the wrist is extended passively the grasp is improved. The patient cannot make a fist properly, as the thumb does not oppose the index finger and the fingers cannot be flexed into the palm, until the thumb has been moved aside by the sound hand. The movements of the interossei in abducting and adducting the fingers are also feeble while the wrist is flexed, but are much stronger when the hand is resting flat on a table with the wrist and fingers extended. The complete reaction of degeneration is

often found in all the paralysed muscles from the onset. Atrophy becomes obvious in a month or two. Its extent and severity give important evidence for prognosis.

Sensory disturbances.—Subjective symptoms are rare. In a few cases, paræsthesiæ are felt on the posterior aspect of the forearm and on the dorsal aspect of the thumb. They are of brief duration, and are commoner with partial than with complete lesions. Severe causalgias are almost never seen in lesions of this nerve. Sensibility to light touch, superficial pain and temperature is impaired over a small area on the radial border of the hand, including the proximal joints of the thumb and first two fingers. The defect is often very slight, and is only discovered on very careful examination. Deep sensibility is rarely affected. Considering the extensive distribution of the external cutaneous branch of the musculo-spiral nerve, it is rather surprising that the sensory disturbances are so slight, when the nerve is injured above the origin of this branch.

Recovery.—It might be thought that recovery would take place in the order of the length of the branches to the various muscles. This, however, is not the case. As a rule the extensors of the wrist recover first, then the extensors of the middle, ring, little and index fingers in this order, next the supinator longus, and the extensors and abductors of the thumb last of all. On palpation of the muscles during attempted extension, contractions can be felt before any movement is produced. Other signs of impending recovery are the disappearance of automatic pronation and of the flail-like drop of the hand, also diminution of automatic flexion of the fingers after passive extension. Recovery of movement is complete when the patient is able to extend the wrist and all the fingers simultaneously or separately. After this becomes possible, restoration of power is rapid.

The Median Nerve.—Whilst the clinical individuality of the musculo-spiral nerve is shown in the preponderance of motor symptoms and in the uniform completeness of the paralysis that follows an injury, that of the median is seen in the frequency of partial and especially of painful lesions. Isolated palsy of this nerve is infrequent except as a result of gunshot wounds and other injuries. It may be damaged by repeated violent contractions of the pronator radii teres, as in one of the forms of "tennis elbow."

Total paralysis.—The muscles paralysed are the pronators, the radial flexor of the wrist, the flexors of the fingers except the ulnar half of the deep flexor, most of the muscles of the thenar eminence (opponens, abductor brevis and outer head of the flexor brevis pollicis) and the two radial lumbricals. Stated briefly the symptoms are: inability to flex the phalanges of the index finger and the second phalanx of the thumb; difficulty in flexing the phalanges of the middle finger; defective opposition of the thumb. The appearance of the hand in total lesions is fairly constant. The hand inclines to the ulnar side, the index and middle fingers are more extended than is normal, and the thumb lies on a level with the fingers—the ape-hand.

Pronation is incomplete and defective. The patient tries to overcome the defect by rotating the whole limb at the shoulder. Paralysis of the *flexors of the wrist* is seen when an attempt is made to flex against resistance. The tendon of the ulnar flexor alone stands out, and the hand is drawn towards the ulnar side. Even at rest, the flexor tendons are more prominent on the sound than on the affected side.

Flexion of the fingers is good in the two ulnar fingers, though weaker than normal. The index cannot be flexed at all, and the third finger only incompletely. Flexion at the proximal joint is usually good in all the fingers including the index, and flexion at this joint with extension at the last two joints is usually well done by the interossei and lumbricals. If the proximal phalanx of the thumb is immobilised, it will be seen that flexion of the terminal phalanx is abolished, owing to paralysis of the *flexor longus pollicis*.

Paralysis of the *thenar muscles* renders opposition and abduction of the thumb defective. By means of the adductor the thumb can be drawn into the palm, but as the radial fingers cannot be flexed nor the thumb opposed, it is impossible to place the tip of the thumb on the tips of the fingers. Atrophy of the muscles becomes obvious in a few weeks. The outer part of the thenar eminence is flattened, and the bulk of the muscles arising from the internal condyle is greatly diminished.

Sensory disturbances.—In almost every case there is complete anæsthesia to all forms of sensation in the two terminal phalanges of the index and middle fingers. The skin outside this area may be unaffected even in complete lesions, but in most cases sensibility is diminished in the terminal phalanx of the thumb, and to a less extent over the remainder of the radial half of the palm, including the radial side of the ring finger. The stereognostic sense is lost in the outer fingers. This defect, together with the loss of power, renders the thumb and index finger useless, and makes paralysis of the median the most serious single nerve lesion of the upper limb.

Vasomotor and trophic changes.—In many cases the skin in the distribution of the median nerve is red, dry and chapped, and the nails white or purple. It is possible that these changes are due to an associated vascular lesion.

Recovery is extremely slow and is rarely complete. Sensation begins to return before power, but the stereognostic sense is often defective, long after movement in the fingers has returned. The pronator and the flexors of the wrist recover first, then the flexors of the thumb and middle finger. Flexion of the index finger and opposition of the thumb, if it is regained at all, remains defective for several years. In searching for signs of recovery, care must be taken lest some "trick-movement," due to contractions of healthy muscles, is misconstrued. For example, when told to flex the terminal phalanx of the thumb, the patient first over-extends and abducts, and then relaxes suddenly. The terminal phalanx then makes a slight passive movement of flexion, which may be mistaken for true active flexion. Recovery is complete when the patient is able to make a good fist with the fingers flexed well into the palm, and the thumb pressed firmly upon the dorsal aspect of the second phalanx of the middle finger.

PARTIAL LESIONS.—Partial paralysis of the median nerve is much commoner than the complete form.

Motor symptoms.—Flexion of the index finger and opposition of the thumb are most impaired. The flexors of the middle finger and of the terminal phalanx of the thumb may suffer also, but to a less degree, whilst the pronators and the flexors of the wrist often escape entirely.

Sensory symptoms.—Apart from the painful lesions to be mentioned later, sensory troubles are usually slight in partial lesions. Anæsthesia is rare, but sensibility to all forms may be diminished in the areas mentioned under complete lesions.

Vasomotor symptoms.—The skin is often cyanosed in the distribution of the injured nerve, and it may perspire more freely than in healthy parts. These changes are more distinct when the paralysis is complicated by a vascular lesion.

Recovery is naturally more rapid than in complete lesions. The order in which the muscles recover and the tests for complete return of function have been mentioned above.

PAINFUL LESIONS OF THE MEDIAN NERVE.—*Causalgia.*—In many cases the most prominent symptom of injury to the median nerve is *pain.*

Motor disturbances are always present, but are usually slight, the weakness affecting mainly the flexors of the index finger and the thenar muscles.

Vasomotor changes are a feature of this type. In many cases perspiration is diminished over the radial half of the palm, and the skin becomes dry and scaly. In others, perspiration is increased over the median area.

Sensory disturbances.—Pain comes on about a month after the injury, at first as tingling or pricking in the finger-tips and palm, later as a constant severe smarting, dragging or *burning* pain—hence the name causalgia. Added to the constant pain, which never ceases day or night, paroxysms occur, in which the pain increases suddenly in intensity. The application of cold water gives temporary relief, and patients often wear bandages or gloves which they keep constantly moistened. Many develop a phobia of dryness. They will not touch dry objects, even with the healthy hand, the sight of another person handling a dry object increases the pain, and any rustling or crackling sound, suggestive of dryness, may bring on a paroxysm.

In severe cases the limb is held flexed at the elbow and wrist, with the hand constantly raised and the fingers extended or hyper-extended. The whole hand atrophies, and irreducible ankylosis occurs with the limb in this position. The skin of the hand is thin and dry. The fingers taper, and the nails are long, brittle, blackened and striated longitudinally. The pain reaches its acme 4 or 5 months after the injury, and then slowly declines, but the limb remains useless. Even in slighter cases, without much deformity, recovery of function is extremely slow, and is rarely complete.

THE ULNAR NERVE.—The ulnar nerve supplies the ulnar flexor of the wrist, the ulnar half of the deep flexor of the fingers, the muscles of the hypothenar eminence, the interossei, the two inner lumbricals, and the adductor and inner head of the short flexor of the thumb. Its sensory area is the ulnar border of the hand, the little finger and the inner half of the ring finger.

Total paralysis.—Paralysis of the *flexor carpi ulnaris* may be detected by palpating the tendons when the wrists are flexed against resistance. The limpness on the affected side contrasts strongly with the firmness on the sound side. Lateral movements of the hand are unaffected, as these are carried out by the extensors.

Paralysis of the ulnar portion of the *flexor profundus digitorum.* In making a fist, flexion of the index finger is perfect and that of the middle finger good, whilst in the ring and little finger it is absent or very feeble. This weakness is best seen when flexion is attempted with the index and middle fingers extended. Even when the fingers can be flexed by the action of the flexor sublimis, the power of resisting passive extension is completely lost in the terminal phalanx of the two ulnar fingers. Paralysis of the *hypothenar* muscles abolishes lateral movements of the little finger, and

diminishes the power of flexion at the proximal joint. Paralysis of the interossei and of the inner two lumbricals leads to the production of the "claw-hand."

The action of these muscles is to flex the fingers at the proximal joints with the distal joints extended. In the "claw-hand" the posture of the fingers is just the opposite of this, namely, extension at the proximal joint with flexion of the distal joints. Although all the interossei are paralysed, the defect is only seen in the ulnar fingers, as the radial lumbricals supplied by the median are still healthy. It is produced by the action of the long extensors, which being now unopposed, over-extend the proximal joints, and by the flexor sublimis which flexes the second joint and draws the distal joint down with it. The clawing of the fingers is greatly accentuated when the nerve is paralysed below the point of origin of the fibres to the long flexors of the fingers. Other features of the "ulnar hand" are atrophy of the interossei and of the hypothenar eminence and persistent abduction of the little and ring fingers. The movements of abduction and adduction are lost in the inner two fingers, and often in the middle finger. Further, these fingers cannot be flexed at the distal joint, whilst the proximal joints are extended.

Paralysis of the *adductor pollicis* and of the inner head of the *flexor brevis pollicis* produces peculiar disturbances in prehensile movements. If the patient is asked to grasp a folded paper between his thumb and index finger, and to resist efforts to remove it by pulling, it will be found that this movement, which is normally very powerful, is grossly defective. He cannot grasp the object beneath the thumb with the second phalanx extended; but presses the tip of the flexed thumb against the outer margin of the index finger.

Sensory disturbances.—In complete lesions, all forms of sensation are abolished in the little finger, and along the ulnar border of the hand. Beyond this there is usually diminished sensibility on the ulnar side of the ring finger, and over a narrow area towards the centre of the hand on both aspects. Spontaneous pains are rare, and vasomotor changes are usually slight.

Partial paralysis.—In partial lesions the same symptoms are found in a less degree. The small muscles of the hand suffer most. Clawing may be slight or absent. Neuralgic pains may be felt in the distribution of the ulnar nerve; but causalgia is never seen in lesions of this nerve alone.

Recovery of sensation is usually complete before movement is regained. The flexor carpi ulnaris recovers first, then the long flexors of the fingers, and last the small muscles of the hand. In these recovery is extremely slow. When recovery of movement is complete the patient can abduct and adduct the middle finger with the palm flat on a table, and he can also scratch the table with the nail of the little finger without moving his wrist.

THE MUSCULO-CUTANEOUS NERVE is rarely affected alone, but is often implicated with the brachial plexus. It supplies the biceps, coraco-brachialis and brachialis anticus. Flexion of the forearm can still be carried out by the supinator longus; but the power of flexion is greatly diminished. Sensation may be diminished or lost along the radial border of the forearm.

THE CIRCUMFLEX NERVE supplies the deltoid and teres minor, and the skin over the deltoid. It may be injured alone in injuries to the shoulder and by pressure of a crutch. The chief symptom is paralysis of the deltoid with almost complete inability to raise the arm.

INTERNAL CUTANEOUS NERVE.—Division of this nerve produces a narrow area of anæsthesia on the inner side of the forearm.

THE LESSER INTERNAL CUTANEOUS supplies the skin on the inner aspect of the upper arm.

In war injuries lesions of the nerves of the lower limb are very frequent; but in civil practice, apart from sciatica, local lesions of these nerves are rare.

THE LUMBO-SACRAL PLEXUS.—The *lumbar plexus* may be damaged by abdominal tumours, and its roots by new-growth or other disease of the vertebræ. In a certain number of cases signs of inflammation of the lumbar plexus are found in association with sciatica or neuritis of the *sacral plexus*.

ANTERIOR CRURAL NERVE (L_2, L_3, L_4).—This is the largest branch of the lumbar plexus. It supplies the psoas, iliacus, pectineus, sartorius, adductor longus and quadriceps femoris. It may be injured alone by fractures of the pelvis or of the femur, by dislocations of the hip, or by implication in wounds, psoas abscesses or new growths.

The most prominent symptoms are loss of power to extend the knee, loss of the knee-jerk, wasting of the quadriceps, and sensory disturbances over the anterior surface of the thigh and inner surface of the leg. The psoas always escapes, unless the plexus itself is also damaged; but flexion at the hip may be imperfect through paralysis of the iliacus. Owing to the rapid dispersion of the branches in the thigh, wounds in this part often cause partial lesions. In these the *nerve to the quadriceps* is most often injured. The resulting paralysis causes serious disability in walking as the knee gives way at every step, especially in going down stairs, and lameness lasts for a long time after complete return of voluntary movement.

OBTURATOR NERVE (L_2, L_3, L_4).—This nerve is rarely damaged alone. It supplies the three adductor muscles, the obturator externus and the gracilis. The symptoms are weakness of adduction and internal rotation at the hip.

EXTERNAL CUTANEOUS NERVE (L_2, L_3).—This nerve supplies an area of skin on the buttock, and through its femoral branch the skin on the antero-lateral aspect of the thigh. As a result of injury, but more often without obvious cause, the skin in the territory of this nerve may show peculiar sensory disturbances, which have been described under the name of *meralgia paræsthetica*. Most cases occur in men. In women it is usually associated with pregnancy. The nerve is tender on pressure at the point where it passes from under Poupart's ligament, and neuralgic pain or numbness and tingling is felt in the skin, which may be slightly insensitive on objective examination or extremely hyperæsthetic, so that the slightest touch causes pain. The symptoms, which are always unilateral, are made worse by walking, and may cause serious incapacity by their persistence and severity. In severe cases the nerve should be excised.

The *sacral plexus* may be damaged by growths or inflammation in the pelvis, by compression during parturition, and by penetrating missiles. It is also often the seat of spontaneous neuritis.

THE GREAT SCIATIC NERVE (L^4, L^5, S^1, S^2).—This nerve supplies the flexors of the leg and all the muscles below the knee. It may be involved in pelvic new growths, or injured by fractures of the pelvis or femur. Next

to the musculo-spiral it suffers in gunshot wounds more often than any other nerve.

Total paralysis.—The foot drops, and the toes point downwards. Walking is possible, but the patient cannot stand on the heel or toes of the paralysed foot. The knee is raised high, but the steppage is not so marked in total lesions as when the external popliteal alone is paralysed. All movement below the knee is abolished. When the wound is in the buttocks flexion of the knee is very weak. The foot becomes œdematous if allowed to hang down. Sweating is often absent on the sole and dorsum of the foot, but is normal on the inner side of the foot, which is supplied by the anterior crural. The skin is dry and thin, and may be scaly. Hyperkeratosis of the sole is common. Subjective sensibility is rarely affected. The skin is completely anæsthetic over the entire foot, except the inner border of the sole and around the internal malleolus. The anæsthesia extends upwards on the postero-external aspect of the calf in its lower two-thirds, embracing the tendo Achillis and external malleolus. Beyond this area of complete anæsthesia there is a wide zone in which sensibility is diminished. The sense of position and passive movement is abolished in the foot and toes. The knee-jerk is present. The ankle-jerk is always lost. Stimulation of the sole may produce a contraction in the tensor of the fascia lata; but there is no response in the foot.

Partial paralysis.—In wounds of the sciatic nerve it often happens that the fibres of the external popliteal alone are wounded, since the sciatic trunk often divides into the internal and external popliteal branches as high as the great sacro-sciatic notch. The symptoms are described below under paralysis of this nerve. In other cases, the fibres of the internal popliteal are damaged either alone, or with some of the fibres of the external popliteal. In this case the outstanding clinical feature is pain of the same nature as that already described in lesions of the median nerve.

External Sciatic Nerve.—This nerve may be injured as it winds round the fibula by wounds or fractures or by compression of a tight bandage. The paralysis is usually severe, all the muscles being equally affected. The foot is dropped and inverted, and the toes are slightly flexed. Dorsal flexion of the foot, extension of the proximal phalanges of the toes, and abduction of the foot are impossible. The patient can walk, and he can stand on tip-toe, but he cannot run, and walking is made difficult by the foot-drop. Subjective sensory disturbances are usually absent. The skin is anæsthetic over a narrow band which extends from the outer surface of the leg in its middle third, downwards beside the outer border of the tibia, and along the middle of the dorsal aspect of the foot as far as the base of the toes. For an inch or so, on both sides of this band, the sensibility of the skin is diminished. The knee-jerk and ankle-jerk are present. The plantar response is always flexor. Vasomotor changes are slight, and trophic changes are absent.

Internal Sciatic Nerve.—This nerve is rarely injured alone. It supplies the popliteus, the calf muscles, the flexors of the toes and the intrinsic muscles of the foot. When it is paralysed, the patient is unable to stand on tiptoe, or to extend or invert the ankle, or to flex his toes. Paralysis of the interossei leads to a claw-like deformity of the foot, associated with lowering of the heel and raising of the metatarsus—talipes calcaneo-valgus.

The calf muscles are flabby and the ankle-jerk is abolished. Sensation is lost on the sole, except along its inner border, on the outer border of the foot, and on the plantar surface of the toes. Causalgia, similar to that in paralysis of the median, is very often present.

Posterior Tibial Nerve.—This nerve may be injured by a penetrating missile or a deep wound in the calf. Movements of the ankle are unaffected, and anæsthesia is confined to the sole of the foot and heel, or merely to its inner half. The paralysis of the intrinsic muscles of the foot may escape detection, and the lesion may easily be overlooked, especially when the nerve is injured below the origin of branches supplying the flexor longus hallucis and the flexor longus digitorum. The symptoms then are pain in the sole of the foot, anæsthesia on the sole, and paralysis of the plantar muscles.

Treatment of Local Nerve Lesions.—Treatment must depend on the nature and degree of the lesion. During the long period which elapses between the onset of paralysis and the first signs of recovery, even in cases of simple physiological interruption of the nerves, every effort must be made to prevent degeneration of the muscles, to keep the circulation of the limb active, and to prevent the occurrence of contractures and deformities. Massage, movements, electrotherapy and suitable appliances all have their uses. With regard to operative treatment, it must be remembered that more than half the cases of nerve injuries undergo spontaneous cure. It is advisable, therefore, to wait three or four months before an operation is undertaken. If, at the end of this time, the wound is soundly healed and all signs of sepsis have disappeared, and if, as a result of repeated examinations, no sign of recovery has been detected, no harm can be done by exposing the nerve. If it is found to be divided completely, the ends should be "freshened" and sutured end to end. If the nerve is notched laterally, the edges of the notch should be pared and sutured, care being taken to preserve the bridge of uninjured tissue. Sometimes the nerve at the site of the lesion appears as a fibrous, flattened band between two swellings on the nerve. In most of such cases the nerve is completely divided, and the condition calls for resection of this fibrous tissue and end-to-end suture. Another common finding, when the nerve is exposed, is a nodule or cicatricial swelling in the course of a nerve which has maintained its continuity. In these cases the continuity of the nerve should not be interrupted. It should be freed from adhesions, and incised in the long axis of the swelling. All operations which involve grafting of nerves are futile. For an account of the great advances in the technique of the surgical treatment of nerve injuries which have been made as a result of experience gained in the Great War, special treatises must be consulted.

The treatment of painful forms of nerve lesions is extremely difficult. In severe cases external applications and internal medication entirely fail. Simple freeing of the nerve sometimes gives relief. Where this fails, it may be advisable to practise complete division followed by immediate suture. Alcoholisation of the nerve trunk often gives immediate and lasting relief. Under general anæsthesia the nerve is freed, and then injected with 1 c.c. of weak alcohol at a point two or more centimetres above the lesion. This, of course, is followed by motor paralysis; but recovery occurs in about six months.

INTERSTITIAL NEURITIS

Synonym.—Neuro-fibrositis.

Definition.—A malady which commonly attacks the large nerve plexuses or nerve trunks, but which may affect any peripheral nerve trunk, and which is characterised anatomically by an inflammation of the connective tissues which surround and bind together the nerve fibres into the nerve trunks. This fibrositis, which may be local or diffuse in the affected nerves, is the result of the causes of fibrositis in general, and is frequently associated with fibrositis elsewhere, as, for example, when sciatica is associated with lumbago. The symptoms are those of irritation of the nerve fibres, namely, pain in the distribution of the nerve trunk, tenderness of the nerve trunk, muscular fibrillation and cramp. Loss of function of the nerve fibres in the way of loss of sensibility or muscular paralysis is the rarest of events in interstitial neuritis, and is seen only as the result of terminal cicatrisation in severe cases. Muscular wasting may occur in severe or in longstanding cases, but it is a general wasting of muscles of the painful region, not confined to the distribution of the nerve involved, and therefore resembling the muscular wasting which is seen in joint disease.

Pathology.—The malady is met with soon after puberty, and is incident chiefly upon the first half of adult life, being unknown in childhood and rare in old age. It is often associated with other forms of fibrositis such as lumbago. Often it arises spontaneously, without external cause; but exposure to cold may directly cause it, as also may injury such as stretching, bruising or wounding of the nerve trunk. Gout and diabetes are well-known clinical associations.

The morbid anatomy is well seen when the nerve is exposed during operative procedures for the relief of the condition. The affected nerve trunk is swollen and pink in colour; the sheath is distended, and droplets of fluid exude when it is incised, and sometimes the nerve is adherent to the surrounding tissues. This inflammatory condition may be local and appear as a pink bulbous enlargement of the nerve trunk, or it may spread widely over a long stretch of the nerve trunk and its branches. When the inflammatory process subsides there may be cicatrisation of the peri- and endo-neurium. Only in the rarest cases does the morbid process become so severe as to interfere with the more important functions of the nerve trunk with the production of motor and sensory paralysis, and even in these cases complete ultimate recovery is the rule. The local inflammatory condition causes a slight shortening of the nerve trunk, and this causes the affected limb to be held in that position which will keep the nerve trunk most relaxed. It is also the cause of the severe pain which occurs on any movement which stretches the nerve trunk.

Interstitial neuritis is sometimes an associate of arthritis. For example, in arthritis of the shoulder-joint it is not uncommon to meet with definite involvement of the brachial nerves, and again in chronic arthritis of the hip-joint the inflammatory process may extend from the capsule of the hip-joint directly into the contiguous sciatic nerve.

The malady may affect any of the nerve roots or nerve trunks, and sometimes several of these may be co-involved. When the nerve roots

are affected "radicular neuritis" results. The sciatic nerve is by far the most common seat of the disease, producing the condition known as "sciatica." Next in order of frequency comes the brachial plexus, causing "brachial neuritis," the anterior crural nerve causing "anterior crural neuritis," the upper part of the cervical plexus producing "cervico-occipital neuritis," and the intercostal nerves producing the so-called "intercostal neuralgia."

Symptoms.—These are the same whatever nerve is affected, and consist in—(1) Pain radiating in the area of distribution of the affected nerve, of a dull, aching character with acute exacerbations and often very long-lasting. (2) Tenderness of the affected nerve to pressure and stretching. (3) Subjective peripheral sensations such as tingling, burning or numbness. (4) General wasting of the muscles of the surrounding region with marked hypotonus, not confined to the muscles supplied by the affected nerve and akin to arthritic muscular atrophy. This wasting may reach a very remarkable degree. (5) Increase of the deep reflexes of the limb. (6) Diminution or loss of the deep reflex in the supply of the affected nerve. This is a valuable indication of the severity of the lesion. In a case of sciatica, for example, all the muscles of thigh and leg are wasted, the knee-jerk and the adductor-jerks are markedly brisk, whereas the ankle-jerk, which is in the sciatic supply, is diminished in slight cases and lost in severe cases. (7) The affected limb is held in a characteristic position to avoid stretching of the nerve, and the gait is similarly modified. (8) Trophic and vasomotor changes are not uncommon. (9) Fibrillation is often present.

Diagnosis.—There is sometimes considerable difficulty in the diagnosis of cases of interstitial neuritis on account of the almost identical clinical picture which may occur in the early stages of pressure upon nerve roots or nerves by tumours. The following points are of value in distinguishing the two conditions: The pain of pressure lesions is rarely so severe as that of interstitial neuritis. Tenderness on pressure or stretching of the nerve trunks is absent in pressure lesions. Signs of loss of function—paralysis and sensory loss—come on early in pressure lesions. The most careful search should be made in every case for any possible cause for local pressure, such as primary and secondary neoplasms, spinal tumours, spinal caries and diabetes. To make a diagnosis of interstitial neuritis in the presence of a mammary or testicular carcinoma, removed or not, is to advocate the highly improbable, whatever the symptoms may be.

Brachial Neuritis.—This form of interstitial neuritis is somewhat rare, and is met with chiefly in women over the age of 35 years. Sometimes it follows injury to the brachial plexus from any violence causing undue separation of head and shoulder. More often it arises spontaneously. The pain, which is often of sudden onset, may be of great severity, and may be at first referred to the region of the plexus itself, the back of the scapula, the axilla, the forearm or the hand, is at first intermittent, but it soon becomes continuous and spreads over the whole upper limb. Tingling and numbness in the hand and trophic changes in the skin and nails of the fingers are the rule.

One of the great difficulties in this malady is that in the upright position the weight of the arm and shoulder carry the shoulder downwards and stretch the inflamed plexus, adding greatly to the pain. Therefore it should be treated with the recumbent position upon the back in bed. Further,

every movement of the hand or arm tends to increase the pain. Splints which keep the arm in the abducted position and the shoulder raised so as to prevent tension upon the plexus are invaluable.

There is little difficulty in diagnosis, the only confusable conditions being arthritis of the shoulder and cervical rib, in neither of which conditions is there any tenderness of the nerve trunks of the plexus.

CERVICO-OCCIPITAL NEURITIS.—This condition, which is by no means rare, is characterised by pain in the upper part of one side of the neck, radiating over the branches of the upper cervical plexus, the great occipital being the most common, and the supra-sternal, supra-clavicular and supra-acromial branches less common seats for the pain. The fibrositis not infrequently co-involves the fibrous structures in the region of the articular and transverse processes, giving rise to pain and stiffness of the neck on movement. When the pain is confined to the great occipital distribution alcohol injection is sometimes most efficacious.

SCIATICA.—In few common and familiar maladies is as much difference of opinion as to ætiology, pathology and treatment as in the case of sciatica. The classification suggested by Barnes Burt is probably the most useful. He recognises three types: (i) root sciatica, sometimes called radiculitis; (ii) trunk sciatica; and (iii) referred sciatica, and believes that the ætiology of the three is different in each case. Root sciatica is commonly due to spondylitis, or strain of the lumbar vertebræ; trunk sciatica depends upon interstitial neuritis of the nerve sheath; and referred sciatica results from inflammation of some structure (muscle, bursa, joint) supplied by the sciatic plexus. He finds in his own series of cases that root sciatica accounts for 36 per cent. of the total, trunk sciatica for 18 per cent., and referred sciatica for 46 per cent. In previous editions of this book, the description was confined to root trunk sciatica. This account now follows, questions of differential diagnosis being discussed subsequently. It has been said that true sciatica as here defined is never bilateral, and that bilateral sciatic pain is always the result of gross lesions involving the nerve. It is important that this error, which has crept into so many textbooks, should be contradicted, for sciatica is occasionally bilateral, and the sciatica which occurs in glycosurics is usually bilateral.

The malady is not met with in childhood, but it begins to be common soon after puberty, and its incidence is greatest upon early middle life. In the majority of the cases it arises without assignable cause, sometimes injury to the nerve of any nature, as from a twist of the leg, a bruise or a fall is responsible. Only in rare cases does exposure to cold and wet seem to have excited the onset. It is important that the urine should be tested in every case of sciatic pain, for glycosuria is more often found in cases of sciatica than is usually believed. In the case of an apparent sciatica, the possibility of rupture of an intervertebral disk should be borne in mind (cf. page 1773).

Symptoms.—The chief symptom is pain along the course of the nerve or of its branches, and since the sciatic nerve often divides within the pelvis into the great internal and external sciatic branches, the pain may be confined to the distribution of one of these alone. One feature of the pain valuable for diagnostic purposes is that it never reaches above the crest of the ilium, but in this connection it must be borne in mind that fibrositis of the back (lumbago) not infrequently precedes or accompanies the onset of sciatica.

The pain may be partly intra-pelvic, for the sciatic nerve is formed within the pelvis. Where the interstitial neuritis is entirely intra-pelvic, tenderness of the nerve trunk to digital pressure in the thigh and buttock fails as a physical sign. The onset is occasionally sudden, and associated with slight pyrexia and constitutional disturbances as in other forms of fibrositis; but, as a rule, the malady sets in gradually with pain in the buttock, back of the thigh or leg, in movements and in postures which make the nerve tense, or cause pressure upon it. The pain gradually increases in severity. It may be both gnawing and burning and sharp and darting in character. It is usually continuous, with occasional severe exacerbations which occur spontaneously or are excited by movement. Its intensity generally increases at night. The seat of the pain often varies from day to day.

Extreme tenderness of the nerve on pressure is rarely absent, except in those cases where the neuritis is intra-pelvic, and the tender region usually indicates the situation of the lesion of the nerve trunk. Stretching the nerve by extending the knee with the thigh flexed is productive of great pain which may be lasting. The best method of testing the sensitivity of the nerve to stretching is to put gentle pressure with the thumb on to the popliteal space as the patient sits in a chair with the knee bent at a right angle. Sometimes there is considerable tenderness of the muscles. The muscles waste not only in the sciatic supply, but throughout the whole lower limb and buttock, surely from reflex irritation as in arthritis atrophy. Cramp in the leg and reflex spasm are common, and muscular fibrillation is often seen. Paræsthesia in the form of tingling, burning and numbness is the rule; but loss of sensibility only occurs in the rarest and most severe cases, and its presence should always suggest the presence of a pressure lesion. Barnes Burt states that in root sciatica (radiculitis) there is also some rigidity of the lumbar spine, tenderness along the lateral aspects of the spine in this region, and also pain along the distribution of the lateral cutaneous nerve of the leg.

Peculiarities of stance, gait and position arise from the tenderness of the nerve to stretching, that position being assumed by the patient which keeps the nerve slackest. In standing, the weight of the body is placed upon the sound limb, and the other limb is flexed at hip and knee and extended at the ankle, with the toes only resting on the ground. In walking, the patient limps in this same position without straightening his knee or extending his ankle, and in bed he lies with knee flexed and ankle extended.

The knee-jerk is sometimes markedly increased notwithstanding the wasting of the quadriceps, the only exception being when sciatica is complicated with anterior crural neuritis. The ankle-jerk being in the sciatic supply tends to be diminished in proportion to the severity of the neuritis, and in severe cases it is always lost. It may not return after recovery from the original attack.

Slight trophic and vasomotor changes in the periphery of the limb are commonly seen.

In very rare cases the cicatrisation which follows the inflammatory process may cause motor and sensory paralysis of all the region below the knee. Such a case came under our care 2 years after the onset, and was explored by Sargent, who found the nerve in the gluteal region densely cicatrised and widely adherent to the muscles. The nerve was freed, and

incised longitudinally in many places, and this patient made a complete recovery. Every degree of severity may be met with from the mildest to the most acute, and from the most rapid lasting but a few weeks to the most chronic lasting 2 or more years.

It is a most remarkable fact that severe sciatica never occurs twice in the same limb. One severe attack seems to free the affected nerve from subsequent liability to the affection, and it is comforting to be able to assure the patient that he will never have the trouble again in the same limb. In a very large experience we have never met with an exception to this rule.

Diagnosis.—Root and trunk sciatica must be distinguished from "referred sciatica," and from pains of sciatic distribution due to involvement of the nerve or its roots by growth.

In sacro-iliac disease pain may be referred along the sciatic nerve, but the nerve trunk is not tender to pressure or to stretching, while the joint is tender, and radiography may reveal a lesion in it. In osteo-arthritis of the hip the signs of sciatica are absent, while there is limitation of active and passive movement of the joint, and pain on movement. In this condition it is more common for pain to be referred down the front of the thigh than along the sciatic distribution. Fibrositis of gluteus medius and minimus may also produce pain of sciatic distribution of some severity.

In new growths involving the nerve, the clinical picture is not really that of a true sciatica. The pain differs in character, is frequently accompanied by muscular weakness and wasting and by sensory loss, and the patient's general condition is cachectic and suggestive of malignant disease. There may also be a history of primary carcinoma. The presence of bilateral sciatic pain is, as has been said, not pathognomonic of involvement of the nerve roots by growth. Indeed this involvement is as commonly unilateral as not.

The pains of tabes and other nervous diseases when confined to the sciatic distribution are distinguished by the presence of other physical signs of those diseases.

Course and Prognosis.—Sciatica commencing acutely tends in the course of time to lessen in severity and become chronic, but some acute cases cure rapidly. When the malady has a slow commencement it usually lasts longer than does an acute case, and it is much more liable to exacerbations than when commencing acutely. The traumatic cases show no essential difference from the spontaneous, except that in the former adhesions of the nerve to the muscles from bruising is likely to prolong the duration of symptoms. The prognosis is always absolutely good as regards recovery, and in severe cases there is no likelihood of relapse. In slight cases, however, subsequent attacks are not uncommon.

Treatment.—The first essential in the treatment of all recent cases is to secure rest and to avoid all those things which excite or increase the pain. The duration of the attack is often considerably prolonged by neglect of this most essential element in treatment. Sometimes the fixation of the limb in a semiflexed position by means of Liston's or Macintyre's splint gives great relief. The use of the bed-pan is advisable to avoid flexion of the hip and stretching or pressure upon the nerve in the act of defæcation. On the other hand, towards the end of a chronic case, active exercise with massage and passive movements are necessary to restore the shortening of

the nerve. The application of heat in the form of hot-water bottles, poultices and radiant heat is invaluable for the relief of pain, and for curative purposes. Counter-irritation is very useful, and is best used in the form of the strong tincture of iodine which should be painted in a broad strip over the course of the sciatic nerve, from sciatic notch to heel, daily until the skin becomes inflamed, just short of blistering. Massive injections of from 4 to 8 ounces of sterilised normal saline solution, made slowly into the region of the affected nerve at a temperature of 104° F., are said to be valuable both in acute and chronic cases. Acupuncture of the nerve with a series of specially designed needles is a useful and ancient remedy which acts by puncturing the sheath of the nerve, and allowing the escape of inflammatory exudation. Attempts to stretch the nerve by flexion of the thigh and extension of the knee may do great harm, and rarely do good. In chronic cases of sciatica or brachial neuritis and in fibrositis of the glutei, iodine given in the following manner is sometimes useful:

℞ Iodi	. . .	gr. 1
Pot. iodidi	. .	gr. ¾
Sp. rect.	. . .	min. 12

Sig. min. 12 to be dropped into half a teacupful of water, and to be taken after being allowed to stand for 15 minutes. This may be administered thrice daily, and continued for 3 weeks. Some patients tolerate the doubling of this dose after the first week. The salicylates are of great service, especially in the form of aspirin, which may be given liberally. Urodonal in doses of 60 grains thrice daily is also often valuable. In the more chronic cases sulphur and guaiacum are serviceable. For the relief of pain heat is generally beneficial, but in some of the most acute cases the application of heat increases the pain, and in these an ice-bag will sometimes give great relief. All the analgesics of the coal-tar series, acetanilide, phenacetin, etc., are valuable adjuvants to relieve pain, and these may be conveniently prescribed with aspirin, or if sleep be difficult with barbitone or carbromal. When pain is very severe and rebellious to the above-mentioned remedies, opium or morphine is indicated. It is essential from the exhausting quality of the pain that the patient should be well fed, and alcohol is often of service.

RUPTURE OF THE INTERVERTEBRAL DISK

Synonym.—Herniation of the nucleus pulposus.

Definition.—A condition of pressure upon the spinal cord or on the roots of the cauda equina resulting from the extrusion into the vertebral canal of the nucleus pulposus of the intervertebral disk. It is traumatic in origin.

Ætiology.—The majority of cases give a history of injury at, or shortly before, the onset of symptoms. The injury is commonly of the variety known as a strain of the back, due to sudden bending, the lifting of heavy weights, or sudden movements of the back, as when striving to avoid a fall. Males are commonly affected.

Pathology.—Formerly the condition under discussion was one recognised on laminectomy, and spoken of as endochondroma of the disk. Actually in the circumstances enumerated above, the disk ruptures and its nucleus

(nucleus pulposus) herniates into the canal. The common seat of such rupture is the lumbar spine, commonly between the fourth and fifth lumbar, or between the fifth lumbar and the sacrum. Multiple ruptures have been recorded.

Symptoms.—The outstanding feature is pain, starting in the small of the back and radiating down one thigh, the outer side of the leg and the ankle. The pain is severe and lancinating, aggravated by stooping and relieved by lying down. There is some flattening and limitation of movement of the lumbar spine. Flexion of the extended leg at the hip may be painful. In some 60 per cent. of cases the ankle jerk is lost, other abnormal signs being absent. Occasionally more severe signs of root compression are present, and in rupture of dorsal disks some signs of compression paraplegia, mild in degree, may be found. The most typical picture is one of pain in the small of the back radiating down one leg. In other words, the symptoms usually mimic those of sciatica.

Diagnosis.—In addition to the history and signs mentioned, radiography of the spine may reveal narrowing of the intervertebral space at the level of the damaged disk, but the intrathecal injection of lipiodol may be necessary to confirm diagnosis.

Treatment.—Attention having been drawn to the condition, there is a not unnatural tendency to diagnose it somewhat too frequently, and to submit patients unnecessarily to lipiodol injection. Careful consideration of all the facts, and conservative modes of treatment, *e.g.* rest, massage, etc., should first be tried. The operative procedure for the removal of the extruded portion of the disk involves laminectomy and is a severe ordeal. For this reason it should not be undertaken unless the diagnostic indications are clear and unequivocal.

CERVICAL RIBS

Ætiology.—The development of the ribs at the thoracic inlet depends on the mode of formation of the brachial plexus, for the nerves are large structure in the embryo at a time when the ribs are soft and pliable. When the plexus is "normal," a well-formed first rib springs from the first dorsal vertebra. If, however, the plexus is "post-fixed," that is, when the contribution to the plexus from the fourth and fifth cervical segments is small and the fibres from the first and second dorsal segments form a powerful cord, this cord in rising over the first dorsal rib may compress and deform it to such an extent that it presents the characters of a rudimentary rib. On the other hand, and this is more frequent, when the plexus is pre-fixed, that is, when the contribution from the upper cervical segments is relatively large and that from the dorsal segments is small, a supernumerary rib is allowed to develop from the seventh cervical vertebra. When this pre-fixation is pronounced, the seventh cervical rib is often very large and is easily felt in the neck. In these cases symptoms are usually absent. In a certain number of cases in which the abnormality is intermediate in degree, symptoms are caused by compression of the lower cord of the plexus as it passes over the supernumerary rib, or over the deformed first rib. This compression may be exercised by the bony portion of the extra rib, but more often the nerves are damaged by a fibrous prolongation of the rudimentary rib which connects it with the first rib.

But these abnormalities in the ribs only cause symptoms in some 10 per cent. of the cases in which they are present. Further, the symptoms are often unilateral with bilateral supernumerary ribs, and the symptoms are often most prominent on the side of the smaller extra rib. Again, the onset of symptoms is usually delayed until adult life is reached. It is clear, therefore, that some contributory cause must come into play. This is found in the dropping of the shoulder girdle, which is normal in adolescents, and is often excessive in persons whose muscular tone is low. In a child the clavicle rises boldly as it passes outwards. In a normal adult male the clavicle is almost horizontal, in women it droops slightly, and in those who develop symptoms of pressure on the nerves, the outer is usually distinctly lower than the inner end. In the latter, the lowest cord of the plexus is submitted to constant rubbing against the extra rib which rises and falls during respiration, and it is compressed by any movement of the arm which depresses the shoulder girdle. Relief is obtained by raising the shoulders, and patients soon learn to support the limb and to assume attitudes in which pressure on the nerves is relieved.

Women suffer most often, the right arm being affected more often than the left. The onset is usually gradual, but occasionally it comes on suddenly after childbirth, or on lifting a heavy weight.

Symptoms.—These may be sensory, motor, or vasomotor, either singly or in combination. Subjective sensory disturbances are most frequent. They take the form of numbness and tingling or neuralgic pains. Paræsthesiæ are most often unilateral, and are frequently confined to the ulnar or to the radial side of the hand and fingers. It is rare for all the fingers to be affected. Pain, when present, is usually felt below the elbow. It is often neuralgic, darting down the arm, and again confining itself to one border of the limb. It hardly ever radiates from the neck.

Objective sensory disturbances are usually slight or absent. They may be found over the ulnar or radial border of the distal portion of the limb in an indefinite area, which does not conform to the distribution either of the ulnar or radial nerve.

Muscular atrophy is not so frequent as subjective sensory disturbance. In the "median type," wasting is confined at first to the abductor and opponens pollicis muscles, and the outer part of the thenar eminence shows a remarkable reduction in size, which contrasts strongly with the inner part, which retains its normal bulk. In the "ulnar type," wasting appears first in the small muscles of the hand supplied by the ulnar nerve. In some cases all the muscles of the hand and, to a less degree, the flexors in the forearm show considerable wasting. The atrophy is frequently bilateral and symmetrical.

Vasomotor disturbances are very common. The hands feel hot or cold, they may be œdematous or discoloured, and the changes may suggest Raynaud's disease. Pressure on the subclavian artery sometimes causes inequality of the pulse. This disappears when the arm is raised.

Diagnosis.—The presence of pain, paræsthesiæ or vasomotor disturbances in the upper limbs, or wasting in the muscles of the hands, should always arouse the suspicion of supernumerary or rudimentary ribs. When pain is the only symptom, its distribution along one border of the arm or hand, and the patient's account of the manner in which it may be increased or diminished by raising the shoulder girdle or performing movements which

depress it, usually direct attention to the cause. Symmetrical atrophy in the hands may suggest progressive muscular atrophy of spinal origin, but this diagnosis is usually rendered untenable by the association of sensory troubles or vasomotor phenomena, or by the findings on X-ray examination of the neck. For the differential diagnosis from syringomyelia, see page 1732.

Treatment.—Pain may be relieved by rest with the arms suitably supported. Atrophy calls for immediate operation to remove the offending rib. Pain is always relieved by operation, either immediately or after an interval of some months. The progress of atrophy is always retarded, and complete recovery may occur if an operation is undertaken early.

OBSTETRICAL PARALYSIS

It is important and useful to group together under this heading all those conditions of paralysis occurring, either in mother or child, which are the result of the processes of labour in the passage of the fœtal head through the pelvis. Autopsies upon the still-born, and upon children who have survived birth for a few days only, have shown that hæmorrhage into the meninges is of common occurrence, and it has been argued that such meningeal hæmorrhages are the cause of many of the conditions of cerebral paralysis which are present immediately after birth, or which appear during the first year of life, and especially the cause of cerebral diplegia. The pathological conditions found in the brain in cases of cerebral diplegia, however, are such as make it absolutely impossible that they could be caused by meningeal hæmorrhage, for no sign of old hæmorrhage is ever found, nor could hæmorrhage cause a general cell atrophy of the brain without signs of any local lesion. It seems clear, then, that though meningeal hæmorrhage may be of common occurrence during birth, and may be the cause of still-birth, yet there is no clinical or pathological evidence to show that it gives rise to any lasting cerebral defect.

The following condition may occur: (1) In the child: facial paralysis; hemiplegia from laceration of the brain substance; fracture-dislocation of the spine with transverse lesion of the spinal cord; injury to the brachial plexus from the separation of head and shoulder in traction; and injury to peripheral nerve trunks at the elbow, axilla or groin, in using traction with the finger.

(2) In the mother: paralysis of the supply of the lumbo-sacral cord and obturator nerve from prolonged pressure of the head against the sacrum and pelvis.

Facial paralysis.—This is usually caused by the pressure of the forceps upon the facial nerve as it crosses the ramus of the jaw, but it has been known to occur where instruments have not been used. When unilateral, as is the common event, it gives rise to little or no difficulty with sucking, and is evidenced by the unsightly deformity of the face, which is drawn over to the sound side. When bilateral, it is one of the causes of complete inability to suck, and on account of the flaccid symmetry of the face may easily be overlooked. It necessitates spoon feeding for a considerable time. Obstetrical facial paralysis invariably recovers within a few weeks and does not give

rise to after-contracture. Gentle stretching and massage of the face with the finger is the only treatment required.

Hemiplegia from laceration of the brain may occur during delivery in contracted pelvis from the pressure upon the sacral promontory, and has been caused by the use of forceps. It is exceedingly rare, and is generally rapidly fatal from the associated hæmorrhage. It may occasionally be survived, with an irreparable hemiplegic condition.

Fracture-dislocation of the spine is produced by traction upon the after-coming head by pulling upon the trunk. We have seen it associated with injury to the brachial plexus. It occurs most often in the lower cervical region, and the transverse lesion of the spinal cord is usually complete.

Injury to the brachial plexus may occur in traction either upon the head, or upon the trunk, if the head is aftercoming, and is caused by an undue separation of head and shoulder on one side rupturing or straining the brachial plexus. The paralysis is usually of the upper arm or Erb type, the fifth and sixth roots being most affected, and the deltoid, biceps and supinator longus muscles being paralysed, but the whole plexus may be involved and even torn completely across. Traction upon a prolapsed arm has caused lower arm or Klumpke type of paralysis, in which the first dorsal and eighth cervical roots are most affected, and the intrinsic hand muscles and the flexors of the forearm are paralysed. The obstetrical lesions of the brachial plexus are for the most part serious lesions, many of the cases making no motor recovery at all, though sensibility is usually regained. The prognosis depends upon the severity of the damage to the plexus, as to whether the roots are actually torn or only bruised. The slight cases recover well enough.

Injury to the peripheral nerves from pressure or traction upon the flexures is seldom severe enough to prevent a rapid and complete recovery.

Paralysis of the lumbo-sacral cord and of the obturator nerves in the mother, immediately after parturition, is an exceedingly interesting clinical condition. In the first place, the lumbo-sacral cord is in a much more exposed position as regards the fœtal head engaging the pelvis than are the other nerves of the sacral plexus, and may be subjected to such severe pressure as causes paralysis, and in the second place, the obturator nerve actually crosses the brim of the pelvis and must of necessity be pressed upon by any large fœtal head which passes the pelvic brim. The lumbo-sacral cord paralysis is evidenced by dropped foot and paralysis of the anterior tibial and peroneal muscles and if it is severe, by loss of sensibility over the distribution of the fourth and fifth lumbar roots. Sometimes the third lumbar root area is affected. The obturator nerve involvement is shown by weakness or paralysis of the muscles supplied by the obturator nerve, namely, all the adductor muscles of the thigh. The paralysis may be noticed directly after parturition, or when the patient begins to get about upon her legs. The lumbo-sacral paralysis is usually unilateral, and is nearly always upon the right side. The obturator paralysis is not uncommonly bilateral, and both forms of the paralysis may coexist. There may be numbness, but no pain. This condition nearly always occurs with a first delivery, and often the child's head has been unduly large. It may recur with subsequent deliveries, but this is not a common event.

The prognosis is absolutely favourable, every case making a complete

recovery in from a few weeks to a few months. The treatment is rest in the first place, with gentle massage and passive movements, and when power begins to return the patient may commence to get about.

POLYNEURITIS

Synonym.—Multiple Peripheral Neuritis.

The clinico-pathological condition we know as polyneuritis, and seen in its most typical forms in diphtheritic paralysis or in alcoholic neuritis, represents a very striking and uniform reaction of the nervous system. Invariably associated with it is a reaction of the myocardium, so that there is in cases of polyneuritis a recognised liability to sudden fatal heart failure. It is in the case of diphtheritic paralysis and of beri-beri, another form of polyneuritis, that this mode of fatal termination is most often seen. Indeed, beri-beri may appear as a rapidly fatal cardiac illness before any signs of involvement of the nervous system have had time to develop.

Ætiology.—At first sight the factors that give rise to polyneuritis fall into three groups: (i) certain chemical poisons, (ii) the toxins of certain bacteria, and (iii) certain disorders of metabolism. Widely differing as these three causative factors may seem to be, there is reason to believe that a common underlying factor which is immediately responsible for polyneuritis may underlie them all. It is probable that in the case of groups (i) and (ii) the pathogenic substance gives rise to a disorder of metabolism in the course of which a toxic metabolite is produced in the body, this acting as the direct poison for nervous system and heart muscle. In the metabolic group (iii) the same process is in action.

Thus, in beri-beri, for example, the illness ensues upon the ingestion of a diet deficient in vitamin Bi. In the absence of this substance carbohydrate metabolism is disordered and a toxic metabolite is produced. Thus, beri-beri is not, as the biochemists formerly insisted, a starvation-degeneration of the nervous system, but an intoxication strictly comparable with that obtaining in other varieties, ætiologically considered, of polyneuritis.

The final and complete proof of this unity of causation of polyneuritis, in whatever circumstances it is seen, is not yet available, but there is an increasing body of evidence in favour of it.

Returning for the moment to the ordinary ætiological classifications of polyneuritis, we see that in the case of alcoholic or arsenical polyneuritis the poison is taken by the mouth, and presumably the final common toxic substance reaches the nervous system by the blood stream. In the case of diphtheritic paralysis, on the other hand, the exotoxins are produced locally at the site of the diphtheritic ulceration, whether on the fauces or, as in extrafaucial diphtheria, at some other local site on the body surface. This unique channel of entry gives rise in diphtheritic paralysis to a group of symptoms not found in other ætiological varieties of polyneuritis. This group includes palatal and accommodation paralyses, which precede the appearance of polyneuritis.

It is noteworthy that in the case of extrafaucial diphtheria this initial paralysis is not palatal, but is anatomically related to the site of the diphtheritic lesion (skin ulceration or wound). Yet the paralysis of accommodation

may occur whatever be the site of the diphtheritic lesion. It is believed, therefore, that the exotoxins gain access to the nervous system by conduction from the seat of the lesion via the axones of the nerves which innervate this region. They pass upwards in the axis cylinders to the central nervous system and produce their toxic action directly there, this action being reflected peripherally again as a motor and sensory paralysis of the muscles and skin (or mucosa) in the region of the lesion. Thus, a diphtheritic ulcer on a finger may be followed by a local paralysis of that part before polyneuritis develops. The subsequently developing polyneuritis is then probably produced in the manner described above, while the accommodation paralysis may indicate a specific action of the toxin upon the nervous mechanism concerned. We thus have a local, a specific and a general group of symptoms. The analogy of the local, specific and general phases of tetanus will occur to the reader.

Many of the intoxications of the nervous system commonly included under the heading of polyneuritis are associated with lesions and clinical manifestations which are not those of polyneuritis. Such substances, to name but a few, are lead, mercury, copper, carbon disulphide and carbon monoxide, and it would be erroneous to regard these as causes of polyneuritis. Many infectious fevers are stated to be not rarely followed by polyneuritis, namely, enteric, malaria and dysentery, but the present writer who spent four years with the Egyptian Expeditionary Force in 1915–19 where the two last named of these infections were common saw no case of true polyneuritis associated with them.

Finally, the categories of toxic polyneuritis, acute febrile polyneuritis and Landry's paralysis have no known causal factors. They make their appearance in apparently healthy persons, adequately nourished and free from all discoverable signs of infection, and it is extremely difficult in the present state of knowledge to account for them on any hypothesis of avitaminosis, or to suggest any possible mode of intoxication. In short, the pathogenesis of polyneuritis presents many unsolved problems.

Clinically, polyneuritis is a lower motor neurone type of paralysis accompanied by a varying intensity of sensory loss of much the same type of distribution as the paralysis, and, as already mentioned, by signs of myocardial poisoning.

1. ARSENICAL NEURITIS

Peripheral neuritis may be caused by a single large dose of arsenic, or it may result from prolonged use of the drug in the treatment of such diseases as Hodgkin's disease, chorea and severe anæmia. It is a rare malady, and the likelihood of its appearing under the last-named conditions is negligible. The toxic action of arsenic with alcohol seemed to be greater than that of either alone.

The description given below of alcoholic neuritis applies to this form as well. Hyperæsthesia of the skin and tenderness of the muscles are more constant and more severe in the arsenical form, and paralysis and atrophy of the muscles are often more wisespread and more rapid in their progress. Hyperkeratosis of the soles and pigmentation of the skin are characteristic of arsenical poisoning. In a suspected case, the diagnosis can be confirmed

by the discovery of abnormal quantities of arsenic in the urine or in the hair and skin.

The mental changes described in connection with alcoholic neuritis under the heading of Korsakow's psychosis may be present, especially when repeated poisonous doses of arsenic have been taken.

2. ALCOHOLIC NEURITIS

In former years alcoholism was perhaps the commonest cause of severe peripheral neuritis. At present it is a rare disease. It occurs most often in women, especially in those who take small amounts of alcohol frequently. It has often been the first indication of secret drinking.

Pathology.—The changes in the nerves are those of parenchymatous neuritis. They are most intense in the small branches supplying the skin and muscles, and they diminish in severity as the larger branches are approached. They are best seen in the terminal branches of the musculospiral and anterior tibial nerves. The wasted muscles often show a reduction in the size of their fibres, and an increase of connective tissue—fibrous myositis. The spinal cord may be healthy, but in almost all cases examination by modern methods shows changes in the nerve cells and degeneration in the tract fibres derived from the posterior roots.

Symptoms.—The onset is insidious, and in most cases premonitory symptoms, such as numbness and tingling in the extremities or cramps in the muscles of the lower limbs, are present for several months before actual weakness occurs. Subjective sensory troubles are a marked feature, even in the early stages. Besides numbness and tingling, the patients complain of feelings of excessive heat or of coldness in the limbs, or of severe aching or cutting pains in the legs. Painful cramp in the calf muscles is a common symptom. It is often worst at night, and may interfere seriously with sleep. Objective examination usually reveals sensory loss, in which the various elements of sensation are affected in a manner which is almost pathognomonic.

Stated briefly, there is anæsthesia of the skin with hyperæsthesia of the deeper structures. Light touches are not appreciated at all or many are missed, the temperature sense is defective, and the prick of a pin causes no pain, whereas even moderate compression of the muscles may cause the patient to cry out. The sensory loss is greatest in the feet and hands and diminishes towards the knees and elbows. Muscular tenderness is usually greatest in the calves. The soles of the feet are also unduly tender. Hyperalgesia is often well marked before anæsthesia of the skin appears. To the disability caused by pains and spasms, weakness of the muscles is added in all but the slightest cases. The arms may suffer first, but in most cases the extensors of the toes, the dorsiflexors of the ankle, and the extensors of the fingers and wrists are attacked in progression, and double foot-drop and wrist-drop result. To overcome the foot-drop, the knees are raised high in walking. This gives to the gait the " steppage " character which is common to all forms of peripheral neuritis. In most cases the distal flexor muscles are also affected, but to a slighter degree. In severe cases, weakness extends to the proximal muscles and even to the muscles of the trunk. The affected muscles become soft and diminish rapidly in bulk. Unless precautions are taken, contrac-

tures occur in the flexor muscles and produce deformities of the limbs, which add greatly to the difficulties of treatment.

At the onset the knee-jerks are exaggerated, but in most cases by the time the patient comes under observation all the tendon reflexes are absent. The cutaneous reflexes may be unaltered, diminished or absent. Sphincter control is retained. Slight bilateral weakness of the face is often present but severe paralysis is rare. Ptosis, nystagmus, and weakness of the external ocular muscles have been observed.

Trophic and vasomotor disturbances in the extremities are common. The hands and feet often perspire freely, and they may be white and cold or red and hot. In some cases œdema of the hands or lower extremities is present. In chronic cases the skin of the hands and fingers is thin, smooth and shiny, and the nails are ridged and brittle.

In almost every case of alcoholic neuritis there is some *psychical defect.* One form—Korsakoff's psychosis—is characteristic of and almost peculiar to this disease. The most prominent feature is failure of memory and loss of appreciation of time and place. A patient who has been bedridden in a hospital for nervous diseases for several weeks, when visited by the resident physician who has attended her daily, will "recognise" him at once as Dr. X, whom she has not seen since he brought her first child into the world some years ago. She is now, she says, in a lying-in hospital which she entered yesterday, and has just been confined with her second baby, who is in bed beside her. She also "recognises" strangers at her bedside, and connects them with events of long ago. Everything is related in the most circumstantial manner, and if the facts were not known her tale might well be accepted as truth. In most cases the mental defects are not so gross. There is merely a failure of memory, to which is added moroseness and irritability, caused by withdrawal of alcohol.

3. DIPHTHERITIC PARALYSIS

The exotoxin of diphtheria is highly selective for nervous tissues, and some form of paralysis occurs in a very high proportion of the cases. The intensity of the paralysis bears no constant relation to the severity of the local infection, for cases, in which the original disease has passed unnoticed, may be followed by serious damage to the nervous system. Walshe has classified the nervous manifestations of diphtheria into three distinct groups, namely, the local, the specific and the generalised paralyses.

Local paralysis occurs in parts related anatomically by nervous connections to the site of the diphtheritic lesion. In faucial diphtheria, the local palsy appears in the palate. In extra-faucial diphtheria, *e.g.* infected sores on the limbs, the local palsy appears in the muscles supplied by the segments of the cord to which afferent nerves from the infected focus pass. The reason for this is, that toxins elaborated by the diphtheria bacillus ascend from the primary focus to the cord or the medulla. Having reached the central structures, they diffuse to neighbouring motor cells and, by injuring them, cause paralysis of the muscles they supply. Paralysis of the palate therefore does not occur except in faucial diphtheria.

The *specific* manifestation of diphtheria is paralysis of accommodation. Like trismus in tetanus, it is not due to a local lesion, but occurs in many

cases, whatever the site of origin of the toxins. It is present in cases of both faucial and extra-faucial diphtheria, and is the local effect of exotoxin accepted from the igeneral blood stream.

The third or *generalised* form of diphtheritic paralysis is multiple neuritis. It follows extra-faucial as well as faucial diphtheria, and is also a result of the action of exotoxin circulating in the blood.

Symptoms.—As faucial diphtheria is the commonest form, the most frequent nervous symptom is *paralysis of the soft palate.* It is shown by the nasal quality of the voice and by the regurgitation of fluids through the nose. As a rule, the weakness is bilateral and equal, but in some cases it is greater on the side on which the local lesion is more severe. It makes its appearance in most instances about the end of the second week, but may come on as early as the fourth day, and as late as the sixth week. The soft palate is relaxed, and its movement on phonation is diminished. The palate may be insensitive, and its reflex is often diminished or lost. Recovery usually occurs in a few weeks. In rare instances the muscles of the pharynx and the vocal cords are paralysed. Together with palatal palsy, it is common to find marked weakness and tenderness of the sternomastoid muscles and masseters. These are also local effects.

Paralysis of accommodation appears about the same time as the palatal palsy, perhaps a few days sooner. The reaction of the pupils to accommodation as well as to light, can almost always be obtained. The trouble is subjective, and is shown by defects of near vision—for example, by inability to read small print. Hypermetropes suffer great inconvenience. In myopes it may pass unnoticed. Paralysis of any of the extrinsic ocular muscles with strabismus and diplopia may occur, and this may be either nuclear or peripheral in type.

Multiple neuritis usually comes on three to six weeks after recovery from the throat infection. Its presence is often detected when patients begin to exert themselves during convalescence. Weakness and aching pains in the legs, unsteadiness in walking, clumsiness in performing fine movements with the hands, feelings of pins and needles in the extremities—all these are common early symptoms. Weakness affects in varying degree the muscles of the neck, trunk and limbs. It is generally slight in degree, greater in the lower than in the upper extremities, and greater in the extensor muscles than in the flexors. Marked local atrophy is uncommon. In severe cases, life may be endangered by paralysis of the intercostals and of the diaphragm, but fortunately one set of muscles has usually begun to recover before the other is seriously affected. The small muscles of the hands and feet and the muscles of the calves and forearms are almost always tender on pressure. They are soft and flabby, and often show a partial reaction of degeneration.

Sensory ataxy is almost always present, and is often severe when the paralysis is trivial. It causes the patient great inconvenience, as it interferes seriously with walking and with the finer movements of the hands. Objective examination reveals sensory impairment of the "glove-and-stocking" type. On the hands and feet, the loss to light tactile stimuli is often complete, pain and temperature being less affected. As the limb is ascended, sensation gradually becomes normal. Even when the sensibility of the skin is but little diminished, the sensations of position and of passive movement

in the extremities are often seriously impaired, and the sense of vibration is often lost.

In the early stages and for a few days the tendon jerks are exaggerated, but are lost later in every case. Their return is often long delayed, and it is common to see patients months after recovery of normal power, in whom the knee-jerks are still absent. It is common also to find them absent many months after an attack of diphtheria in patients who give no history of nervous symptoms during the attack. The skin reflexes are usually retained, and stimulation of the sole gives a normal response.

Cardiac failure is a grave but uncommon complication. It is of myocardial origin. Vasomotor paralyses and disturbances in the nutrition of the skin, which occur so often in other forms of peripheral neuritis, are never seen in diphtheria. In those that survive the attack, complete recovery from the nervous troubles always occurs.

4. DIABETIC NEURITIS

In many patients with glycosuria, symptoms are present which point to changes in the peripheral nerves, or in the fibres of the posterior roots. In many respects they resemble tabes rather than pheripheral neuritis; but as the exact pathology is still unknown, it is convenient to describe them here.

Pathology.—Degenerative changes have been found in the peripheral nerves in some cases, in others these were healthy, whilst the intramedullary portion of the posterior roots showed degeneration, similar to that found in tabes.

Symptoms.—In some cases the only symptom is neuralgic pain in the distribution of one or more peripheral nerves. This is commonest in the lower limbs, where it simulates sciatica, and sugar is found in the urine in the absence of any other sign of diabetes.

In severe cases of diabetes the knee-jerks and ankle-jerks are diminished or lost in more than half the cases. This may accompany subjective sensory troubles in the lower limbs, or it may appear as an isolated symptom. The muscles are very often tender and the vibration sense of the feet is frequently absent. To objective examination, the sensibility of the skin is usually intact. Perforating ulcers of the feet have been observed.

Diagnosis.—The diagnosis of multiple neuritis from other diseases rarely presents any difficulty. It is made from the combination of symmetrical flaccid paralysis with sensory loss of the "glove-and-stocking" type, and tenderness of the muscles and nerves, confined to or most intense in the distal parts of the limbs. When sensory disturbances and diminished tendon reflexes are prominent symptoms and muscular weakness is slight, *tabes* may be suggested, and the resemblance is still greater when ataxia is present. Difficulty usually arises when the distinction has to be made between tabes and alcoholic neuritis, in a patient who has courted both diseases. In most instances the diagnosis can be made from the nature and distribution of the sensory changes. The lightning pains of tabes cannot be mistaken by any one who is familiar with their peculiar characters. Anæsthesia of the extremities is common to both diseases, but diminished sensibility around the

nose and across the chest is peculiar to tabes and is present in almost every case. In neuritis the calf muscles and nerve trunks are tender, whereas in tabes the sensibility of these structures is usually greatly diminished. Hyperæsthesia to touch and temperature, and great exaggeration of the abdominal reflexes, also suggest tabes.

5. ACUTE FEBRILE POLYNEURITIS

Synonym.—Acute Infective Polyneuritis.

At various times small epidemics of a form of polyneuritis characterised by a febrile onset and by the involvement of the facial nerves have been described (Osler, Gordon Holmes, Rose Bradford and others). Nothing is known of its ætiology and it is probably not essentially different from Landry's paralysis in nature, though less fulminating in onset and not so liable to grave involvement of the trunk muscles.

Symptoms.—The onset is with slight fever, headache and malaise, pains in back and limbs, and such general symptoms as a coryza or gastro-intestinal irritation. The fever persists for 2 or 3 days only. A few days then elapse before the signs and symptoms of polyneuritis develop. It is said that the proximal limb muscles are more severely involved than the distal muscles, a point of distinction from other forms of polyneuritis, but this relative incidence of weakness is not invariable and has probably been over-stressed. The trunk muscles do not escape, and the face is usually bilaterally paralysed. As in other forms the paralysis is of the lower motor neurone type, flaccid, atrophic and with loss of tendon jerks. As in Landry's paralysis sensory loss is very slight, and there is relatively slight muscular tenderness. The cerebro-spinal fluid may show a high rise in the protein content, but is otherwise normal.

The clinical course is variable, and sometimes fluctuating in the individual case. Death may ensue from paralysis of the respiratory muscles, and recovery in the majority of cases is fairly rapid. There is the usual tachycardia of polyneuritis.

Treatment.—The first essential in treatment is to remove the patient from the influence of the existing cause. In alcoholic cases, rigid precautions are necessary to prevent secret access to alcohol. To attain this, treatment in an institution is almost a necessity. In most instances when the cause, whatever it may be, is removed, gradual improvement sets in and complete recovery ensues, in a time that varies with the severity of the symptoms. The administration of vitamin B_1 preparations has now a great vogue in the treatment of both multiple (parenchymatous) and interstitial neuritis. In the latter its use has no theoretical justification or practical value, and even in the former, though its use is rational, it yet remains to be proved that the course of the malady is materially influenced. This may be due to inadequacy of dosage in the past, and the parenteral injection for from 2 to 4 weeks of 500 to 1000 units daily is the minimum dosage likely to be efficacious. During this time the physician's most important duty is to prevent the occurrence of deformities and contractures. From the beginning, each joint in the affected limbs should be moved passively to its full range several times each day, and care should be taken to ensure that the attitude of the limbs during rest is a suitable one, especially that the feet are main-

tained at right angles to the legs by the use of appropriate apparatus. Drawing up of the heel must be prevented at all costs.

Gentle massage is soothing in the acute stage. Later, more vigorous rubbing may be given, and the patient should be encouraged to move the limbs voluntarily. Electricity is of no value. Analgesic drugs and soothing applications may be needed at the onset. Thereafter, local treatment to the limbs is combined with measures to improve the patient's general condition. The possible rôle of B avitaminosis in the production of many, if not all, varieties of polyneuritis has naturally led to the administration of the B_1 complex as an important element in treatment. Not less than 1000 to 2000 units daily and given over a period of two or three weeks is adequate, but even with this dosage it is not yet clear that the course of any ætiological variety of polyneuritis is materially influenced, and extravagant claims should be treated with great reserve.

6. LANDRY'S PARALYSIS

In the year 1859 Landry applied the name " acute ascending paralysis " to a case in which acute flaccid paralysis with loss of reflexes and without sensory disturbances commenced in the periphery of the lower limbs, and rapidly spread upwards. The arms were next involved, first in the periphery, and later the trunk, respiratory muscles, neck, and lastly the cranial muscles were involved, and death occurred from respiratory failure. He made a careful microscopic examination of the spinal cord with the methods then at his disposal, and failed to detect in it any morbid changes. He subsequently described this symptom complex, which has since borne his name, from an analysis of 10 cases.

Since this time a large number of cases have been recorded which, from the acute nature of the onset, and from the spreading nature of the paralysis, have been described as cases of Landry's paralysis. This name should be restricted to those cases of acute spreading paralysis, in which disorders of sensibility and sphincter trouble are absent or little marked, and in which recovery is complete if the patient survives, and in which no gross lesion is found within the nervous system after death.

Acute poliomyelitis may also, in rare cases, give rise to a spreading paralysis, and cause much difficulty in diagnosis; but it is invariable that some permanent paralysis remains upon recovery, and, further, the lesions of poliomyelitis are both gross and characteristic.

The majority of authors who have written upon this subject have made the attempt to separate Landry's paralysis from the group of " acute toxic polyneuritis," both on pathological and on clinical grounds. Such a separation would appear to be entirely unsupported by the evidence. In both these conditions all the nervous pathological changes which have been discovered are confined to these lower neurones, motor and sensory, and are often in polyneuritis confined to the lower motor neurones. The clinical separation of Landry's paralysis and polyneuritis is equally artificial and impossible, though much stress has been laid upon the presence of disturbances of sensibility, and the strictly peripheral distribution of the paralysis in polyneuritis. As regards sensory disturbance, this clinical feature is dependent upon the peculiar selective capacity of the poison. The following

description of this malady is based upon the personal observation of 10 cases with 4 autopsies which have come under our observation at the National Hospital and at St. George's Hospital.

Ætiology.—What is known of the causation of the disease in general resembles very closely that of acute polyneuritis. It affects males much more frequently than females, and occurs chiefly in adult life between the ages of 16 and 54 years. The cases which have been reported in children were probably examples of the spreading type of poliomyelitis.

Pathology.—Slight hyperæmia of the spinal cord, and especially of the grey matter, with a few punctiform hæmorrhages, is the only change noticeable upon naked-eye examination. Very definite histological changes are found upon microscopic examination in the anterior horn cells and in the cells of Clarke's column, where any degree of change may be found, from an early pericentral chromatolysis to a complete loss of the chromatin granules and concentration of nuclei.

The cerebro-spinal fluid is in excess, and clear. In two of the cases under our care, it presented no abnormality either as regards cell or albumin content. In other cases there is an excess of albumin, and in this respect it resembles the cerebro-spinal fluid of polyneuritis, which is usually albuminous, and sometimes so highly so as to clot spontaneously.

Symptoms.—The onset is in some cases abrupt, with the appearance of the characteristic spreading paralysis. Much more frequently the paralysis is preceded by certain premonitory symptoms, which may last from a few hours to days or weeks. These symptoms may consist in malaise, headache, lassitude, insomnia, anorexia, constipation, gastralgia, vomiting and diarrhœa, and there is not infrequently slight elevation of temperature. More characteristic still among the prodromal signs are subjective disturbances of sensibility. Pains in the back and limbs are common, and may be of a dull aching nature, or they may be sharp and shooting in character. Numbness, tingling, "pins and needles" and other paræsthesias may occur over any part of the body, and are most commonly complained of in the periphery of the limbs. The muscles may be locally tender during this prodromal stage.

It is not uncommon for the paralysis to commence in the periphery of the lower extremities, to ascend rapidly, and to involve the muscles in the order of their innervation from the spinal cord, the trunk becoming affected before the upper extremities, and the intercostal muscles before the diaphragm. The muscular weakness may commence in any group of muscles, as, for example, in the face, neck, upper extremities or trunk, and when so commencing the spread of the paralysis is downwards, constituting a descending type of paralysis.

In Landry's paralysis, as in acute polyneuritis, the innervation of the respiratory muscles seems to be peculiarly resistant to the toxin.

In those cases which recover the advance of the paralysis ceases, and those muscles which have been most recently affected begin to show some recovery quickly.

When the disease does not prove fatal either from respiratory failure, pulmonary complications or sudden syncope, the paralysis ceases to spread, and the patient enters upon the stage of recovery, which presents many features of interest. The flaccid muscles show a moderate degree of wasting within 2 or 3 weeks on the onset, this wasting being much less in those cases

which recover rapidly. It is a general atrophy, and is not limited to particular groups of muscles. In rare cases, though fair power is regained, yet the muscles remain conspicuously small for life; but generally the muscles recover their bulk and tone completely. The paralysed muscles retain their excitability to faradism throughout, though there may be some slight diminution of faradic excitability in proportion to the general wasting of the muscles. Contractures and deformities do not occur.

The paræsthesias, which have been described with the onset, often persist, and there may be cramp-like pains. Not uncommonly the muscles are tender upon deep pressure; but there is never that severe degree of tenderness met with in some forms of peripheral neuritis as, for example, in alcoholic neuritis. There is exceptionally blunting of sensibility, most marked in the periphery; but this is never deep, and is rapidly transient.

Though from the general weakness of the trunk muscles there may be some difficulty in emptying the bladder and rectum during the first few days, and even retention with overflow incontinence that may require catheterisation from the same cause, yet these last but a few days. The deep and superficial reflexes disappear early with the onset of the first signs of the paralysis in the affected regions. The psychic functions remain unimpaired throughout.

Diagnosis.—The rapidly spreading character of the paralysis in Landry's disease is so striking as to necessitate distinction only from those few maladies in which a similar rapidly spreading paralysis may occur, and these are acute spreading myelitis, intrathecal hæmorrhage, acute poliomyelitis (spreading type) and acute polyneuritis. Acute spreading myelitis is at once distinguished from Landry's paralysis by the severe sensory loss and sphincter paralysis, which in the former condition develop *pari-passu* with the motor paralysis and, further, if the myelitis does not involve the lumbo-sacral enlargement of the spinal cord, an extensor plantar reflex will be observed.

The rare, spreading form of poliomyelitis presents difficulty in diagnosis, especially in the acute stage. The general symptoms and the pyrexia are apt to be more severe in poliomyelitis. An onset in childhood is more suggestive of poliomyelitis than of Landry's paralysis. A fairly high polymorpho-nuclear leucocytosis in the blood, and a lymphocytosis in the cerebro-spinal fluid, are in favour of poliomyelitis. The persistence of local atrophic palsy on convalescence is absolute evidence of poliomyelitis. The distinction of Landry's paralysis from acute polyneuritis is held by the writers of this article to be entirely artificial, since they argue that *Landry's disease is merely a striking type of acute polyneuritis.*

Prognosis.—In about one-half of the cases the paralysis advances until the respiratory and bulbar muscles are involved, and death occurs from respiratory failure, usually on the third or fourth day, but sometimes not until ten days or more have elapsed. So long as the paralysis is extending, and especially when the respiratory and bulbar muscles are failing, the prognosis is very grave. The extension of the paralysis may, however, cease at any stage, and when this occurs the prognosis at once becomes favourable, even though there be considerable involvement of the respiratory and bulbar muscles.

Treatment.—The patient must be placed at complete rest, and the discomfort and panic which are likely to arise from the utter inability to move must be assiduously relieved by frequent changes of posture. The greatest

care must be taken that the patient is adequately fed with nutritious and light food. Stimulants are usually indicated. A mercurial aperient should be administered early and the bowels regularly relieved, for in some cases obstinate constipation occurs. The bladder should be catheterised, if there is a difficulty in micturition. Both pain and pyrexia may be relieved by the administration of salicylates or aspirin.

Atropine tends to check accumulation of secretion within the bronchi. Oxygen may be administered where cyanosis occurs. When once the patient has shown signs that the malady has passed its height, and that recovery is commencing, little treatment is required except careful nursing and feeding. Gentle massage may then be employed.

7. PROGRESSIVE HYPERTROPHIC POLYNEURITIS OF DEJERINE AND SOTTA

Definition.—An extremely rare progressive form of polyneuritis, sometimes developing in infancy, showing an heredo-familial incidence, and characterised by thickening of the nerve trunks due to hypertrophy of the sheaths of Schwann.

Pathology.—The thickening of the nerves may be palpable during life, but is not invariably so. Microscopically this thickening is found to be due to masses of non-nucleated tissue arising from the sheath of Schwann.

Symptoms.—The malady develops and progresses very slowly with weakness, muscular wasting, sensory loss, loss of tendon jerks. There may be noted, in addition, kyphoscoliosis, nystagmus and ataxy of movement. It was formerly thought that the Argyll Robertson pupil was an integral part of the symptom-complex, but this is not the case.

Prognosis.—Death ultimately ensues from intercurrent disease.

Treatment.—There is no known treatment.

NEUROFIBROMATOSIS

Synonym.—Recklinghausen's Disease.

Definition.—A rare and complex disease characterised by multiple benign tumours on the skin and on the nerves and the ganglia of the somatic and autonomic nervous systems. Cutaneous pigmentation, and multiple tumours on brain and spinal cord may also be present.

Ætiology.—The malady is probably developmental in origin, and heredo-familial incidence is not uncommon.

Pathology.—The skin presents spots of varying size and number that have the colour of freckles. When these are extensive they are known as café-au-lait patches. They tend—like the cutaneous tumours—to increase in size and number with age. The skin is adorned with numerous soft fibromatous tumours, some sessile and some pedunculated. In some cases the trunk may be thickly sewn with these. Large plexiform neuromas on cutaneous nerves may form large masses on the skin, flattened and of irregular outline, and when this aspect of the disease is prominent it is given the name of *molluscum fibrosum.*

On the nerve trunks are more or less numerous, fairly firm nodular tumours of varying size. The cranial nerves may also bear similar tumours, especially the fifth and eighth nerves. Marked kyphoscoliosis is common.

Symptoms.—The cutaneous pigmentation and tumours are readily visible and tend to increase throughout life. Sometimes the neurofibromata on the nerves give rise to symptoms of irritation (pain in the distribution of the nerve) or of paralysis. Intrathecal tumours may give rise to spinal cord compression, while the symptoms of an auditory nerve tumour (unilateral or bilateral) may first bring the patient to notice.

Treatment consists in the removal of fibromata on the nerves when these give rise to irritative or paralytic symptoms.

LEAD PALSY

The effects of lead are confined almost entirely to motor neurones. Subjective sensory disturbances are often slight or absent, and in most instances there is no objective sensory loss.

Pathology.—Aub in 1923 showed that the first event was the local concentration of lead in those muscles which were about to be paralysed and that the paralysis was a muscular event primarily, and that, secondarily, the lead ascends along the motor axons and may finally cause the death of the ventral horn cell. The degenerative changes in the nerves are confined almost entirely to the motor fibres, and are most intense in the intramuscular twigs supplying muscles of the extensor groups. Normal and degenerated fibres are found side by side, the former becoming more numerous as the nerve is traced upwards. Degenerative changes due to the action of lead are also found in the affected muscles.

Symptoms.—In most cases of the common *antebrachial* or *wrist-drop type*, paralysis is limited to the extensor muscles of the fingers and wrists—that is, to the muscles supplied by the musculo-spiral nerve. But the supinator longus and the extensor ossis metacarpi pollicis, also supplied by this nerve, usually escape. Inability to extend the first phalanges of the two middle fingers, owing to weakness of the common extensor, is usually the first difficulty. The special extensors of the index and little fingers, the long extensors of the thumb and the extensors of the wrist are next attacked, and the characteristic wrist-drop appears. As a rule the paralysis becomes severe about a week after it is first noticed. By this time it is usually bilateral and symmetrical, but for several days, or even for several weeks, it may be confined to one side. The affected muscles waste rapidly and the back of the forearm becomes flattened, thus rendering the intact supinator longus more prominent. In this form, loss of power always precedes atrophy, and some muscles may show weakness without any wasting. Recovery is almost always complete. Simple weakness without atrophy usually passes off in a few weeks. If the wasting is moderate and the muscles still react to faradism, recovery may be expected in a few months. When the atrophy is severe, a year or more may elapse before recovery is complete.

Occasionally the deltoid, biceps, brachialis anticus and supinator longus muscles are affected, either alone or in company with the forearm muscles —*upper arm* or *brachial type*. Less often paralysis occurs in the legs, the muscles supplied by the peroneal nerve, namely, the long extensors of the toes and the peronei, being chiefly involved—*peroneal type*. Like the supinator longus in the arm, the tibialis anticus, although supplied by the peroneal

nerve, usually escapes. This type is usually associated with paralysis of the forearm muscles, and runs the same course.

In the form of paralysis described above the features are those of a traumatic lesion to a nerve. Loss of power precedes, and may be more extensive than wasting, faradic irritability of the muscles is lost or diminished while the reaction to galvanism is retained, and recovery is usually complete. It is therefore called the degenerative form. In the second form, the paralysis has the characters of progressive muscular atrophy. Weakness and wasting come on together, faradic and galvanic irritability of the muscles are both diminished in proportion to the wasting, and the paralysis is often permanent. This is known as the primary atrophic form. It occurs especially in the small muscles of the hand—*Aran-Duchenne type*—but is sometimes irregular in its distribution and affects many muscles in all four limbs. It is often associated with the first form, but may occur alone. Wasting comes on slowly, and accompanies the loss of power, instead of succeeding it. It is much more intractable than the degenerative form, and often persists after muscles showing the first form of paralysis have recovered. (See also Lead Encephalopathy, p. 366.)

MUSCULAR DISEASES

MYOTONIA CONGENITA

Synonym.—Thomsen's Disease.

Definition.—A very rare malady, commencing in early childhood, which is hereditary and familial, and characterised by a striking slowness in the relaxation of the muscle after voluntary effort. The muscles pass into a spasm on voluntary contraction, which relaxes very slowly, resembling the contraction of the veratrinised frog's muscle, and its subsequent slow relaxation. Peculiar changes in the electrical excitability of the muscle and hypertrophy of the muscle fibres are constant.

Ætiology.—Beyond the facts that the malady is usually hereditary and familial, only a few sporadic cases occurring, and its incidence in early childhood, nothing is known of the causes. Cold, heat, fatigue and hunger conspicuously increase the symptoms.

Pathology.—The affected muscles are actually hypertrophied, and are always firmer to the feel than normal muscles, while sometimes they show a board-like hardness. The individual fibres show considerable hypertrophy.

Symptoms.—The presence of the disease first becomes evident from slowness, clumsiness and awkwardness of movement, with a great tendency to fall if the balance is upset. This is often most noticeable after rest, when, on attempting to move, the limbs seem glued down and move very slowly. Often the patient is able with exercise to work the stiffness off, and the myotonia lessens in the muscles which are being used; but if he is suddenly called upon to put another set of muscles into action, as, for example, by losing his balance, he is at once caught up by the myotonia and so is apt to fall. In other

cases the myotonia increases or is uninfluenced by exertion. The muscles of the legs are as a rule most affected, but sometimes all the muscles of the body may be involved.

Passive movement does not reveal the presence of any rigidity except that following voluntary contraction. The abnormality affects the voluntary contractions and relaxations of the muscles only, and the peculiarities of these are—(1) their slowness, (2) their tonic character, and (3) the continuance of the contraction after voluntary impulses have ceased. The peculiarities of electrical excitability bear the name of the " myotonic reaction " of Erb. The contraction, either on faradic or galvanic stimulation, lasts much longer than the normal and relaxes very slowly, and this is more marked the stronger the current used ; with the stabile application of galvanism, slow wave-like contractions of the muscle are seen to proceed slowly from the cathode to the anode. There is no pain, no sensory disturbances or loss, and the sphincters and reflexes are unaffected.

Diagnosis.—The only malady which can be confused with Thomsen's disease is myotonia atrophica, in which the myotonic symptoms and signs are identical. In the latter malady, the onset is at a much later age, the incidence of the spasm is upon local groups of muscles, and the characteristic weakness of the facial muscles and atrophy of the sternomastoids, etc., at once distinguish it.

Course and Prognosis.—Thomsen's disease has no tendency to shorten and destroy life. It tends to become more marked from infancy to puberty, and then less marked again as age increases. It has never been cured.

Treatment.—This is entirely unavailing, except in the way of the avoidance of those conditions, such as fatigue, cold and hunger, which are known to increase the condition. Thomsen himself, who was afflicted with the disease, was always better with free exercise.

DYSTROPHIA MYOTONICA

Synonym.—Myotonia atrophica.

Definition.—A disease of familial incidence, which begins usually in the third and fourth decades of life, and which is characterised by muscular atrophy of peculiar distribution and unlike that of any other disease. This atrophy occurs first and most in the sterno-mastoids and facial muscles, next in the muscles of the forearms, and may also be found in the muscles of mastication, in the vasti, and in the dorsiflexors of the feet and peronei. Associated with this wasting, but not commensurate with it, nor necessarily occurring in the same muscles, is a peculiar difficulty in relaxing the muscles after effort, called " myotonia," which gives to this malady an especial feature which at once separates it from all other forms of muscular atrophy. Signs of bodily dyscrasia are often present, the most important of which are cataract, premature baldness, atrophy of testicles, loss of sexual power and general bodily wasting. This disease was first placed upon a firm clinical basis by Batten and Gibb, and Steinert in 1909. Curschmann in 1912 adopted the term Dystrophia Myotonica as being more correctly descriptive.

Ætiology.—This condition is probably always familial, and the heredity is homologous—that is, it tends to appear in the same child-rank, in a number

of apparently unconnected families at a common distance from one and the same ancestor, and often it seems to be entirely confined to one child-rank. The descent of the latent tendency is equally through the males and females, but the males more frequently transmit. The presence of the heredo-familial disease in earlier generations is often betrayed by other signs, such as cataract, frequent celibacy, childless marriages, high infant mortality, and a dying out of certain branches of the family. The malady has been observed at the age of 10 years, but usually the onset occurs between the ages of 20 and 35 years. A large number of the patients have been unusually gifted and proficient in athletics prior to the onset. Both sexes may be affected. No exciting causal factors are known.

Pathology.—No definite changes have been found in the nervous system. The muscles presenting the myotonia have repeatedly been examined and found normal. In the atrophic muscles the morbid process singles out certain fibres especially, so that quick and thin fibres are found lying together. There is increase of the muscle nuclei round thick and thin fibres alike, though some atrophic fibres may be found with no increase of nuclei. Recent biochemical and electrographic studies by Brown and Harvey of a form of congenital myotonia in goats suggest that there is no functional disorder of neuromuscular transmission of the motor impulse, but that the disorder is in the muscles themselves.

Symptoms.—The onset is gradual and the course extremely slow. The first symptom to call attention may be, either the difficulty in relaxing after muscular effort—the clinging of the hand to the tool which has been grasped, the smile that is so slow to disappear—or the weakness and wasting of the muscles. The two chief signs of the disease—the myotonia and the wasting—seem to have no connection the one with the other, either as regards coincidence in time or place. The myotonia may appear years before there is any obvious wasting. Moreover, the muscles which show the most conspicuous myotonia are often those which are not wasted, and finally those muscles which waste greatly tend to lose any sign of myotonia which they may have had. The extent and the intensity of the muscular atrophy and of the myotonia show great variations. The atrophy may be widely spread, and many muscles may be myotonic, or the former may be severe and the myotonia slight, or both may be present in minor degree only. Lastly, there are cases in which only the atrophy or only the myotonia is present. The myotonia consists in an inability to relax a muscle immediately after it has been put into voluntary contraction, and the greater the effort used in contracting the muscle, the greater the difficulty with relaxation. The patient grasps one by the hand, and is unable to disengage the hand, but pulls it away still grasping, and it may take seconds to relax. He smiles quickly to a suitable stimulus, and the face remains fixed at the height of the smile for long after the emotion has vanished. In eating, his jaw becomes fixed, he is unable to perform any alternate movements in the muscles which are affected, but at a very slow rate. When the myotonia is severe and general, he is liable to fall like a log when walking, from inability to relax muscles which have been put into contraction. The myotonia is seen most often and to a greater extent in the flexor muscles of the forearm and in those of the face, but it may be quite general. In the same patient it may be very marked at one time and absent at another.

The muscular weakness and wasting usually have a most typical distribution, involving the sterno-mastoids and other muscles of the neck, the facial and masticatory muscles—giving rise to the sad "myopathic" face, the vasti of the thighs, and the dorsiflexors of the feet, and this is the usual order in which the muscles are affected. It is always in one or other of these groups that the wasting commences, but sometimes the sequence of muscles attacked is quite different. Fibrillation does not accompany the atrophy. The electrical reactions show a reduction both to faradic and to galvanic stimuli, with a tendency to a polar change. Some modification of the "myotonic reaction" is often superadded in those muscles which are wasted, and this usually is present in the muscles which are myotonic and are not wasted. This "myotonic reaction" consists in a very long, lasting contraction when the muscles are stimulated with every form of stimulus, and if the latter be strong it may last as long as 30 seconds.

The affection of the muscles of the face and jaw entails some alteration of articulation and phonation. The voice is low, it lacks intonation, and has a definite nasal quality. Sensibility is not affected.

The rule is for the muscle-jerks to be diminished or lost, and it is very rare for all the jerks to be present in any case.

Apart from symptoms and signs connected with the muscles, the most important sign of the dystrophy is cataract, which occurs in more than half of the cases. This cataract is often met with in otherwise healthy brothers and sisters of those who have the muscular changes, and in otherwise healthy members of earlier generations in the afflicted families. In succeeding generations after its first appearance, the age of occurrence of this cataract shows remarkable "anticipation"—that is, commencing at first as senile cataract, it appears at an earlier and earlier age with each successive generation, until with fully developed myotonia atrophica it appears in youth. The presenile cataract of the dystrophic generation begins as a star-shaped opacity, first in the posterior and later in the anterior cortical lamellæ, sometimes with fine point-like opacities scattered through the lens. It ripens quickly to a total soft cataract, with a small central nucleus.

The genital organs remain infantile in some cases; celibacy and childless marriages are common. More often sexuality is normal until the onset of definite symptoms, after which desire and power disappear. Early baldness is the rule. A general wasting of all the tissues of the body is seen in many cases. Ultimate atrophy of the testicles is usual.

Diagnosis.—There is no difficulty in the diagnosis when the distribution of the muscular atrophy is typical and when myotonia is obvious; it simply involves a recognition of the unique characteristics of the disease. When the myotonia precedes the wasting, the age of onset will distinguish this malady from Thomsen's disease, or myotonia congenita, and the oncoming of any sign of facial weakness or muscular wasting will make the diagnosis certain. When the myotonia does not appear until long after the wasting is apparent, the diagnosis is much more difficult.

Course and Prognosis—This malady usually progresses very slowly, but occasionally very extensive and incapacitating wasting of muscles and weakness may develop within a year of the first symptom. Some cases seem to remain stationary for very long periods. The tenure of life is certainly short in all cases, and does not appear to be prolonged beyond the middle of

the fifth decade. The oldest patient reported in the records as still living was aged 50 years.

Treatment.—It has been found that the administration of quinine, grs. 10 to 15 daily, lessens the myotonia considerably. Neither electrical treatment nor massage has the slightest effect in altering the course of the disease.

JAMES COLLIER.
Revised by F. M. R. WALSHE.

MYASTHENIA GRAVIS

Definition.—A chronic malady of adult life characterised by—(1) a variable paralysis of muscles which is produced or rapidly increased by exertion, and which tends to disappear slowly during rest; (2) a permanent paralysis which shows no improvement with rest, and which succeeds the variable paralysis. This permanent paralysis may be very local in distribution, and may be associated with atrophy of the muscles; and (3) the affected muscles on strong faradisation soon cease to respond to faradism, but remain excitable by galvanism.

Ætiology.—The malady seems to be much more prevalent in England during the past 20 years than formerly. Rarely occurring before puberty, it commences most commonly in the third decade of life, and affects the sexes equally. Nothing is known of any causal factors either immediate or remote. The one clinical association which cannot be ignored is with exophthalmic goitre, for not only may myasthenia follow that malady, but the ophthalmoplegias which occur in Graves's disease bear no small resemblance to those of myasthenia.

Pathology.—The only changes found within the nervous system are slight atrophy of those nerve cells which supply long paralysed muscles, and these changes are certainly not primary. In a certain number of the cases a large peristent thymus gland, showing proliferative and degenerative changes, or thymic rests showing similar changes, have been found. The view expressed in earlier editions of this book that the seat of the disorder of function responsible for myasthenia gravis is at the myo-neural junction has recently received confirmation from observations made with physostigmine and the synthetic substance "prostigmine." It is believed that the normal transmission of impulses from nerve to muscle through the motor nerve endings depends upon the liberation in the endings of acetyl-choline. In myasthenia the failure of effective innervation may be due either to premature destruction of acetyl-choline, or to a failure in its liberation. The administration of physostigmine temporarily delays the destruction of the acetyl-choline by the choline esterase normally present in the blood, and during its period of activity renders muscular contraction normal.

Symptoms.—The first sign of myasthenia is the variable paralysis which may commence in any of the voluntary muscles. It may be unilateral at first, but soon becomes symmetrical. The paralysis appears first upon exertion and fatigue. The schoolmaster finds that towards the end of the day's work he cannot raise his arm readily to write upon the blackboard, or that his voice fails him in speaking. The housemaid finds that her broom

slips in her hands, because of an ever-weakening grasp. The theatre-goer, towards the end of the performance, finds himself tilting his head farther and farther back to escape from an oncoming ptosis, or he develops diplopia. Next morning these symptoms are gone with the night's rest, to reappear with fresh exertion perhaps earlier each day, until work becomes impossible. The affected region may be narrowly confined, the eyes alone, the face, the muscles supplied by the trigeminus, or the larynx alone may be affected, or it may be the muscles of the upper extremities, or of the lower extremities, or of the back which may be solely involved. Lastly, the myasthenia may be quite universal, though never in the same degree in all the affected regions.

The incidence is greatest upon the muscles innervated from the brain stem, next upon the upper extremities and trunk, and least upon the legs. When the initial incidence of the malady is upon the eye muscles, diplopia and ptosis are the first symptoms. The paralysis is usually of the nuclear type, involving both eyes in terms of the conjugate movements; but inequality in the paralysis upon the two sides usually gives rise to decided strabismus and diplopia, and we have observed one case in which the initial paralysis was confined to one external rectus. When the permanent paralysis sets in, the axes usually become parallel, and the diplopia ceases. Until this event occurs, the great feature of myasthenic ocular paralysis is its variability, and its increase with fatigue. An ocular paralysis which is well each morning on waking, and which develops in the course of each day, is always due to myasthenia. Short, very quick, jerky movements of the eyes on attempted voluntary movements are often characteristic, and are quite different from the movements of nystagmus. Though ptosis is the rule, sometimes there is retraction of the lids, and both von Graefe's and Stellwag's signs may be present. Permanent nuclear ocular paralysis follows the variable paralysis in nearly every case, though it varies in degree. When the face is affected, epiphora, dysarthria and lack of facial expression with a peculiar weak "nasal smile" are conspicuous. The facies of myasthenia, with inability to close or pucker the eyes and mouth, the motionless and slightly dysarthric speech and peculiar smile are unmistakable.

Involvement of the muscles supplied by the fifth nerve causes trouble with mastication, and when the palate is affected there may be nasal speech and regurgitation of liquids. We have seen one case in which total unilateral paralysis of the larynx preceded the onset of typical symptoms by twelve months. When the tongue is affected it usually shows some wasting, especially of the linguales, and dysarthria results. Sometimes a widely spread involvement of this region causes severe dysphagia and dysarthria, and the former may be so great as to necessitate nasal feeding. The permanent paralyses are rarely seen, except in the muscles supplied by the nuclei of the brain stem. The neck muscles are usually affected when the malady extends on to the trunk, and it is a common thing to see the patients sitting at rest, either with the head supported by the hands, or resting upon the table. In the extremities the variable paralysis appears more marked at the proximal joints in most cases, and the test for myasthenia in the upper extremity is to ask the patient to extend his upper limbs level with the shoulder, when they will be seen to fall slowly down from the increasing fatigue paralysis.

Involvement of the respiratory muscles is common, and constitutes the gravest danger in the disease, since any effort, and especially an emotional

outburst, may in a few seconds fatigue the respiratory muscles into a complete and fatal paralysis. Myasthenia often remains long confined to one region, and subsequently spreads rapidly. Wasting of the muscles occurs only when there is marked permanent paralysis, and may be seen in the muscles of the tongue, face and in the masticatory muscles. In one fatal case under our care there was marked wasting of the intrinsic hand muscles on both sides.

The myasthenic reaction is only seen in those muscles which are showing conspicuous fatigue paralysis. If a strong interrupted faradic current is applied to such muscles, there is at first a strong contraction, but this is not maintained as in normal muscles, and it rapidly decreases until there is no response. If the stimulation is discontinued for a few minutes, and again applied, there is a further response, which tires more rapidly than the first. After exhaustion of the muscles by faradism, some volitional contraction remains. Exhaustion of the muscles does not occur from galvanic stimulation. Sensibility and sphincter control are not affected. The reflexes are normal in all but the rarest cases. The knee-jerk is not abolished when the quadriceps is exhausted, either by voluntary exertion or by faradisation.

Diagnosis.—This is never a matter of any difficulty if the variable paralysis, increasing with fatigue and lessening with rest, is conspicuous, for this phenomenon occurs in no other disease. When permanent paralysis only is present, the diagnosis requires care. It must be remembered that any unilateral or bilateral palsy of muscles supplied by the brain stem may be myasthenic. Here the history of a slow onset with variable paralysis and fatigue phenomena can nearly always be obtained, and the absence of the usual signs of gross lesions of the brain-stem nuclei, or progressive diseases affecting the latter, should avoid confusion. When, as sometimes happens, myasthenia begins with a unilateral ophthalmoplegia or laryngoplegia, the diagnosis may really be difficult. The possibility of such a commencement should be borne in mind, and a careful watch kept for the appearance of conclusive evidence. Other forms of nuclear ophthalmoplegia do not show a long history of variability and fatigue phenomena.

Course and Prognosis.—Myasthenia is always a very dangerous disease, as the term "gravis" implies. Some of the cases, and especially those in which the brain-stem region escapes, recover completely; but no records are as yet available to prove in what proportion of the cases this event occurs. The disease has proved fatal within a fortnight of the onset of symptoms, and, on the other hand, in our two cases here recorded, strenuous work was followed for 24 years after the development of permanent ophthalmoplegia. Improvement and relapses are very common. Frequently a patient will get rapidly worse, and become bedridden, in spite of careful treatment; to recover completely for the time being, when treatment has been abandoned as useless. Sometimes a patient with severe myasthenia will live for many years, if life be carefully protected. We have had one patient under observation in this state for 20 years, and she is not materially worse.

Sudden death is very liable to occur in any of the cases, but especially in those with bulbar paralysis and implication of the muscles of respiration. Death has been attributed to respiratory failure and asphyxia; but some of the patients die much too quickly for any such explanation. Two of our patients, seated at a table with their heads supported by their hands, and

engaged in pleasant, quiet conversation, smiled, lowered their heads on to the table, and were dead without the slightest sign of distress or reaction, as if from syncope.

Treatment.—The life must be so ordered as to exclude all fatigue. Massage, electrotherapy, endocrine therapy and strychnine medication are ineffective when not harmful. Claims have been made for many different drugs and preparations, but they are based upon an ignorance of the fluctuating course of the malady and of its occasional spontaneous cure. Few things in clinical medicine can be more dramatic than the rapid and complete disappearance of all weakness and disability upon the hypodermic injection of prostigmin 2 to 4 c.c. (1 to 2 mgms.) combined with atrophine sulphate, gr. $\frac{1}{100}$. This abeyance of symptoms endures for some four or five hours only. When the effect passes off the patient lapses into his original state, or may even be weaker than before. In severe cases, this possibility of increased weakness after physostigmine or prostigmin administration has its dangers. It is not yet possible to use these drugs by repeated injection as a mode of treatment for myasthenia gravis, though their occasional administration may enable the subject to meet special calls from time to time. The drug may be given orally in tablets of 15 mgms., four to eight daily.

A few patients maintain an improved level of power in the affected muscles when given ephedrine sulphate or chloride (grs. $\frac{1}{2}$ to 1, t.d.s.).

FAMILIAL PERIODIC PARALYSIS

Definition.—A flaccid paralysis affecting the muscles of the trunk and of the extremities, associated with loss of the deep reflexes and diminution or loss of faradic excitability in the muscles. The paralysis is temporary in character, though it may be fatal during the attack, and it recurs at intervals. It is a rare malady, some 200 cases having been reported in the literature.

Ætiology.—It has been noted as early as the fifth year, and as late as the thirtieth year; but usually it appears about the age of puberty. Most of the cases occur in the male sex. Heredity is very marked, and the malady has been traced through five generations. Transmission may occur either through the male or through the female, and not infrequently a generation is skipped. Several members of the same family are usually affected.

Pathology.—Several cases have come to autopsy, but no lesion which could be associated with the symptoms was found. Biopsy of the muscles has given entirely negative results.

Symptoms.—The clinical picture is so striking as to be almost dramatic. The patient retires to bed feeling perfectly well, and awakens in the morning without pain or malaise, but with a flaccid motor paralysis, which always involves all four extremities, and which may reach all the muscles of the body, except those of the organs of speech, deglutition and respiration, and even these are often partially involved. Severe involvement of these vital muscles during an attack has caused death. The bladder and rectal functions are retained, and it is unusual for the patient either to void urine or fæces during the attack. The paralysis is usually at its height on waking; but it may subsequently increase. After lasting for a variable time, from a few hours to

a few days, it passes off, sometimes gradually, sometimes rapidly. In the family under our care it was astonishing how the patients on waking in an attack could judge invariably how long the particular attack would last. They could judge with unfailing certainty when ability would return, and were in the habit of arranging their business accordingly. Most of the patients in addition to the severe attacks of paralysis suffer from what they call "morning weakness," temporary inability to grip with the hands, and slight disability with the feet on waking. It is curious that similar morning weakness, lasting a few minutes, is not very uncommon in normal children. The paralysis in periodic paralysis is flaccid, and there is loss or marked diminution of response to faradism during the paralysis. The deep and superficial reflexes are lost in the paralysed region. Objective sensation is not affected; but there may be subjective sensations of tingling and numbness, and the muscles may be a little sore and stiff after the attack. We have noticed flushing of the surface and sweating during the attack. There is an invariable tendency for the attacks to diminish in frequency and severity after middle life is reached.

Diagnosis.—This must be evident to any one acquainted with the symptoms of the disease.

Treatment.—Potassium chloride in large doses (up to 30 or 40 grs.) will avert or cut short an attack. No other remedial measure is known.

MUSCULAR DYSTROPHY; MYOPATHIC ATROPHY

Synonym.—The myopathies.

Under this heading, a disease is described in which the voluntary muscles undergo primary degeneration, independent of detectable disease in other parts. To facilitate description, a number of clinical types have been distinguished according to the age at which the disease appears, to the group of muscles first attacked, to the presence or absence of pseudo-hypertrophy, or to the prominence of the hereditary factor. The chief of these are—(1) the pseudo-hypertrophic type; (2) the juvenile type of Erb; (3) the facio-scapulo-humeral type of Landouzy and Dejerine; (4) the distal type.

The first type is fairly constant, but there is in reality no sharp division between the different forms. That the others do not represent separate diseases is proved by the appearance of more than one of them in members of the same family. The disease is familial, and it is also hereditary in the sense that it may appear in some or all the members of a family through several generations.

The changes in the muscles in the myopathies are the same as those which occur when muscles degenerate from any other cause, namely, a slow and progressive atrophy of the contractile elements, with a concurrent increase of fat and fibrous tissue. In the pseudo-hypertrophic form the connective-tissue hyperplasia is excessive in some of the affected muscles and their bulk is increased. In the other forms of the disease, and in those muscles in the pseudo-hypertrophic form which become weak without any increase in size, the overgrowth of connective tissue may balance the loss of bulk due to atrophy of the contractile tissues, and the diseased muscles retain their normal size; or atrophy may proceed faster than hyperplasia, and the muscles waste from the beginning.

1. PSEUDO-HYPERTROPHIC PARALYSIS

Ætiology.—The cause of the disease is unknown. In many instances no antecedent cases can be traced in the family. In others, a family history is obtained, always on the mother's side. Isolated cases occur, but more often several children are attacked in each generation. Boys suffer more frequently than girls in a proportion of about 5 to 1. Sometimes one sex alone suffers, sometimes both. It is rare for all the children to be attacked. The males who escape beget healthy children, whilst the females, who appear to have escaped, may transmit the disease to some of their offspring.

Symptoms.—The symptoms appear in early childhood. The onset is often delayed to the fourth or fifth year, rarely until towards puberty, and very rarely until as late as the twentieth year. In cases of late onset, enlargement of the calves has usually been present for many years. Weakness appears first in the muscles of the pelvic girdle. The child, who usually looks fat and strong, begins to walk late, he falls easily, and rises again with difficulty. He does not romp as other children do. He cannot skip or jump, and he has great difficulty in mounting stairs. At first the muscles may be normal in size, but, as a rule, some show obvious enlargement before the fifth year is reached. The enlargement is most conspicuous in the calves, the buttocks and the infraspinati. The erector spinæ, the quadriceps in whole or part, the deltoid, the supraspinatus and the triceps often show considerable hypertrophy. Occasionally the masseters are enlarged. At the same time other groups of muscles atrophy. This is most severe and most frequent in the latissimus dorsi and in the lower part of the pectoralis major. Later it extends to other muscles, and ultimately to those which were at first hypertrophied. The neck and face are spared. There is no exact correlation between the size of the diseased muscles and their power, but weakness is usually greatest in those which show most atrophy. The defects are greater in the proximal muscles, and diminish distally. The hands often retain good power to the end. This distribution of paralysis gives rise to certain characteristic defects of attitude and movement.

In standing the legs are placed far apart, and the upper part of the trunk is thrown back, so that a plumb-line from the most prominent vertebra falls behind the sacrum. This attitude compensates for the forward tilting of the pelvis, resulting from weakness of the glutei, which normally raise the anterior border of the pelvis by lowering its posterior border. In the sitting posture the lordosis disappears, for now the attachments of the flexors of the hip are approximated, and these muscles no longer lower the anterior border of the pelvis. On lying down the lordosis appears again, but can be abolished by relaxing the flexors of the hip-joint, that is, by flexing the hips passively. In walking, the feet are widely separated, and to clear the ground with the advancing foot the body is inclined first to one side and then to the other. This "waddling" produces a gait like that seen in congenital dislocation of the hip. The early preponderance of weakness in the extensors of the hip and knee is betrayed by the great difficulty experienced in mounting stairs.

The manner in which the child rises from the supine to the erect position is almost pathognomonic of the disease. He first tries to sit up, but fails. He then rolls over on his belly, and raises himself first on his knees and elbows, and then on his hands and feet. Next he places his hands on his

knees, and as it is impossible for him to raise the trunk actively owing to weakness of the extensors of the hip, he literally climbs up his thighs, pushing the trunk passively almost to the erect position. The remaining power in the extensors may be enough to enable him to complete the movement. If not, he jerks the shoulders back suddenly and gains the erect posture by a writhing movement, whose details are difficult to follow. To climb the thighs successfully a certain amount of power is necessary to hold the knees slightly flexed. When this power is lost he is no longer able to rise. The arms are also used to assist the weak legs in sitting down and in getting up from a chair.

As time goes on the weakness increases, and invades all the muscles of the trunk and limbs. Some of the muscles become shortened, and distortions are produced by permanent alterations in the position of the joints. The knees and elbows become flexed, the feet take up the attitude of talipes equinus, the spine becomes curved, and the whole body is grossly deformed.

The deep reflexes and the electrical excitability of the muscles diminish gradually as the wasting increases. Sensation is unaffected. The sphincters are not involved. The mental condition shows no abnormality.

Diagnosis.—The diagnosis is usually simple if a few of the outstanding features of the disease are known. The defects of attitude and movement, especially the mode of rising from the supine position, together with the characteristic association of enlargement of the infraspinati and calves with atrophy of the latissimus dorsi, form an unmistakable combination.

Prognosis.—This is most grave. Few patients reach adult life, and most die within 10 years of the onset of the disease.

Treatment.—Drugs have no beneficial influence. Massage and passive movement are useful in the prevention of contractures, and the efficiency of the muscles may be prolonged by suitable exercises. Walking should be practised daily, until it becomes impossible. Very often this is lost owing to contractions of the calf muscles, and is regained after tenotomy.

2. OTHER TYPES OF MUSCULAR DYSTROPHY

Ætiology.—The separation of the remaining types of myopathy from the pseudo-hypertrophic form is not an absolute one, as isolated cases are occasionally met with which seem to form a connecting link between the several varieties. The varieties, however, are habitually separate in occurrence, and in families in which numerous cases conforming to the types to be described hereunder have occurred throughout several generations, no cases presented the peculiar features of the pseudo-hypertrophic form. Moreover, the sex incidence as well as the period of onset is different in the two varieties, and it is possible that there is some essential pathological difference between them, and that they are separate diseases. With regard to the types of myopathy unassociated with pseudo-hypertrophy, no doubt exists as to their fundamental unity. They are merely varieties of one disease.

The influence of heredity is much more prominent than in the pseudo-hypertrophic form. Isolated cases occur, but they are rare. In most instances several members of a family are affected in the same and in succeeding generations.

The sexes suffer equally. The time of onset varies within wide limits—

from infancy to old age. When the wasting begins in the face (*facio-scapulo-humeral type*) the disease frequently begins in childhood; but sometimes it begins there late in life. In the cases where it is first noticed in the muscles of the shoulder and pelvic girdle the onset is most frequent between the ages of 15 and 35 (*Erb's juvenile type*); but here, again, it may begin in childhood or early old age, and the term juvenile is hardly applicable to it. The same variations in the age of onset are noticeable in cases where the atrophy begins in the forearms and legs (*distal type*).

The various types may be exemplified in members of the same family, and in the same family the age of onset may show extreme variation.

The cause of the disease is quite unknown.

Symptoms.—In the so-called juvenile form weakness and wasting come on simultaneously. In most cases they are first noticed in the arms; but in some families the legs suffer first. Of the arm muscles the biceps, triceps, and supinator longus are most often first affected. The lower part of the pectoralis major, the latissimus dorsi, trapezius and rhomboids are attacked in most cases. Atrophy of the serratus magnus is common; but it may escape even in severe cases. The deltoid, supraspinatus, infraspinatus and subscapularis usually escape. Atrophy of the forearm and hand muscles is rare.

In the legs, the flexors of the hip, the extensors of the knee and the glutei are most frequently affected. The muscles below the knee often escape entirely.

In the face the zygomatic muscles and the orbicularis are attacked. The face is dull and expressionless, the naso-labial fold is obliterated, the lips are habitually separated and the lower lip projects—myopathic facies. The face does not light up in conversation, in blinking the eyes are incompletely closed, and the articulation of labial consonants is defective. In smiling the mouth forms a straight line, instead of its angles being drawn upwards and outwards by the zygomatici. The power of whistling is lost. When the patient closes his eyes, or compresses his lips as forcibly as he can, they can be forced open with great ease. The buccinators are often affected, the tongue and the masticatory muscles never. The spinal muscles often atrophy, and in a few cases the abdominal muscles have been involved. The excitability of the muscles to faradic and galvanic stimulation usually diminishes in proportion to the wasting. The muscles never show fibrillary tremors. Sensibility is unaffected, and all the other functions of the nervous system are normal. Deformities are neither so common nor so severe as in the pseudo-hypertrophic form.

Diagnosis.—When a family history of atrophy is obtained, myotonia atrophica and peroneal muscular atrophy must be excluded. Myotonia atrophica is distinguished by the peculiar prolonged response of some of the muscles to voluntary, electrical and mechanical stimulation, and by the distribution of the wasting. Atrophy of the sternomastoids, which is constant and severe in myotonia atrophica, is never seen in the forms of myopathy now under consideration. In peroneal muscular atrophy the combination of atrophy in the lower limbs and small muscles of the hands, together with sensory disturbances in the lower limbs, is distinctive. In an early case, when the hand muscles are still normal and sensory changes are absent, the differentiation from myopathy may be impossible for a time.

In isolated cases myopathy is suggested by the appearance of muscular atrophy in childhood or youth. The diagnosis of myopathy is based on the distribution of the wasting in the absence of any sign of disease of the nervous system.

Prognosis.—The disease shows wide variations in its course and duration. The atrophy may remain confined to the group of muscles in which it begins, or extension may take place after an interval of several years. It rarely extends beyond the muscles mentioned above. In most cases, even in those that begin in childhood, progress is extremely slow, and as no symptom of the disease is necessarily fatal, death usually results from other maladies unconnected with the disease.

Treatment.—Owing to the variable course of the disease, it is impossible to estimate the value of any treatment that may be employed. Massage, and especially voluntary exercises designed to bring the weakened muscles into play, seem sometimes to retard the progress of the disease.

AMYOTONIA CONGENITA

Synonyms.—Oppenheim's Disease; Myatonia Congenita.

Definition.—A malady of early childhood, usually congenital and sometimes familial, characterised by extreme flaccidity, smallness and weakness of the muscles, which are not actually paralysed, by lowering of the faradic excitability of the muscles, by loss of the tendon jerks, and by contractures in the region affected.

Ætiology.—In most cases the disease is present at the time of birth; in a few cases it has appeared during the first year of life in an apparently healthy child, and sometimes following an acute illness, such as bronchitis or diarrhœa. Usually sporadic, it has occurred in several children of the same parents.

Pathology.—The chief morbid changes are found in the muscles. In these very conspicuous pathological conditions are present, closely resembling those found in the myopathies. The three most striking conditions are—(1) the minute size of the majority of the muscle fibres, from 7μ to 12μ; (2) the presence of a few very large or "giant" fibres reaching 140μ in diameter, and larger than any fibre occurring in normal muscle; (3) marked regressive changes are seen in the giant fibres. There is increase of the connective tissue between the muscle bundles and a notable determination of fat. Reduction in numbers of the ventral horn cells of the spinal cord occurs, and the ventral roots are small and poorly myelinated.

Symptoms.—The extreme flaccidity of the affected muscles is noticed from the time of birth. They are small and weak, and though there is no muscular wasting and no absolute paralysis, yet in many cases the limbs cannot be raised against the action of gravity, nor can the head be held up. The great relaxation of the muscles and ligaments allows of the most fantastic attitudes being assumed without pain. When the child gets older, he is unable to sit up, but when placed in the sitting position the spine bunches up from absence of any muscular support, and he is unable to support his weight upon the weak legs. The amyotonia is symmetrical, and affects the legs always, the trunk often, the arms not infrequently, but never the face.

Notwithstanding the flaccidity, some degree of flexor contracture is usually present. The faradic excitability of the muscles is much lowered, but not lost. Sensibility and the sphincters are not affected. The superficial reflexes are normal, but the deep reflexes are invariably absent in the affected regions. The children are usually intelligent, with good bodily development, and growth proceeds normally.

Diagnosis.—This presents no difficulty on account of the presence of the flaccidity at birth, the absence of the deep reflexes, and the tendency slowly to improve. It has to be separated from those maladies to which it bears a superficial resemblance, namely, the myopathies, rickety weakness, obstetrical, infantile and diphtherial palsies.

Course and Prognosis.—Some of the children succumb during the early and severe stages of the disease, but the tendency of the disease is to improve slowly in the course of years, and in some cases almost complete recovery with return of the knee-jerks occurs.

Treatment.—This consists in aiding the natural tendency to improve with massage, passive movements and exercises, in treating contractures with tenotomy, and in attending to the general health and nutrition.

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SECTION XXI

PSYCHOLOGICAL MEDICINE

INTRODUCTION

PSYCHIATRY is concerned with forms of illness as widespread and diverse as those of somatic medicine. There are almost as many beds in mental hospitals as in all other hospitals put together; and there is an undoubtedly large, if unnumbered, part of the population who have mild mental disorder not needing mental hospital care: hysteria, obsessional neurosis, hypochondria, chronic depression, paranoid states, and so forth. The diversity of this widespread group of illnesses depends on their being disorders of mind—disorders, that is, of the human function which comprehends and sums up all other functions of the organism, serves to relate a human being to his complex environment, and is the chief token that he is an individual, and not a sample. Mental disorders are therefore varied, as are the people who suffer from them. It is only by ignoring most of what is individual in these illnesses that a few common types or categories can be recognised, comparable to the "diseases" of somatic medicine. Such a procedure is necessary for practical ends; material must be classified. Moreover, a biological foundation may be assumed for the syndromes with which psychiatry works. They stand for the main ways in which a human being can become mentally unhealthy. There are only a few such ways, and they are determined by the structural and functional patterns inherent in the organism. Diversity arises through their becoming manifest under the influence of each individual's special environment and in combination with his other inherited tendencies. Diversity, therefore, can be due to a combination of single hereditary causes and to the effect of each individual's environment throughout his life upon his development and behaviour. There is always interplay between inheritance and environment. Part of the psychiatrist's business is to discover how this interplay has led to the present illness. The interplay, moreover, is sufficiently varied in the course of each patient's life to make prognosis and the effect of treatment a matter of individual study, rather than of summary inference from the diagnosis, once made.

Treatment is only another special instance of the environment acting on the patient; its power and limitations for him must be studied by seeing what effects this or that experience has had on his previous life. Consequently the psychiatrist, even more than the general physician, must study illness in two ways: first, as showing some typical pattern of morbid behaviour, and tending to run along well-known lines; and secondly, as a patch of personal biography, something to be understood, rather than classified in terms of psychology and biology. The two methods are complementary,

though, in a brief text-book presentation, the former must be the more prominent.

There is no dividing line between somatic medicine and psychiatry. Psychiatry, although it has to work in part with social and psychological conceptions of which general medicine has felt little need, suffers greatly when it limits itself to this way of regarding mental phenomena. It cannot safely ignore the relationship between bodily happenings and the patient's state of mind. Crude instances of this relationship are the delirium that accompanies an acute fever and the irritable fatigue (neurasthenia) that may follow it; the insanity that is due to cerebral tumour or general paralysis of the insane; the obsessional neurosis that follows encephalitis lethargica; and the hysterical symptoms of disseminated sclerosis. There is no mental disorder, mild or severe, in the causation of which bodily disease may not play an important part. Moreover, it is not only in crude instances of structural or chemical disease that the relationship between bodily and mental illness may be recognised. A human being does not exist as a rarefied mind united with a solid body; he is an organism all of whose subsidiary functions contribute to this highest function—his mind—which brings him not only consciousness, but also an integrated behaviour in relation to his surroundings. Disturbances, transient or permanent, of these part-functions (for example, in the sensory apparatus or the circulatory system) will have some effect on his state of mind. Changes in the central nervous system are the most obvious instance of this, but the endocrine glands, the autonomic nervous system, and the metabolic processes are often of notable significance in the various maladjustments summed up as mental disorder. A human being is constantly responding to, and influencing, his surroundings; but his doing so is conditioned by the various parts of his body and the way they are working.

Before the categories and clinical features of mental illness are described, the principles of psychopathology, prognosis, and treatment call for some very brief consideration, since without them psychological medicine written down is a repellent catalogue of details. Though the principles set forth may seem trite or too obvious to be worth stating, it is unfortunately the case that they are seldom applied as fully as they might be to the clinical study and treatment of mental disorders.

Psychopathology.—Intrinsic Causes.—The intrinsic causes of mental disorder are those which depend on heredity and on normal phases of development, *e.g.* puberty or the climacteric. Extrinsic causes, which come from the environment, are either mental experiences or physical damage. The distinction between intrinsic and environmental, like that between physical and mental, is convenient but artificial; a long sequence of related happenings both within and without the patient's body goes to the causation of any mental illness. It is, of course, possible in many instances to discover some indispensable link in this chain of causes—an intoxication with alcohol, for example, a syphilitic infection of the brain, an inherited predisposition to periodic insanity, a bereavement—which may legitimately be singled out as the chief cause and classified as intrinsic or extrinsic, but this is more valuable for formal and didactic purposes than clinically. Actual cases usually show a complicated ætiology. Thus, a man whose parents had both been subject to melancholia became himself profoundly depressed after the death of

his wife, and attempted suicide by drowning. He survived, but during the resulting pneumonia he was delirious and threw himself from an upper window, crying out that he must go to his wife. The causes of the mental disturbance in this case were many and obvious; numerous they always are, but not always obvious. One cause may, of course, be prepotent.

The more detailed the analysis of a patient's endowment and experiences, the more entangled physical and psychological, internal and external factors seem to be.

Heredity and constitution.—The hereditary factor is not a general neuropathic taint; there are specific predispositions to one or other anomaly. These predispositions are transmitted in accordance with familiar genetic principles, summed up in the modern gene-theory of inheritance. Studies of families and of twins have proved the importance of the hereditary factor in the major non-organic psychoses, though they have not yet sufficed to reveal the number of genes concerned in the transmission of the hereditary types of morbid reaction.

Among the main reasons for this incompleteness in our knowledge is the impossibility of concluding that an inherited trait is not present, merely because it is not manifest in some recognisable form. Other inherited factors and, most of all, the environment, will in many cases determine whether an individual predisposition is to become evident or not. Thus a man may have an inherited tendency to melancholia which remains latent until a financial reverse or disease of the cerebral arteries provides the conditions necessary for its manifestation. It is true that some inherited predispositions, *e.g.* to Huntington's chorea, are almost independent of the environment in this respect, but such are exceptional.

Since the Mendelian and other conceptions of modern genetics are held to obtain for the heredity of mental disorders, it can be understood that more than one type of proneness to mental disorder can be inherited by the same person. He may, for example, be prone not only to periodic insanity, but also to schizophrenia. Mingled proclivities of this kind account for anomalous clinical pictures, frequently met with and difficult to classify as either one syndrome or another. The "either-or" kind of diagnosis is often out of place or misleading in psychiatry because of the commonness with which more than one constitutionally rooted type of illness may be found in the same patient. Syndromes are frequently combined; to grasp their clinical meaning it may be indispensable that one investigate the patient's family not only as to mental disorder, but as to normal characteristics too.

The signs of a transmissible tendency to some mental disorder may not be actual illness, but only a special kind of personality. There are certain varieties of personality which show some or all of the essential features that characterize certain types of mental illness; the differences between personality and illness seem then to be of degree rather than of kind. Moreover, those who manifest one or other type of illness are often found to have had the type of personality that is functionally similar to it. So close may the similarity be that it is difficult to decide when the illness has begun, because there was no sharp dividing line, in time or in form, between the more or less normal previous personality and the actual disorder. This frequency of association and similarity of form

between the normal state and the illness points to the constitutional background of mental illness, and shows how hereditary tendencies can express themselves in more or less normal ways in personality before the catastrophe of an obvious illness has directed attention to them. Nor is it only in the personality that inherent proclivities may be revealed; certain types of bodily structure, too, occur much more frequently in those with a particular mental constitution or mental illness than in the rest of the population. The most striking instance of this is the frequency with which a "pyknic" bodily habit and a "syntonic" personality are found among those who have periodic attacks of mania or melancholia (see p. 1855). Such constitutional features, whether mental or physical, indicate that inherited tendencies can body themselves forth in normal physical and psychological structure before morbid exaggerations of them make an appearance. The varieties are sometimes called by appropriate names, *e.g.* schizoid, cyclothymic, syntonic, obsessional, hysterical, paranoid. The relationship is not a simple one. There are very many people with these types of personality who never fall mentally ill.

A pronounced personality, belonging to one or other of these types, does not indicate that the person who exhibits it is likely to have a mental illness, but only that if he should have a mental illness, it will probably be of the corresponding type. As with all inherited anomalies of which the crude manifestation is delayed until adult life, there may be for many years none or only mitigated signs of the proclivity; these may be indistinguishable from what occurs in normal people. The more pronounced the anomaly of personality, the more likely that it portends a mental illness, or, at any rate, a proclivity to the mental illness in specially adverse circumstances.

In the foregoing, personality and constitution have been spoken of as though they were static, innate attributes of the human organism. Neither of these epithets, however, is appropriate, not even in respect of bodily constitution. Responsiveness and plasticity are essential to human development of every kind; there is a constant interplay of personality with the outer world, modification of it and by it. The main pattern of development is doubtless determined by innate, inherited factors—bodily structures grow, instincts come into play, and the general direction of functional activity is predetermined. But general directions and main patterns mean little unless they are given body and content by individual experience. Nutrition, for example, can deflect the body from its ordained pattern or enable its fulfilment; all sorts of physical interference can maim it or improve it: the same is profoundly, if obviously, true of the mental side of human growth and maturity. Consequently, each patient's personality is not only to be assessed as conforming to a frozen artificial type, but as a complex of dynamic functions, changing in outward form, sometimes in unstable equilibrium, and none the less powerful for being subterranean. Here, as was said earlier of psychiatry in general, there must be two ways of viewing the data: in classes, and as individual living biographies to be understood rather than schematised. Both methods are necessary to any complete psychopathology.

Phases of development.—A concrete instance of the foregoing is the change that occurs at certain turning-points, such as puberty, pregnancy, or the climacteric. Endocrine and other physical changes at these epochs are

accompanied by psychological disturbances, the severity and form of which may bring them under the notice of the psychiatrist. They are dramatic episodes in a lifelong and universal process of growth, maturity, and involution or decay, which is marked by plasticity and development of varied functions in the first stage, stability and differentiated adaptation in the second, emotional lability and suspicion, intellectual narrowing of interests, rigidity, failing grasp and memory, in the last. The mental disturbances which may occur at different ages are much influenced by these intrinsic factors and tendencies.

Extrinsic Causes.—The outer world impinges on human beings from the day of their birth, or even their conception, in more and more complicated ways, as they themselves become more complicated. In other words, the environment is, for the individual, as complicated as he can make it; and that will depend on how far he has himself developed hitherto. Human beings deal selectively, not merely passively, with experience. At each stage of their growth, previous experience helps to determine what they will select from their environment, and how they will use this and integrate it, to serve in its turn as the partial determinant of further growth and integration (the other determinants being innate ones). "Experience" is here being used in the widest sense to denote the response of a human being to the impact of the outer world upon him, whether it be consciously recognised as such or not at the time.

It is, therefore, impossible to give adequate consideration to any aspect, including the psychological, of a human being's way of dealing with the outer world unless one pays regard to his previous experience, mental and physical, and to the present state of his whole organism, mental and physical. The cultural milieu in which he has grown up must be taken into account. Too partial a regard for subsidiary functions, whether physiological or psychological, may lead one away from the living human being, who is an integrated organism, not a collection of disparate mental and physical systems; similarly, too concentrated a gaze on this latter aspect, *i.e.* on the socially organised person, to the neglect of part-functions, may make one see only a disembodied spirit, as remote from medicine as from daily life.

Physical experiences.—Some external happenings influence the mental state chiefly by way of the body: infection, physical trauma, intoxication, and metabolic and endocrine disturbances due, wholly or in part, to environmental influences may result in mental disorder. In many of these instances, the mental change is mediated by way of some cerebral damage, and the clinical picture is of the organic neurogenic kind, *e.g.* dementia. It would be wrong to attribute the whole of the mental disorder to the cerebral damage; but to it is referable the core of the psychosis. Some diseases have an incidence on special functions and parts of the central nervous system, which determines characteristic features in the mental picture, *e.g.* the anxious fidgetiness of the patient who has had chorea, the stiff mind and obsessional thoughts and movements of the post-encephalitic, the hysterical phenomena of the elderly arterio-sclerotic patient or the man poisoned with carbon monoxide, the aphasia and apraxia of the post-apoplectic, the silly "moria" of the cerebral tumour. In the main, however, it is not possible to correlate mental symptoms with special areas or kinds of cerebral damage—partly because the brain is not the only structure concerned, partly because it acts as a whole,

and also because the presumptive changes in it are too evanescent and delicate to be accessible to our crude methods of examination.

To limit oneself to the brain in studying the somatic correlates or basis of mental phenomena would be an error. In the physical accompaniments of emotion, the whole body participates through the mediation of the vegetative nervous system and the endocrine glands. This is significant, because emotional upset is one of the most important phenomena of mental disorder. The sequence of psycho-physical happenings of which an emotional upset is the climax and the outward sign, may be started not only by some mental happening, but also by physical experiences—intoxication with a drug, or a circulatory disturbance, or a metabolic upheaval such as acute hypoglycæmia. Whether, for example, this hypoglycæmia comes from outside, as an injection of insulin, or arises (as it rarely may) from within the body, as a "spontaneous" deficiency, is of little consequence in its bearing on the mental disturbance engendered. The chief emphasis lies on the physical apparatus through which so widespread an affection of the whole organism can be evoked, just as in other circumstances the emphasis would lie on the psychical apparatus which serves the same end. This applies more widely than to emotional disturbances alone. Where a symptom is, on the face of it, definitely physical or definitely mental, its causation may not be inferred to be exclusively of the same order; the chief cause of, say, an anorexia may be a series of mental experiences or an attack of migraine or a uræmia or a pituitary disease. Study of the anorexia alone cannot serve to discriminate them; not even study of the psychological state alone, or of the physical state alone may suffice. Very often the physical and psychological factors in causation are mingled almost inextricably—they represent, in fact, different facets of the same series of phenomena.

Mental experiences.—Mental growth is dependent on daily experience for its material. Experience can be subdivided into perceptual, emotional, and other kinds, but such a division is fictitious. The means by which daily experience is incorporated with our mental equipment and acquires an influence over our subsequent behaviour in all respects can only be understood if we avoid thinking of emotions, instincts, perceptions and other abstractions as real entities, as distinct and separately operative forces. Memory, for example, is not merely an intellectual function by which we recall a happening into consciousness in more or less verbal terms, but a device, or function, by which past happenings are able to influence subsequent behaviour; the ways in which they do so, and the form in which the earlier experience is reproduced into consciousness, will be greatly influenced by its original emotional, as well as more purely perceptual, aspects, and by other physical and mental experiences—a distressing repetition of the experience, for example, or a physical happening like concussion or cortical atrophy.

There are general tendencies in mental life—instinctual tendencies—which bring us into relation with our immediate surroundings, direct us to feed ourselves, maintain our lives, reproduce, and aim at other ends, which are variously formulated by philosophers, saints and psychologists. These biological forces, however denominated or classified, are not peculiar to human beings, but in respect of human beings are so much more accessible to minute inquiry along verbal lines, that an unduly complex conceptual system has been built up to describe them. Comparative, behaviouristic and experimental

psychology have partly corrected unreal refinements of a verbal kind, as also can physiology and a truly medical psychology. Metaphysical subtleties and speculations, *e.g.* psycho-analytical ones, cannot meet medical needs, nor enable one to understand the human being as a whole organism in the way that the doctor must. The influence of previous experience on all subsequent behaviour is as evident in physiological happenings as in the mental field; the special language and formulations and hypotheses of psychology are not to be taken as wholly and permanently separate from those suitable to less highly integrated functions, though something must be conceded to the special complexity of psychological phenomena. Such terms as projection, sublimation, conversion, symbolism, identification, repression, amnesia, perseveration, displacement of affect, cover special instances of the general relationship between inherent tendencies of the organism and their material substrate, and the influence of past on present experience and behaviour.

In dealing with the multifarious world about him, a human being is constantly obliged to select what he will perceive, and in what form he will perceive it; pure " objective " perception never occurs. To perceive things at all, he must give them meaning by relating them to himself and to his previous experience. Unless he can do this, not necesarily consciously, he is at the mercy of his environment, as a new-born baby is. Perception is therefore an active process; it has instinctual and emotional, as well as cognitive aspects. It depends partly upon memory for being able to give meaning to what it perceives; such memory need not be conscious. Consciousness, it is well to bear in mind, is only an attribute of psychological happenings, not their essence or their criterion; mental life goes on with varying degrees of consciousness attaching to it. There is no sharp division between conscious and unconscious mental life: no region called " the Unconscious " with its own rules and contents. Many of the psychological happenings most significant for psychiatry go on without clear consciousness of them, but in appropriate conditions they may be accompanied by much more, or by full, consciousness. Biologically and psychologically regarded, consciousness is an attribute, like memory or movement, immensely important for us human beings, but not a " present-or-absent " factor decisive for our mode of mental conduct.

Perception being thus an active process, which makes use of past experience, it not only selects its material and invests it with meaning, but in doing so may distort it, and give it a special " false " meaning. Unwelcome emotions may be thus projected on to external objects or happenings, which are then regarded as hostile or contemptuous, or in some other way significantly related to oneself. This is not remote from the process in visual perception, whereby one projects the image on one's retina into the external world, and is convinced of its reality there; the further process of clothing it with emotional significance depends on one's inherent tendencies and one's previous experiences. Paranoid symptoms, ideas of reference, grandiose and self-reproachful delusions exemplify this. Hallucinations and kindred phenomena are a special instance of the interplay between material substrate (*e.g.* in cocaine poisoning), inherent tendencies (*e.g.* visual fantasies of children), and past experience (*e.g.* hallucinations of homosexual abuse or divine commands). Similarly, by fantasy and imagination the outer world can be manipulated or denied according to the heart's desire, just as by body-images

of proposed movement the way is prepared for purposive muscular action. In giving meaning to present things, personal connections between them and earlier experiences are established; whether normal or morbid, this ascription of "symbolic" meaning to every-day objects is indispensable to thought, and is most striking in our use of spoken or written language, where sounds and shapes are conventional symbols for the most diverse experiences. Some of our words are personal to ourselves, and are used in an individual way; in morbidly heightened form, this process may issue in schizophrenic neologisms, or oddities of expression. Similarly an obsessional patient may feel towards some word or object a superficially incomprehensible mixture of attraction and repulsion, which is due to this word or object being the symbol of some earlier experiences that have been of great moment in his life. To see how it has come to be such a symbol calls for minute study of his earlier experiences. Physical happenings in one's own body may symbolise present emotions or earlier experience of a momentous and emotionally painful kind. A gesture of disgust may normally be evoked unconsciously by a banal happening, which has somehow become emotionally coloured by past experience. A headache may embody our dissatisfaction with a present situation. So hysterical "conversion" symptoms may reflect and symbolise an inner emotional struggle, as may also some obsessional movement, schizophrenic stereotypy or hypochondriacal fear. The body, with all its functions, is the background of psychic life, and resonates to it.

What experiences will be important in determining the form of mental symptoms, depends much on the emotional disturbance they originally provoke, and this, in turn, on the instinctual drives which they touch on and disturb. Instincts may conflict, and the emotion accompanying the conflict prove so disturbing that it cannot be borne in its naked form; "repression" serves the end of making this more or less tolerable, through disguising or distributing it. So emotion may be shifted from one object to another, and paradoxical or unexpected emotions be thus aroused by objects on to which the affect has been displaced. Or energy mainly directed to plain ends, *e.g.* sexual love, may be diverted into less obvious channels, and when thus "sublimated" and mingled with features derived from other instinctual sources, its origins may be hard to recognise. Sexual instincts so often conflict with others that many of the most powerful motives for the production of mental symptoms come from the struggle.

To describe the whole of instinctual life, however, in terms of sex and aggression, as is sometimes done, is only possible if one strains the meaning of these words out of all knowledge. It is as unwise to make the sexual paramount in explaining psychogenesis as to burke it.

The patient's present symptoms, it is clear, must be examined in the light of his earlier experience. Thus one elucidates in detail the content of his illness and some of the causes of its occurrence. In doing so it is not necessary to push back one's inquiries to a supposedly crucial stage of early childhood. The experiences of the first two or three years of life are, like all subsequent experience, contributory to mental development, and they show certain sequences of phenomena characteristic of such development. Moreover, their relative simplicity makes it possible to recognise in these early reactions the instinctual drives, or (more correctly) the "inherited functions" which become manifest when the environment supplies the

necessary material, though, of course, it cannot supply the necessary energy and direction; these last must come from within. On the other hand, the functions recognisable in the relatively simple reactions of early childhood are not the same as those which may be seen in later years when the organism is more fully grown, any more than an infant's physical structure and functions are identical with those of the more differentiated adult. The obvious continuity of the actual happenings in a human being's lifetime does not justify one in trying to analyse and reduce all adult mental phenomena into terms of supposed child psychology, nor does clinical practice usually require it.

The effect of war upon the incidence of mental illness has obvious importance. The psychiatric disorders which occur in war do not differ in kind from those of more normal times, but certain forms of disorder, especially panic, psychogenic stupor and gross hysteria in men, become commoner and sometimes more severe. People are exposed to unaccustomed dangers; their privations are both material and emotional; they have to surrender some of their independence and individuality; and they are thrown together in groups and therefore prone to share in group-feelings and group-behaviour. It is doubtful whether the losses, fears and psychological infections of war directly lead to an increase in certifiable mental illness, though such exogenous factors as syphilis, alcoholism and malnutrition may do so, under the conditions of thoroughgoing modern war. It is, however, neurotic disorders that are most prominent then.

Course and Prognosis.—The making of a correct diagnosis may in psychiatry indicate the general drift of an illness — towards recovery, chronicity, progression, or relapse—but is of even less use than in the rest of medicine for showing how far this will apply to a particular patient. For this, careful study of the individual history and illness are indispensable. The prognosis can be inferred from the ætiological factors, the mode of development, and the form of the disorder.

Where a known external cause has been at work, its point of attack, its severity and persistence will affect the issue. This applies equally to such "organic causes" as poisons and cerebral diseases and to "mental causes," like economic misery or frustrated love. The physician must consider how long the environmental cause has been acting, what changes it is known to produce—whether in the way of cell-degeneration or habitual gloom, fibrosis or fantasy—and whether it is likely to persist. He must also ask if the patient's previous history has shown that he is specially sensitive to such a trauma. This brings in the intrinsic ætiological factors. How has the patient previously reacted to this sort of interference or to any disturbing circumstances? Has he fallen more and more into unsatisfactory habits in meeting his daily life and its difficulties? How has his whole character developed? Is there good evidence of his being able to cope with partial deviations from mental health? Has he inherited tendencies to benign or to progressive illness? Which seem to be the most useful reparative or stabilising features in his personality? How far are his struggles with the world an outcome of his intrinsic endowment, evident in various guises since his childhood, how far have they been forced upon him by an adverse milieu? How old is he? There is more chance, if he is young, of his being adaptable, so that the removal of various stresses

may help him, and his instinctual energies be diverted into less morbid channels; as he grows older, he may gain in stability, but gradually become more disposed to fear and suspicion, bodily preoccupations, and fixed attitudes of mind.

An abrupt onset is favourable, other things being equal. A gradual, especially an insidious, onset may indicate a rooted abnormality that will be hard to shift. The longer an illness has gone on, the more will it have become autonomous, *i.e.* independent of its immediate causes of occurrence, and prone to become a gross or text-book example of some chronic anomaly. A study of the ups and downs in the course of an illness may show favourable influences that can with profit be deliberately brought to bear on it, as well as harmful ones that must be avoided. The more reconciled the patient has become to his illness the less satisfactory the outcome.

As to the form of the illness and its prognostic value, there is much empirical knowledge at our disposal. Thus, a predominantly affective attack will very likely clear up, but may recur; a schizophrenic syndrome is in the long run usually ominous; hypochondria and depersonalisation, especially in young people, tend to last a long time, even years; sexual perversities can seldom be got rid of; hysterical symptoms can easily be changed, but hysterical reactions are persistent; obsessional attacks are either periodic or very chronic; melancholia is often a fatal disease, through suicide or refusal to eat; delirium tremens commonly ends by crisis or lysis after about seven days; untreated general paralysis of the insane goes downhill towards dementia and death, with partial remissions on the way: and so forth. There is a wealth of such special prognostic knowledge, based on clinical observation and statistics.

Obviously prognosis must always take account of treatment. Will treatment be efficacious? Will it be practicable? It is absurd to forecast how general paralysis will turn out if one does not know whether one will be giving artificial fever and tryparsamide, or how hysteria will turn out before one has decided whether psychological and social treatment will be possible. In every mental illness this is one of the essential points to be weighed in prognosis: what will be the conditions, beneficial, neutral and adverse, under which the patient is going to live henceforth; and, in particular, what will be those specially devised conditions of every kind, social, psychological and physical, which can be regarded as likely to have therapeutic effect?

Treatment.—PROPHYLACTIC.—Much can be accomplished by social measures; also by individual care, though that is less certain. A striking instance of social influence in preventing mental disorder may be seen in alcoholic psychoses, which have been cut down in this country to a third of what they were before the War of 1914–1918. Morphine and cocaine addiction and lead encephalopathy are now rare, typhoid delirium is exceptional, and typhus unknown. It is the organic mental disorders that have been more accessible to these preventive methods so far, because they have one indispensable cause that can be controlled. The "functional" disorders are partly dependent, it is true, on social factors, such as economic security, lack of employment, imposed moral, cultural and educational standards, competition and ill-judged interference. But the remedy for these is to seek, and their total removal is utopian. There is, nevertheless, much

room for prevention here. A preventable social cause may be well seen in " compensation neurosis " where the administration of a humane statute involving lawyers, insurance companies, doctors, employers and employees often has the inhumane effect of evoking hysterical symptoms, anxiety and a depressive or paranoid invalidism in the injured man.

Individual preventive measures cover both the intrinsic and the extrinsic causes. Eugenic precautions, such as birth-control or voluntary sterilisation (if legalised), may under skilled guidance prevent some mentally unstable persons from being born to parents who, having had mental illness themselves, do not wish to propagate it. If physical factors, *e.g.* diabetes, be prominent in causation, it may be possible to prevent this mental illness, or at any rate to scotch it in its early beginnings, by dealing with the somatic disorder. Thus, there are far fewer cases of syphilitic psychoses now that syphilis is less often contracted and earlier treated. The psychological reactions to a physical disease or blemish may be favourably modified or averted, when foreseen. It is for obvious reasons impossible to counteract mental disorder by regularly protecting the patient from physical or psychic trauma : a life that is guarded against risks and painful experiences is almost certain to issue in mental ill-health, out of its very emptiness. By altering a patient's environment and way of living one may, however, be able to avert an impending illness : only study of the individual patient can show how this end may be achieved.

The difficulties in the way of making the patient's environment easier for him are immensely greater during war, and it may be inadvisable to attempt any such change. Social needs have to come before individual ones in so many instances during war that the measures which would appear most favourable to the patient's mental health are often quite impracticable. Much, however, can be done by careful selection to lessen maladaptation among soldiers and other large groups. The mental hygiene of war is a complicated problem which cannot be divorced from the political and economic issues, as well as the military ones.

How far the treatment of behaviour disorders and neurotic traits in childhood can be trusted to avert outbreaks of definite mental illness in later life is a disputable matter, but it is certain that by taking advantage of his plasticity and responsiveness, a bent can often be given to the energies of the maladjusted child, which will result in his being socially better adapted and better able to deal with his problems. The more persistent the beneficial influences one can bring to bear on development at this impressionable age, the more valuable the prophylactic effort.

Measures of mental hygiene that may be recommended to the community as a whole are still of a negative kind : what to avoid rather than what to do. This applies most obviously in the field of sexual practice and belief where needless fears and harmful education are rife, as with regard to the masturbation of adolescence—a normal and comparatively harmless phase of sexual development.

Treatment of the Actual Illness.—This is almost as varied as æetiology and symptomatology. To use only one method of treatment, however simple or complicated its theory, is to fight illness with one hand behind one's back. There is no valid distinction between palliative and curative therapy : the distinction should be between more efficacious and

less efficacious.

with those mental disorders which are closely related in time and form of occurrence to some indispensable cause, *e.g.* a toxic delirium, a reactive depression or anxiety, an interstitial syphilis of the brain. But these are rare conditions if one considers the whole of mental illness. The treatment of general paralysis by fever is not causal, its theory is dubious, its basis quite empirical; yet its success is such that it is the most important therapeutic advance in psychiatry for a hundred years. One cannot despise any measure that promotes the recovery or well-being of the patient: the giving of drugs, the prevention of suicide, occupational therapy, analysis of motives, removal into favourable surroundings, hypnosis, re-education and other means of helping the patient are not to be graded in a hierarchy with an arbitrary scale of values, in which recovery is called spontaneous unless psychotherapy or a novel chemical treatment has been employed.

Sometimes a patient's condition demands energetic intervention; sometimes it demands restrained symptomatic treatment; sometimes social adjustment is called for; sometimes endocrine injections. Whether the accent in treatment shall fall on the physical or the psychological or the social side will often be less important than care that all the available resources are used. It should not be regarded as a matter of course that a diagnosis should connote a method of treatment: *e.g.* that psychoanalysis is the only thorough treatment for obsessions, while for mania continuous narcosis is the "proper" method. Nor, to mention another common error, should it be lightly assumed that a heavily tainted family history or other evidence of a strong constitutional factor indicates that treatment is out of the question, a superfluous struggle against fate.

Treatment may be considered as social, psychological and physical. For some types of illness obviously much more stress will fall on one than on another of these, *e.g.* in hysteria, general paralysis of the insane, epilepsy.

Social and occupational treatment.—The first task in social treatment is to decide where the patient is to be looked after. Is he fit to be at home, should he be in a mental hospital, or in some environment intermediate between these extremes? The decision as to the need of a mental hospital rests in the first instance on the danger the patient presents to others, or the chance of his committing suicide. These two problems of behaviour were at one time almost the only grounds of admission to a mental hospital, but such questions of "certifiability" need no longer preoccupy the psychiatrist, since voluntary treatment has broadened the scope of the mental hospital and modern conditions made it suitable for many patients who would ordinarily be regarded as "neurotic," rather than "mental" "psychotic" or "insane" (*e.g.* early cases of general paralysis masquerading as neurasthenia, or obsessionals who fear their own impulses and want to be protected against themselves). Psychiatric hospitals and clinics dealing only with voluntary cases also bridge the gap between out-patient care and certification.

The social decisions in treatment cover much more than merely the mental hospital issue. If the patient's immediate environment contains many disturbing influences, it will be desirable for him to be away from them temporarily at least, so long as this does not entail worse troubles; summary decisions are here impossible. It may be useless, for example, to get a woman who is

paranoid about her neighbours to move to another district to escape them, unless it is the actual conduct of the neighbours and not the patient's morbid attitude that is provoking her suspicion of them. It requires a close knowledge of the facts as well as wisdom and psychiatric experience to give advice on matters that may wholly alter the course of a patient's life—advice, say, about separating from his wife, giving up his job, or emigrating to the Dominions. Many instances of this might be offered. Neurotic patients are often advised to get married, especially if loneliness and sexual needs trouble them, as though marriage were a panacea; such advice by rule of thumb too often makes their condition worse, ruins the life of the person they marry, and results in offspring that have to be treated at a child guidance clinic. Weary, depressed patients are often harmfully urged to go to dances and lively seaside resorts where they must try to look happy. Hysterical patients do not benefit by being put among people who are hostile and contemptuous, any more than in an atmosphere of mawkish sympathy and compliance.

In the social treatment of patients indispensable help can be given by trained psychiatric social workers. Their assistance is not restricted to the patient's economic problems, though it is most obvious in that field.

Occupational treatment is important for all kinds of mental disorder. Where there is acute overt emotional disturbance, rest is at first desirable, as also for confusional and delirious states. In these conditions opportunity for occupation must be gradually offered to the patient as his disorder subsides; steady, simple work is preferable to the restless unsatisfying fickle activity in which he would often engage, if left to himself. The less acute any mental disturbance, the more necessary is it that occupation should be urged upon the patient, and that it should be disciplined and congenial. This applies equally to gross psychoses and minor affections of the neurotic sort. Allowance must be made for the patient's bent, his symptoms and personality, and especially his more or less conscious reasons for working and not working; hence there will be much diversity in the conditions of his occupation, whether it be therapeutically contrived in a hospital, offered at a Rehabilitation Centre, or sought out as remunerative work in the open market. Mental health cannot be permanently retained unless one does some satisfying work; often it cannot be recovered unless one does. Work is not satisfying, in the long run, if it is done mainly as a diversion, to fill in time.

Psychological treatment.—There is no form of treatment which has not a psychological aspect and result. The term psychological treatment or its synonym "psychotherapy" is, however, conventionally limited to those forms which depend upon direct and personal relationship between the patient and the physician. They have separate names, and are divided into schools and techniques. Stress may be laid upon the prestige of the physician (as in hypnosis), the patient's attachment to him, in all its complicated phases ("transference"), the trained understanding and thoroughness with which he clears up the patient's problems (persuasion, re-education, distributive analysis), or on his qualities of personality—enthusiasm, energy, warmth, candour, wisdom. In so far as psychological treatment is necessarily based on a personal relationship it cannot be made a routine except in its non-essentials: whatever rules the psychiatrist follow or whatever the training he has undergone, he himself will be more important than his method in

benefiting the patient. To that great extent psychotherapy is not a scientific procedure. That is not to say that method and training are of no consequence—far from it—but only that they are devices whereby the influence of one human being upon another's mind and conduct can be turned to the best medical ends, and the dangers inherent in such a relationship minimised.

The more specialised, intricate or esoteric the method, the less suitable is it to be used by any but the most expert. It is not proposed here to detail the many kinds of technique that have been employed. The general rules that must be followed in any psychotherapy are:

1. To regard the removal of symptoms as a good thing, but the maintenance of normal social adaptation as far better. It is bad to get rid of one symptom only to see it replaced by another, but much worse to get rid of all symptoms only to see the patient at the end of treatment a dependent and introspective hypochondriac of the mind, a social invalid.

2. To seek for the psychological cause of the patient's illness only to the extent that the patient's wellbeing demands, which is often far short of what one's own interest and psychological curiosity would demand.

3. To consider carefully whether any shock to the patient, any aggravation one produces in his illness even temporarily, may be a sign of bad treatment. It is on the whole unnecessary to make the patient worse in order to get him better, though many psychotherapists believe the contrary.

4. To be satisfied with the patient's recovery, and not to aim at his promotion to a state of ideal mental health and self-understanding. It is better that treatment should be quick and effective than drawn out to meet theoretical standards.

5. To understand the development of the patient's illness, and to interpret it both to him and to oneself, in terms of real experience and not of hypothetical forces.

6. To treat the patient without allowing one's own emotions to be more concerned in the course and outcome of the treatment than is usual in the treatment of a physical illness.

7. To aim at harmonising the patient's mental life by giving his ill-managed energies fitter material to work at, and release from the burdens laid on them by past experience.

It is impossible to describe in general terms what the psychotherapist does, otherwise than by metaphor or analogy: he promotes the ventilation and desensitisation of emotional disturbances; he elucidates latent or obvious muddles, disentangles conflicting tendencies, giving them new incentives and a different direction; and so guides the patient through the maze of his life's experience, as recalled in memory, that he is afterwards better fitted for dealing with current experience, knows himself better and has somewhat purged himself of past harms. All "analytic" methods review the patient's life as he recalls it under special conditions, *e.g.* of free association, hypnosis, biographical scheme, etc. They stop at different points, some aiming at emotional clearance by abreaction, some at a redirection and liberation of the instinctual bases of character, while others remain content with an educational achievement.

Whether psychotherapy, in the above sense, is to be applied to a case will depend on the following factors: the patient should be willing to co-operate in the treatment; free from such hindering disabilities as, say,

deafness; able to give the necessary time; of at any rate average intelligence; still capable of modification (as he would not be in old age, or with very long-standing and indurated habits of faulty reaction, or with organic cerebral disease); and, finally, endowed with a considerable residue of normal mental functions with which one may work. The more profound his aberrations, as in schizophrenia, or the more extreme his emotional disturbance, as in agitated melancholia, the less is he fit for psychological treatment of this individual and specialised kind. Psychological treatment, however, in the literal and larger sense of the words, is essential for every variety or stage of mental illness, and every degree of co-operativeness or intelligence. It is a wide notion, including all that may ease or reassure the patient, bring him to a better relationship to those around him and with himself, and protect him from being distressed by the ignorance, lack of tact, or thoughtlessness of others. It is as much negative as positive. One must avoid arguing with the patient, telling him lies "for his own good" or to avoid unpleasant scenes, cajoling him, making promises that will not be kept, threatening or punishing him, jesting at his expense, losing one's patience with him, assuming he is indifferent to what goes on because he looks indifferent, provoking him by petty supervision or frequent rebukes; one should not assume that he is quite irresponsible or quite responsible, nor talk theory to him, nor get on a false footing through ready assent to his delusions and his point of view. The physician and the rest of those who are in contact with the patient must do certain positive things: make due allowance for his disorder influencing his conduct, use their understanding of the psychological happenings without saying so, take advantage of every opportunity created by other methods of treatment. When occupation, narcosis, hydrotherapy, massage, a physical illness or other happenings bring him more closely into contact with nurses and physicians there are chances of unobtrusive psychological treatment in the wide sense.

Physical treatment.—"Mechanical restraint" and violence are now foreign to the treatment of insanity; the patient may be unrestrained and violent, but his treatment may not. It is still necessary, however, to restrain a patient who is bent on harming himself or others, and physical force may be the only way of doing so, or of giving a patient by tube enough food to keep him alive when he abjures the natural way of eating. But force must always be a last resort; and chemical substitutes for it seem only a little less of an evil. Drugs have their place in the treatment of all kinds of mental disorder, but their use easily turns to abuse. Whether one is giving morphine and hyoscine in an emergency to an acutely excited catatonic, or prescribing aspirin for a mild hysteric, the chief danger must be borne in mind, which is not overdosage, habituation, or suicidal misuse, but the habit of stupefying or satisfying a patient with drugs when other means might be taken, better suited to his condition. Sedative drugs should not be a short cut; neither should they be eschewed. They should be given when other measures will not serve, as for some obstinate form of insomnia, anxiety, agitation and restlessness, or when their use obviates greater troubles, *e.g.* the pulling of bandages from an operation wound. The symptoms of intoxication must be watched for with more than usual vigilance when bromide is being given, because if unrecognised as such they may lead to certification—for an avoidable drug-made psychosis. Continuous narcosis for nearly a fortnight,

with the patient sleeping through 18 or more of the 24 hours, is sometimes efficacious in abbreviating an acute attack of mental illness; it is a dangerous method except in skilled hands.

There are other drugs to which the above cautions scarcely apply, *e.g.* endocrine preparations, remedies specific and otherwise for the physical basis of "organic psychoses" (*e.g.* arsenical treatment for syphilis of the central nervous system), and aperients. Insulin for promoting hunger, calcium for those with hysterical hyperventilation fits, amphetamine (benzedrine) for anxiety, and a number of substances—from nitrous oxide to amytal—that relieve catatonic stupor, or facilitate psychological inquiry and treatment, have all been found useful on occasion, though their field of application is small.

Two methods of treatment have been widely employed of late years, especially in the treatment of schizophrenia. Insulin has been employed in large doses to produce hypoglycæmic coma repeatedly; and certain convulsant drugs (pentamethylenetetrazol and cyclohexylethyltriazol) given to produce fits. The benefits to be obtained by these methods are not yet clear. Undoubtedly in some cases the duration of a schizophrenic illness can be shortened by the insulin treatment, and recovery brought about in cases regarded as having a bad prognosis. It is, however, in those that would have a favourable outlook by other methods of treatment that the majority of insulin successes are obtained. The technique demands skill and experience, if considerable risks are to be avoided. It consists essentially in daily administration of the appropriate dose of insulin to produce coma. The duration of the treatment is usually not more than two months. Treatment by the artificial production of convulsions was first instituted for schizophrenia, but the results have not proved as satisfactory as was at first supposed, and it is of very limited application. The method has proved effective in terminating obstinate melancholia, chiefly involutional, and in abbreviating attacks of depression which would otherwise have taken months to clear up. The chief objections to the method are the disagreeable experiences many patients have immediately after the injection, and the likelihood of cerebral impairment, and of fracture of the long bones or dorsal spine during the fit. The last complication is not infrequent, and may occur also when the convulsions are induced, not by a drug, but by electrical stimulation of the brain, a method employed within the last two years.

Exercise or massage and hydrotherapy are beneficial as much for their psychological as for their physiological results; the latter, however, are not negligible, as may be seen in the effect on an excited or an anxious patient of a continuous bath at body temperature. The chief importance of diet lies in the frequent refusal of food by patients depressive, hysterical, stuporose, paranoid, hypochondriacal, or over-active. Feeding by the nasal or œsophageal tube is a necessity in many such instances, after every other method has failed. Rarely, special diet is called for, as in epilepsy, the symptomatic psychoses of diabetes, pernicious anæmia or pellagra, and also for some temporary disabilities of the alimentary tract—anorexia nervosa, psychogenic hyperchlorhydria. As a rule, however, such dietetic regime, and indeed all physical treatment of localised psychogenic disturbances of function in a bodily system, is an expedient rather than a settled and adequate mode of treatment. Many patients with a visceral neurosis, a hypochondriacal

preoccupation, a hysterical anomaly, or a somatic delusion are greatly harmed by the prolonged physical investigation and treatment they receive: it confirms the symptom, localises it all the more, and brings fresh ones in its train. Sometimes one has no choice; a progressive hysterical contracture, a dermatitis artefacta, a sore infected by constant picking, a tooth loosened by obsessional knocking at it demand treatment.

The caveat against lightly resorting to physical treatment of psychogenic anomalies is especially applicable to operative surgery. In general there is no more reason for "cleaning up the septic foci" in a person with mental disorder than if he were a mentally healthy person—other things being equal. Removal of teeth, appendix or tonsils, scraping of sinuses, and searchings of the pelvis are operations that in psychological medicine seldom yield the results expected of them.

CLASSIFICATION

The ideal classification would be on a uniform basis, according to the nature of disordered physical and psychological function, or according to innate and external causes. Since we do not know enough to do this, a mixed ætiological, functional and clinical grouping is used, whereby the same illness can belong in several categories. It is obviously provisional. The chief division is between those mental changes accompanying distinctive somatic disorder and those for which no such physical relationship has been demonstrated. The former are called symptomatic, or organic; the latter constitutional or functional. It is needless to illustrate the point that everything found in the latter may be seen also in the former. The reverse of this is not true, because there are some symptoms—due to the loss or damage of essential tissues, especially in the central nervous system—which can only occur when the material substrate is grossly damaged.

Although the "functional" group is made up of those conditions for which no distinctive somatic disorder can be found responsible, it by no means follows that their causes or basis are therefore purely psychological. Theoretically, such a belief is untenable; and as a matter of observation certain physical disturbances so regularly accompany these disorders and a physical configuration may be so linked with them that there is small doubt that eventually the somatic disturbance of function in them will be well enough worked out for the terms "organic" and "functional" to lapse, and only the crudity of the physiological changes remain as a point of difference.

As mental disorder thus comes closer to general medicine so must the whole of general medicine reveal its psychiatric side, which is now as little illumined as the physiological side of the psychoses.

The first or toxic-organic group is large, the chief syndromes in it being neurasthenia, confusion, and delirium and dementia. Such phenomena as apraxia, aphasia, agnosia, amnesia and hallucinosis are fairly frequent in this group.

The second group, comprising three-fourths of the recognisable mental illnesses, includes the insanities or psychoses, and those anomalies, outwardly less alien to the normal mind, commonly called "neuroses." The distinction

between neuroses and psychoses is at times convenient, but without substance. To argue whether a dubious case is neurotic or psychotic is like arguing whether a man of medium size is thin or fat: he is both and neither. A genuine decision as to ætiology, prognosis or treatment turns not on whether a case is regarded as neurotic or psychotic, but on more solid findings. Since such words die hard, the best use of them is to term a patient with mental disorder "neurotic" if he has insight into his illness, is co-operative and unlikely to need care in an institution, and to term him "psychotic" if the contrary is the case.

The toxic-organic group is divided into diseases located in the nervous system and those affecting it indirectly, as uræmia or lead poisoning may. Some are toxic, *e.g.* delirium tremens; some degenerative (senile psychoses); some inflammatory, *e.g.* encephalitis lethargica; some plainly hereditary, *e.g.* Huntington's chorea or "primary" mental defect; and some privative, *e.g.* pellagra or myxœdema.

The "functional" conditions are arranged according to whether emotional disturbance is evident and predominant (affective disorder), or whether there is profound derangement of thought, feeling and contact with the real world (schizophrenia), morbid false beliefs have become fixed without intellectual or emotional deterioration (paranoia), repetitive and seemingly irrevelant phenomena hamper mental activity (obsessional), signs of physical or mental ill-health, expecially dissociation, readily appear when an unpleasant situation may thereby be escaped from (hysteria).

As will be seen in the special sections, the personality of the patient may also be a criterion of these groupings, with the proviso mentioned earlier that illness does not only occur in those with the appropriate psychopathic anomaly of personality, nor does the latter by any means regularly issue in definite symptoms. Unless, however, psychiatry takes account of the psychopathic personality, even when not accompanied by symptoms of illness, it cannot study delinquency, disorders of behaviour in children, sexual perversions and other not obviously medical anomalies which touch very closely on psychiatric problems in the stricter sense, but are omitted here for reasons of space.

The following is the classification used here:

1. Organic Disorders:

   (*a*) Degenerative and Hereditary Brain Disease.
   (Senile dementia, cerebral arterial disease and hypertension, Huntington's chorea.)

   (*b*) Syphilis of Central Nervous System.

   (*c*) Other Cerebral Diseases.
   (Lethargic encephalitis, Sydenham's chorea, disseminated sclerosis, cerebral tumour, cerebral trauma, epilepsy, etc.)

   (*d*) Intoxications.
   (Alcohol, morphine, cocaine, bromide, etc.)

   (*e*) Infections and Exhaustive Disorders.
   (Infectious toxæmias, hæmorrhage, etc.)

(*f*) Metabolic, Endocrine and Visceral Disorders.
(Diabetes, pernicious anæmia, pellagra, exophthalmic goitre, myxœdema, tetany, pituitary diseases, sexual epochs, cardiac disease, uræmia, etc.)
(*g*) Mental Deficiency.

2. Affective Disorder.
   (*a*) Excitement.
   (*b*) Depression.
   (*c*) Anxiety.
3. Schizophrenia.
4. Paranoia.
5. Hysteria.
6. Obsessional Disorder.

In the above classification mental deficiency is given a separate heading, though properly it should be systematically distributed among the preceding groups, since it differs from the rest of mental disorder only in the age at which the damage is done. Custom and convenience compel the old distinction to continue.

The above are great clinical groupings, types of morbid reaction, which are the nearest to a valid and useful classification we can get at present. There are subordinate symptom-complexes or syndromes, which are likewise innate and preformed, and likewise evoked by circumstances, but which are not limited to any one of the major groupings—they are the weft that runs across the psychiatric pattern. The most important of these are depersonalisation, hypochondria, twilight states, stupor and other disorders of motility, and spasmodic attacks and seizures of different kinds. Between symptoms (classified on a psychopathological basis) and the main groupings which best serve clinical purposes, these symptom-complexes have an intermediate place, comparable say, to that of mononuclear leucocytosis or coma in general medicine.

All the categories of psychiatry stand for mixtures of symptoms due to disturbance of control, capacity or co-ordination and synthesis in mental life. Nor is this true only of mental life, since the same symptoms may arise through physical disturbances of function which may be classified in the same way; this may be plainly seen in such a disease as encephalitis lethargica.

ORGANIC DISORDERS

A. GENERAL DESCRIPTION OF TYPES

The varieties of form and course in organic psychosis are essentially few and simple, in contrast to the causes, which are numerous. In other words, there is no support for the hope that to each physical disease there corresponds a characteristic mental disorder. It is not possible in an organic psychosis by study of the mental picture alone to infer its physical cause; for that the methods of somatic medicine are needed. Many different poisons and lesions

may produce the same effect on the mental state. Differences depend on the degree and duration of the physical damage and its site, which may determine neurological and other symptoms of a typical kind; *e.g.* in G.P.I. or encephalitis lethargica.

They are the least constitutional of all mental affections, yet even in them constitutional factors are far from negligible. To such factors it is due that one man will show a psychosis with physical illness that in another would lead to no such mental upset, and that one patient responds with a manic extravagance to the cerebral disease that makes another patient depressed. Moreoever, hereditary factors can be of great importance in these organic affections, as may be seen in amaurotic idiocy or Huntington's chorea.

The few syndromes commonly met with here, though they are not restricted to organic disease, must be described before seeing how particular diseases colour them and determine their course and treatment. In the organic syndromes, a diminution in mental capacity is the central finding. Nearly all of them may occur in cases and types of illness in which no structural damage can be found, as might be expected seeing that the available patterns of structure and function are in all cases much the same. Delirium or confusion may occur typically in non-organic syndromes, though much less frequently than in organic ones.

(1.) NEURASTHENIA.—This term has been over-used and ill-used, like most of the more palatable diagnoses (cf. anxiety neurosis), but it need not therefore be discarded now. It denotes a form of irritable, hypersensitive weakness and depression that is not uncommon after infections, exhausting experiences (*e.g.* hunger, lactation, insomnia, worry, hemorrhage), cranial injuries and chronic poisoning (*e.g.* with alcohol or coffee). It is true that a clinical picture indistinguishable from it frequently arises where physical causes are unlikely and emotional causes are obvious: this clinical finding has the same significance as the fact that the anxiety of exophthalmic goitre is like psychogenic anxiety. Just as the anxiety of exophthalmic goitre or constant fear can pass into delirium, so can physiogenic neurasthenia be aggravated until it becomes plain dementia.

The symptoms are partly somatic—active deep reflexes, increased sensory irritability, feelings of pressure on the head and pains in the muscles and elsewhere, giddiness, vasomotor lability, delayed peristalsis and feelings of fullness in the abdomen, diminished libido, slight clumsiness, and tremor of the muscles of the face, tongue and hands. On the more psychological side, there are feelings of languor, and incapacity to concentrate on any mental work, doubts as to the accuracy of memory, loss of interest, slight depersonalisation, irritability and tenseness, lessened control of emotion, and perhaps slight paranoid, obsessional or hypochondriac trends. This general condition is, when physiogenic, less influenced by a change in mood than would be the case with psychogenic neurasthenia, and the patient is better able to control his motor unrest than his features, which are expressive of his agitation. The chief reliance, however, must be put on the history and physical findings for telling whether the neurasthenia is physiogenic or not; psychological causes which seem adequate to explain the illness may be deceptive.

The course of neurasthenia is towards recovery unless the noxa continues to act; where the noxa persists, extreme chronicity can result. Sometimes

an original physical noxa ceases to act, but meanwhile other emotional ones have entered the field, *e.g.* unemployment, domestic fears and frustrations, and so the illness drags on. Treatment depends on assessment of the causes and the possibility of removing them.

(2) DELIRIUM.—Delirium, most familiar in fevers, can also be produced by drugs and other causes of acute cerebral disturbance: severe affective disturbance also may be accompanied by delirium. Its characteristics are general malaise, restlessness, irritability and sensitiveness to external stimuli, headache, anxiety and troubled sleep, or insomnia. Mild forms of this are met with in so transient an affection as cold in the head. Severe forms are marked by illusions and hallucinations of all the special senses, especially vision. Anxiety often becomes extreme, and the patient is terrified of his fantastic visions. Thought becomes as chaotic and fleeting as in dreams, activity is incessant and past experiences of daily life are revived, as in the occupational delirium of alcoholics. Attention is weakened, and orientation in time and space much impaired. There are striking variations in the severity of the condition in the same patient: it becomes worse in the evening or when the patient has hardly any external stimuli to keep him in touch (cf. delirium at night and after a cataract operation). The extent to which consciousness is clouded usually corresponds to the amount of perceptual and affective disturbance. Auditory hallucinations occur with clearer consciousness, visual ones very profusely with a clouded mind. The auditory hallucinations are commonly of an elementary, undifferentiated kind—not voices. Vestibular hallucinations may occur, *e.g.* of floating in the air. Distressing and incoherent ideas pursue each other—ideas of being torn to pieces, burnt, poisoned, buried alive, and so on; also ideas of grandeur.

Closely akin to delirium, and indeed shading into it, is the *confusional state*, in which thought is very incoherent, but the patient is more eager to get in touch with his environment than in typical delirium. If consciousness is not grossly clouded, the patient is perplexed and troubled by the disordered perceptions through which alone he can learn what is going on about him. The picture may be indistinguishable from that seen in some forms of manic excitement and in some catatonic states. Differentiation rests, not on the immediate psychiatric symptoms, but on the history and discoverable causes of the illness. The same is true of *acute hallucinosis* in which orientation and grasp are very little impaired, but auditory hallucinations—especially threatening sounds and voices—abound, and there is a tendency to the formation of delusions on the basis of these and other perceptual disturbances. The name "*twilight state*" is applied to another syndrome in which consciousness is changed chiefly because of some powerful affective influence; anger or fear may so overwhelm psychic life that the patient cannot grasp his surroundings, his thinking is interrupted and slow (except where it falls in tune with the affective disturbance), and his motor behaviour is in keeping with his mood. It is as often of psychogenic as of organic origin—one can hardly, for example, by direct observation tell an epileptic twilight state from a hysterical one. Like delirium and the other conditions just mentioned, it is prone to subside and to be followed by amnesia for what happened during it: where there is some recollection, it may be associated with a conviction that the hallucinations and other morbid phenomena were real external happenings.

(3) DEMENTIA.—Of all gross encephalopathic syndromes this is the gravest and most typical. It corresponds to a diffuse cerebral disease, and is made up of intellectual impairment and lessened control of emotion. Its form depends so much on the stage of the patient's development at which it occurs, that it is customary to consider as dementia only those cases in which the cerebral damage has occurred in later childhood, adolescence, or adult life, and to regard earlier cases, *e.g.* cretins as showing mental deficiency or arrest of development. The distinction is rather artificial, at whatever age it be made. For convenience, only the adult form will be described here. The order in which functions are impaired corresponds to Hughlings Jackson's principle of dissolution: thus, recently acquired memories are soonest lost. There is intellectual weakness—the patient cannot reason, grasp and remember as he could, his attention is less concentrated and sharp, his ideas are fewer, he cannot take in anything complicated or be sure about time and place, he loses himself. His emotions are likewise affected—he weeps over trifles in spite of efforts to control himself, his feelings are shallow and transient, he may be foolishly euphoric, or may burst into anger whenever he cannot get his own way. There are wide variations in the severity of the condition, and its symptoms may be much influenced by the local incidence of the pathological changes in the brain. The extent to which various cerebral functions are impaired may differ widely in the same patient: a man who seems hopelessly demented may be able to play a good game of chess, while another in whom it is hard to demonstrate any intellectual impairment may micturate into his shoes or do something equally stupid and inappropriate; unexpected sexual misdemeanours are not uncommon in demented persons who do not as yet show gross intellectual damage.

Closely connected with dementia are the *amnesic* syndromes, known by the name of Korsakoff. Here the memory disturbance is in the forefront. The incapacity to receive, store and reproduce experience is remedied, as it were, by lying, *i.e.* the patient confabulates to fill up the gaps in his memory. These patients are often ready to adopt suggestions, so that one can lead them to tell absurd tales about their recent movements, *e.g.* that they were yesterday at Vladivostock to see some polar bears. They do not show an intellectual damage or incapacity to deal with ideas that is at all comparable in degree to their memory disorder, but they are always out in their appreciation of time-relationships, especially where the present is concerned. At first blush they often seem to be behaving like mentally healthy people, but one presently discovers that their memory is much impaired, their orientation as to space, time and personal identity correspondingly poor, and their interest and general mood duller than is normal. The disorder of memory is never, as in dementia, a general weakness reaching back even to childhood.

The Korsakoff syndrome is most often seen in alcoholics, in whom it was first described associated with polyneuritis, but it also occurs in a great variety of organic disorders, *e.g.* intoxication with lead, carbon monoxide, and other poisons, uræmia, cranial trauma, cerebral syphilis, and arteriosclerosis—apoplexy may precede it and the amnesic syndrome be thus complicated by aphasia. That it should sometimes follow on delirium is not surprising, since in delirium the same memory disturbance is present,

but covered up by the concomitant excitement, disturbance of consciousness, and hallucinations. Whether a Korsakoff syndrome will clear up depends on the cerebral damage which produces it; the alcoholic form occasionally does so eventually in uncomplicated and treated cases.

Mental deficiency is a special instance of cerebral impairment, as is dementia. It is considered, for the sake of convenience and tradition, in a separate section. (See p. 1846.)

B. DEGENERATIVE AND HEREDITARY BRAIN DISEASE

There is a group of disorders occurring in late middle life and old age, which are clinically and even pathologically near to one another. At the one end of the scale is senile dementia, at the other climacteric anxiety and depression. It includes Pick's presenile dementia, Alzheimer's disease, cerebral arterial disease, and arterial hypertension.

1. Senile and Presenile Dementia

Ætiology.—Constitutional factors are obviously the most important. A tendency to become dotards may be evident in successive generations of a family; heredity is held responsible for the wide differences in mental health among elderly people. The symptoms of senile psychosis may not be revealed until the patient is exposed to some sudden stress—the death of his wife, the need to move house, the loss of his occupation, some new set of circumstances. Senile psychoses are more common in people with lifelong nervous symptoms.

Pathology.—Physical.—The tissues show the general signs of age, *i.e.* a diffuse atrophy, which makes the convolutions narrower and the weight of the brain less. The nerve cells and fibres are fewer, while the mesodermal and neuroglial tissues are increased; fatty pigment accumulates. There are also, however, in senile dementia striking histological features in the grey matter, especially of the cortex, namely, thickening of the neurofibrils, which are characteristically twisted and aggregated, and there are remarkable plaques, seldom seen except in this condition. There is no close correspondence between the kind or extent of the tissue changes and the mental state. Plaques and neurofibrils are reported to occur also occasionally in the brains of mentally healthy old people.

Psychological.—The previous tendencies of the patients may greatly colour the symptoms. Obscure somatic preoccupations and disturbances in time appreciation lead often to fantastic delusions about eternity and what is happening in their body.

Symptoms.—Memory is poor for recent events; the extent of the damage may increase until only the recollections of childhood and early adult life remain. People and places are falsely identified with those once familiar, and transient pseudo-memories are invented. Events with a strong affective tone, especially if unpleasant, are remembered better. The memory of the remote past is not entirely spared; even matters of personal identity may at last be forgotten. Grasp and judgment, the capacity to follow a train of thought and to eliminate the irrelevant are faulty. Obstinacy and

perseveration go with a rigid adherence to old habits. Prolix and garrulous, the patient does not recognise how little interest there is for others in his repetitive and ill-arranged talk. He may partly cover its emptiness with long and sounding sentences; on the other hand, some patients become monosyllabic, because of their failure to find words to express themselves, and others again will use a word loosely associated with the one they are vainly seeking, or will quite seriously give a punning meaning to a word, and even act accordingly (*e.g.* whistling because " You said I could whistle for my money ").

There is a narrow range of interests, in which food, possessions, and bodily well-being are prominent. Grotesque hypochondriacal delusions are common. Patients hoard rubbish and are angry if interfered with in this. On the whole, however, their affective responses are greatly reduced; they meet calamities with composure, partly due to their failure to grasp what has happened. Now and then they show depression and resentment at a slight, and may bear a grudge long after. Their activities are sometimes considerable, on the lines of determined rummaging and collecting; in others a dull inactivity is all. They become dirty and unable to look after themselves. This applies as much to those who are excited and active as to the inert. The former may fight against being fed and washed, and it is not possible to get them to understand what is being done. Delirium and confusional states are prone to occur at night, accompanied by fear and bewilderment. Sleep is bad, and often the patients busy themselves about the place all night long.

Legal difficulties arise through the heightened readiness to accept some suggestions (as in the matter of making a will, or giving away property), the poorer judgment and the lessened capacity to control sexual desire, which is sometimes seen in the early stages. Hoarding may lead to petty thieving. Occasionally the patient sets fire to the house during his nocturnal prowlings.

The symptoms need not be obvious. Often the illness has so slowly developed that no one can say when it first passed beyond what is normal in old age. An apparent change of character—a kindly man becoming selfish, a respectable churchwarden assaulting little girls sexually—may usher it in; this is not so much a change in character as a release of primitive trends, hitherto controlled. The psychosis may take various forms—depressive, manic, and paranoid. In the *depressive* variety there is seldom retardation, the affect is rather empty, the patient is irritable, and hysterical symptoms may be commingled with hypochondriacal ones. Ideas of poverty, wickedness and disease are often grotesque in their exaggeration—the patient's urine drowns the whole world, his body is an undying shell of corruption, he is as tiny as a baby—and are monotonously reiterated. The *manic* variety is rarer: pointless activity and a diarrhœa of words, with silly boasting, may be accompanied by a disturbance of memory, giving a total picture of the Korsakoff type: it is sometimes called " presbyophrenia." Many of these patients have always been of hypomanic temperament; their illness may be only slightly progressive and not so severe as to call for hospital care. The *paranoid* variety is especially likely to occur in people who have always been of a suspicious turn of mind. They hide things because they feel surrounded by thieves, and then forget where they have hidden them;

their failing senses, especially of hearing, feed their distrust, and they project their awareness of sexual impotence or waning intellect. Hallucinations and delusions are mingled—gases are pumped into their room, their food is poisoned, people throw bombs at the house by night, greedy heirs are doing them out of their possessions. Some of these patients barricade themselves against their enemies or call in the police. Whereas the depressive and manic forms are commoner in people with corresponding heredity, this paranoid form is genetically often connected with schizophrenia, though the distinction between the three varieties is not a sharp or important one. The name " involutional paranoia " has been given to the chronic delusional condition of this type that may develop in single women between the ages of 40 and 52.

Bodily symptoms are those of old age, especially in the central nervous system, where it leads to a slow, careful gait, with short steps and legs wide apart, apraxia and poor co-ordination, tremulous rather whining utterance, small sluggish pupils, and occasionally epileptic seizures. The disorder of movement is conspicuous in the handwriting—pointed, small or erratic in size, and sometimes jerky and tremulous.

The conditions known by the names of Pick and Alzheimer are to be regarded as atypical senile or presenile psychoses.

Pick's dementia consists pathologically of a circumscribed cerebral atrophy, mostly in the frontal or the temporal lobe, or in both; the motor area, however, is seldom affected, nor are Wernicke's zone and the transverse temporal convolutions; other areas of the brain may be involved. Histologically, the ganglion cells are swollen and contain argentophil globules. There is a hereditary determinant. The onset, which is gradual, can be at any age from 40 onwards, but is usually between 50 and 60. Symptoms depend on the localisation of the atrophy. Memory and affect are not impaired till late; they are preserved at a stage in which the patient behaves stupidly—stealing, lying, or otherwise making a fool of himself. Spontaneous attention is poor; at first moody, the patient becomes dull and unresponsive; judgment deteriorates and initiative fails. Stereotypies, echolalia, and repetition of empty phrases, monotonous talking and laughing or singing, and outbursts of bellowing or whining appear in the later stages. There may be aphasia. Diagnosis is difficult during life; it may be assisted by an encephalogram showing the shrinkage of cerebral tissue from atrophy.

In *Alzheimer's disease* the senile plaques and neurofibril changes are very numerous. The onset may be between 40 and 60. Indefinite premonitory symptoms (headache, irritability, forgetfulness) are quickly followed by progressive dementia; aphasia and apraxia are prominent, though less coarse and sudden than in cerebral arterio-sclerosis. In the earlier stages the patients are in fair contact with their environment, and look as though they grasp much more than they actually can. Their deficiencies are shown up in writing and talking. As the disease advances they are less open to affective influences: they sink into themselves and say little. Stereotyped words or syllables and movements take the place of embarrassed remarks and gestures. In the aphasia there is a rather characteristic stringing together of syllables like each other in sound, but meaningless. Muscular rigidity may lead to contractures. The progress of this disease to severe

dementia is faster than in typical senile deterioration and the onset is rather earlier.

Prognosis.—This depends on the previous rate of development of the condition, the general physical health of the patient and any special pathological basis, *e.g.* Pick's atrophy, that may be recognised. Delirious and confusional phases may give a deceptively bad impression, for sometimes, after they clear up, the patient can resume his old routine tolerably well.

Treatment.—This consists in providing for the patient as easy and familiar an environment as possible. Whether institutional treatment is necessary depends not only on the mental impairment but also on the patient's social level and the willingness of his relatives to look after him well enough. Patients often fit surprisingly well into hospital life and routine. Drugs are best avoided, and caution is necessary in letting the patient have the aperients he demands to relieve his—mainly delusional—constipation.

2. Cerebral Arterial Disease and Hypertension

The characteristic features here are the focal symptoms. All else is indistinguishable clinically from senile and other cerebral conditions; of course, pathologically many senile brains show arterial degeneration too. The early or mild symptoms of cerebral arteriosclerosis are the same as those of "essential" hypertension; and very like those of many benign melancholias of late middle age.

Pathology.—Atheroma of the cerebral arteries is accompanied by nutritional changes—softening—in the brain tissue, falling into three stages, *viz.* necrosis, degeneration (with masses of granular phagocytes, containing fats and hæmosiderin) and sclerosis (in which cavities and scars of glial—astrocyte — and mesodermal tissue take the place of the necrotic cells). (See also p. 1597.) The cortex on the convexity of the brain may show microscopic areas of perivascular gliosis, but no softening. It is not yet possible to correlate the mental and the cerebral changes in these psychoses, except for the focal lesions.

Symptoms.—Since "essential" hypertension often precedes definite vascular disease and itself produces mental symptoms, a description of these symptoms serves also to describe the earlier stage of cerebral arterial degeneration. Along with headache, giddiness, tinnitus, faintness and insomnia, there may be disturbance of speech and writing—the former becoming slow and at times indistinct—and transient pareses and apraxia. Certain traits of personality may be intensified: the patient becomes irritable, egotistic, moody and easily tired, his conversation lumbers along where once it moved easily: he is depressed or paranoid; but there may be wide variation in the intensity of these changes, which are by no means always found. Brief phases of disturbed consciousness, lasting up to three weeks, may suddenly occur either in a form very like the "absences" of the epileptic, or as twilight states with hallucinations, ecstasy, incoherence, disturbed motility and agitation.

After this stage of neurasthenia and episodic disturbances, the patient with cerebral vascular disease may begin to have trouble in finding words: he perseverates a little, and is at a loss when anything unusual is required of him. His depression and hypochondriacal worries increase, he is distressed

by his own slowness and failures, and may attempt to kill himself. Emotional control falls off so that he weeps and storms when he would rather be calm. Nihilistic ideas may abound—his bowels have not been opened for six months, his trunk is a hollow cavity. Nocturnal delirium is frequent. Aphasia and apraxia are commonest after a focal complication.

The most important feature is the way the patient continues to look normal and sensible when already mildly demented. Sometimes transfer to the strange surroundings of hospital is too much for the hitherto well-preserved outward normality, and the patient goes to pieces, as he also may if he has to give up his usual work or move house.

Diagnosis.—Because a patient has generalised arterial disease, it does not follow that any neurotic symptoms he may show are due to the cerebral vessels being thus affected. Unless there are definite focal symptoms, or evidence of dementia, it is unsafe to hold the cerebral arteries responsible and to give a prognosis based on this. There is no known means of distinguishing many benign " neurasthenic depressions " and involutional hypochondrias from those due to disease of the cerebral vessels. If there has not been any history of such tendencies until an attack at the age of 60 odd, the probability that it is an organic vascular disease is much higher. The distinction is all the more difficult because so many unstable persons develop arterial disease in later life ; especially those prone to anxiety and other affective disorders. Neurological findings (see p. 1599) may be decisive in a doubtful case. The condition of the retinal arteries is not a reliable guide.

Course and Prognosis.—In definite cases of cerebral arterial disease with mental disorder the prognosis is necessarily bad, though the mental symptoms may only progress slowly, and the patient live another ten or twenty years. Much will depend on such sudden accidents as thrombosis or hæmorrhage. An episodic confusional state, perhaps even one produced by drugs, may suggest a needlessly gloomy prognosis. In cases of " essential " hypertension, the course of the mental illness is dependent on the general disturbance, and is often quite favourable. Symptoms that are apparently hysterical, occurring for the first time in middle life, are of bad omen.

Treatment.—Besides the general medical care of such patients, not a little can be achieved by psychiatric methods. In the early stages, where there is much anxiety and depression, too energetic physical investigation and treatment may do harm : reassurance and sedation can do much good. The less said to the patients about their blood pressure and their arteries the better. They should keep at work and in their accustomed surroundings as long as they can, unless an acute phase of the illness or depression intervene. Emotional upsets oftener aggravate their condition than physical ones, so they should be cushioned against such jolts. Their depression may necessitate hospital care, especially because of the risk of suicide, or because they are too irritable and neglectful to be at home any longer. If there be dementia, even of mild degree, the patient will probably remain in a mental hospital once he has gone there. It is, however, not easy to be sure about mild dementia being present; it can be counterfeited by passing disturbances, *e.g.* emotional ones.

3. Huntington's Chorea

(see p. 1703)

C. SYPHILIS OF THE CENTRAL NERVOUS SYSTEM

Only the mental symptoms will be described here. Hypochondriacal and depressive reactions sometimes follow infection, or the risk of infection: such psychogenic illnesses do not belong under this rubric; occasionally, however, a patient's anxiety lest he be developing neuro-syphilis turns out to be justified. A syphilitic neurasthenia can occur in the early stages of the disease, due to a mild meningitis. The more severe meningo-encephalitis—*cerebral lues*— may be accompanied by disturbance of consciousness, even to the point of delirium or mild dementia: loss of initiative, euphoria or moroseness, poor judgment and impaired memory may persist and the patient be aware of them in greater measure than he is in general paralysis. These conditions are often complicated by the signs of premature arterial degeneration in the brain. The psychoses that accompany tabes are due to syphilitic changes in the brain, often complicated by alcohol, trauma, heart and kidney disease, and other exogenous factors; there are also depressive hypochondriacal reactions to the pains and other disabilities which the patient suffers.

General Paralysis of the Insane.—Dementia is the constant sign of this mental picture; the old descriptions of a "classical" course with an expansive onset are fallacious, but general dementia is almost certain to occur in every case that is not treated early. All the other symptoms are either neurological and focal, or due to the patient's constitutional predisposition and previous experiences.

The dementia may at first be quite undetectable as such, because it appears under the deceptive guise of a neurasthenia, melancholia or mania; only gradually does the intellectual impairment become manifest. In the beginning of general paralysis, which is seldom abrupt (though it may need a careful inquiry to verify the prodromal symptoms), "functional" syndromes can be so "typical" and organic changes so slight that the most expert psychiatrist is misled; only by physical and serological examinations can he avoid a blunder. A faint degradation of personality, a lapse in social refinements may be the first indication of what is wrong. Then memory for the events of yesterday and last week becomes less trustworthy, what seemed at first a trivial absence of mind becomes serious incapacity, and yet the patient remains serene and outwardly indifferent to his lapses. As in senile and arteriosclerotic dementia, he may be all right so long as he is in an accustomed rut, but a holiday or a change reveals his infirmity. His mood and interests as the illness goes on become dull or labile, his rages are fleeting, his activities fussy; if, however, he is in a manic excitement, with little dementia as yet, the affective changes can be violent, and indeed dangerous, just as in a depressive phase the patient may kill himself. Sleepy and slow, careless about social usages, inattentive and ignorant of what he once knew well, the more demented patient cannot escape recognition as having an organic cerebral affection. Elementary problems in arithmetic and questions of general information are more than he can cope with. He gives easy assurances that he can do them, or puts his questioner off with airy explanations (*e.g.* that he has not had his spectacles by him lately); when pressed, he makes bad mistakes or becomes angry. The extent of his failure will, of course, depend not only on his dementia, but on his previous

intelligence and habits (*e.g.* a bank manager retains the capacity to do mental arithmetic when much else has gone). Inability to receive new impressions and to relate them to earlier memories co-operates with impaired judgment to give a gross but patchy and fluctuating amnesia. Because of these disturbances, and especially the bad judgment, patients may commit offences, ruin themselves by grotesque extravagance and brush aside facts that stare them in the face. They will put up with restrictions on their freedom, forgetting their protests soon after making them; silly reasons are sufficient for their compliance, and a tactfully offered cigarette or joke may divert their thought and feeling from some serious matter that angers them. Their delusions are due to the same disorders of memory and judgment, coloured by their general personality; sometimes they are confabulations, rationalisations for their having forgotten or spoilt something. If the patient had in health tendencies to euphoria and expansive behaviour, grandiose delusions and boasting will be to the fore. It is, however, not uncommon to find a fatuous euphoria, though there had not previously been affective swings and hypomania; in such patients one finds abundant proof of gross impairment of judgment, especially shown as defective insight. The most advanced dementia appears as a helpless, vegetative, bedridden state, sometimes accompanied by gross focal symptoms, such as aphasia and agnosia. The physical symptoms (see p. 1638) are much intermingled with the mental ones, as in the patient's clumsy movements and disturbed speech and handwriting: thus, in his writing he leaves out letters, syllables and words, repeats and transposes them, messes the paper with blots and sputters, writes across the lines, puts in meaningless strokes and leaves his mistakes uncorrected; the tremulous script shows interruptions in the usual smooth alternation and tempo of movement, the letters are of very uneven size and ill spaced. Articulatory and aphasic disturbances may affect the sense, intonation, timbre, rhythm and precision of utterance; they must not be evaluated in diagnosis, any more than the writing disorder may, without regard to the patient's previous normal script and speech and the circumstances under which he was writing or talking, since people, habitually untidy in their enunciation or handwriting, can exhibit many of these symptoms when tired or in a hurry.

Besides the above, atypical mental pictures may be seen either ordinarily or as the outcome of treatment with artificial fever. Paranoid states, hallucinosis, a Korsakoff syndrome, epileptiform excitement, hysterical disorders and catatonic symptoms of every kind (except flexibilitas cerea) may occur. Hallucinations are uncommon, except during fever or after malarial treatment; in the latter case they are often of paranoid colouring. Not the expansive form, but a simple progressive dementia is by far the commonest clinical picture; depressive, confusional, and hyperkinetic states are almost as frequent as the expansive.

In the "Lissauer" form the slowness of the dementia is remarkable in comparison with the conspicuous focal symptoms, such as the seizures without convulsions or loss of consciousness.

The effects of treatment upon the mental state are of great social moment. In a majority of the cases who do well the personality has the edge taken off it, there may be less initiative and force in mental activity, and emotion may be less controlled, especially in the proneness to anger or to frivolous

levity, yet the patient is able to return to his former work, even though it is responsible and complex; he could scarcely, however, except in the most favourable cases, learn a new job or adapt to new and exacting situations.

In the "*juvenile*" form there may be premonitory symptoms of excitability, grizzling, timidity and backwardness at school. Gradually the symptoms of dementia become plain, and if the onset be early enough, symptoms usually found in severe mental deficiency naturally appear, such as rhythmic or iterative movements, grimaces, repetitive chewing and sucking of an automatic kind, great restlessness and screaming attacks. Simple dementia is the usual form; grandiose ideas are exceptional. If the illness begins before the age of 10 or 11 years speech and writing may be completely lost, or reduced to a senseless smattering.

For *prognosis* and *treatment*, see pp. 1640, 1641, and 1653.

D. OTHER CEREBRAL DISEASES

LETHARGIC ENCEPHALITIS.—The mental disturbance of the acute attack may merge into a hyperkinetic excitement, with choreiform and athetoid movements, insomnia, generalised pains, mild delirium and, occasionally, catatonic symptoms: this seldom lasts more than a few weeks. There may be subsequently a neurasthenic fatigue and irritability with headaches and poor sleep. The distinction between what is neurological and what is psychiatric in the symptoms could scarcely ever be more difficult than in this disease. The motor disturbances, such as oculogyric crises, are not merely responsive to emotional and other psychogenic influences, they are inseparable from concomitant mental happenings (*e.g.* the surging up of anxiety or obsessions), and whole patterns of complicated behaviour, *e.g.* breathing, may be involved. The motor rigidity of the patient's Parkinsonian state may be paralleled by a lack of the normal drive and fluidity of thought or behaviour. Memory, however, and grasp are unaffected. The obsessional symptoms sometimes occur quite apart from oculogyric crises, and may greatly distress the patient. Depressive phases may result in suicide, which is fostered, as it were, by the keen appreciation which many patients have of their ruined careers and their almost imbecile appearance, so different from what they were and, indeed, from what they still know themselves to be. Paranoid, and especially schizophrenic, symptoms may develop in the later stages.

The younger the patient the more likely is it that he will develop disagreeable anomalies of personality, and have attacks of restlessness or even be permanently restless. Many children and adolescents after their acute attack become social problems: they play stupid or cruel tricks, they set everyone they can by the ears, they may steal, behave sexually in an outrageous way or accuse others of sexual offences against them. Their activity is not always purposive, nor always antisocial; they make the same impression as a monkey might who is sometimes mischievous but always on the move. There may be no Parkinsonism in these cases. The prognosis is not good, and they almost always do better when subjected to the regime of an appropriate institution; they do badly at home or in places where

what may be termed normal delinquents and "social problems" are cared for.

SYDENHAM'S CHOREA.—The usual mental changes here are lability of affect and irritability. These are seen as naughtiness, outbursts of anger or crying, resentment at sudden noise or light; in others there is lessened spontaneity, often masked by the choreic movements. In more severe cases, especially in older children, these changes are accentuated; in the fleeting phases of anger or terror there may be slight delusional trends. Still more severe forms, with delirium, hallucinations, delusions of persecution and much excitement, are seen in adults, *e.g.* in chorea gravidarum.

The tics and compulsive utterances (Gilles de la Tourette's disease) which may follow chorea are evidence of the interplay between hereditary, psychic and structural factors. Chorea is more prone to occur in those whose families show nervous disorders, especially schizophrenia. The motor after-effects, especially tics, appear and disappear under emotional influences; they are also conditioned by the original choreic disturbance of neuromuscular function. The obscene ejaculations of la Tourette's disease are dependent on much the same articulatory and respiratory hyperkinesias as are the breathing spasms of encephalitis lethargica, though they are also dependent on psychological tendencies and experiences. They illustrate how psychological influences work through available bodily structures and functions, whether morbid or healthy. The obsessional element in this affection is comparable to that in encephalitis lethargica.

DISSEMINATED SCLEROSIS.—Slight deviations from mental health are frequent, but obvious ones rare in this disease. Affective lability may be conjoined with a slight disorder of judgment, so that a baseless euphoria develops, but this is not universal, and many of the patients are depressed. Acute outbursts of excitement, hallucinosis or delirium occur in a few cases, and dementia in the advanced stages. The most important mental disorder in them is that which appears as hysteria. A hysterical personality has not been present in these patients before the disease began, and the symptoms are in that respect only dubiously hysterical: they do, however, in other respects conform, in that they can be evoked psychologically and removed psychologically; they may centre on, and elaborate, actual anomalies, *e.g.* of movement or sensation, and may still yield to hypnosis or other psychological measures. They can greatly confuse the diagnosis.

SCHILDER'S DISEASE.—In this disease profound dementia gradually develops along with the blindness, deafness, aphasia and agnosia and other focal symptoms. In the juvenile cases there may be at first disturbances of behaviour like those of juvenile encephalitis lethargica.

PARALYSIS AGITANS.—This may be accompanied by hypochondriacal depression. Sometimes this is an expression of the cerebral disease which also causes the Parkinsonism, and in that case the prognosis is bad; sometimes it is a recurrence of depressive attacks which have occurred at times of stress earlier in the patient's life and then the outlook is fairly favourable. Senile dementia is, of course, not infrequent in these elderly patients.

CEREBRAL TUMOUR.—Apart from any aphasia and apraxia, the mental state here is more closely related to general intracranial tension than to any local disturbance. The size and rate of growth of the tumour are therefore important in this regard. If rapidly growing, there is more disturbance of

consciousness, with impaired memory, disorientation, incoherence and, sometimes, hallucinations and confabulation; this clouding of the mind fluctuates a good deal. In more slowly growing tumours, lucidity is preserved and change of disposition is the prominent feature. The patient's earlier tendencies get freer play, unsuspected ones appear, and a series of foolish investments, for example, or homosexual escapades may for years divert attention from the organic disease. The moria, or fatuous wit and cheerfulness, often attributed to frontal tumours but also found in other cerebral diseases, may give the impression of being a hysterical pseudo-dementia; other apparently psychogenic symptoms may prove misleading. A straightforward depressive attack can occur, or indeed any "functional" syndrome.

Hallucinations may depend on a focal lesion, as in the cases in which they are limited to the hemianopic field, or are solely of taste and smell.

In CEREBRAL ABSCESS the mental symptoms are those of tumour with or without others due to meningitis. In ACUTE MENINGITIS there may be delirium, preceded during the prodromal stage by irritable apathy, and followed by months of moody neurasthenia.

CEREBRAL TRAUMA.—After concussion there is retrograde amnesia; the extent of this and the rapidity with which it diminishes depends on the amount of cerebral damage. In rare instances delirium ensues: it has little that is characteristic, and is more frequent in alcoholic and elderly people; a Korsakoff syndrome may develop. Twilight-states are rather more common; during them acts of violence may be committed, as in epilepsy, and afterwards quite forgotten. Traumatic epilepsy may follow. The later changes in personality are commonly those that may be found lingering after any toxic or other structural impairment of the brain. But sometimes the disturbance of consciousness is more persistent, the intellectual damage greater, the deterioration progressive; in such cases there is usually cerebral arterial disease, an unrecognised alcoholism, cerebral tumour, G.P.I., or some other complicating factor. In predisposed persons the cranial injury may be responsible for a melancholic attack, schizophrenia, or other "functional" syndrome; the prognosis is usually good even if the illness lasts many months.

Hysterical symptoms occur frequently after cerebral trauma. This is partly because of the site of the injury, which favours vague physiogenic symptoms that respond readily to emotional and other psychological influences. Many of these symptoms are, however, produced by psychical rather than physical mechanisms. Not injured cells, but mental attitudes are at the bottom of the tremblings, faintings, weakness, paræsthesiæ and other troubles so often the sequel of a trauma in itself little likely to have such effects. They are not responses to the actual injury, but to the situation created by the injury. Compensation may play a large part in this. It is as unwise to dub all such vague post-traumatic phenomena hysterical as to attribute them entirely to the direct injury. If there is slight amnesia of the typical kind, with difficulty in concentration and headache, it is fairly probable that these are physiogenic residues; if there has been an interval between the actual concussion and the appearance of the indeterminate symptoms, and an adequate psychogenesis (*e.g.* claims for compensation, with repeated medical examinations, and patent uncertainty among the experts) the condition is likely to be hysterical. Much will, of course, depend on the neuro-

logical and other findings, including the demonstration of localised lesions; thus, damage to the frontal lobes may much change the personality, and in other sites be responsible for an apraxia, say, or a visual defect.

EPILEPSY.—Although the motor seizure is the chief symptom of epilepsy and the only decisive one in diagnosis, there are minor or equivalent symptoms, as well as delirium, twilight-states and dementia, to be included among the mental disorders of this illness. The minor symptoms are much rarer in symptomatic epilepsies than in the "idiopathic" form.

Instead of a major fit the patient may become unconscious; or he may pass into a twilight-state in which for a few minutes or longer he wanders about in a dazed way and does inappropriate things, having afterwards complete amnesia for all this; or there may be a sudden interruption of action and speech, during which the patient remains immobile or makes some automatic or aimless movements. Epileptic furor is a delirious state in which acts of violence may be committed: it lasts often for several days, is accompanied by disorientation and hallucinosis, and is much rarer than is popularly or forensically supposed. All the states of disturbed consciousness mentioned above are most often seen as equivalents for a seizure; the twilight-states, however, may precede the motor attack, follow it, or be accompanied by a few violent clonic movements.

Apart from their seizures epileptics are prone to swings of mood—towards anger, shallow sentimentalism or depression—which may pass over into a fugue, during which the patient wanders a long way from home.

The likelihood of dementia later cannot be inferred from the symptoms of the epilepsy, except that it is greater if attacks occur very often. Apparent dementia may be the result of intoxication with bromide, or of the idleness and sterile life in an institution. When there is genuine dementia, it begins as a faint loss of interest and concentration, with increased sensitiveness to supposed slights, then memory falls off somewhat, the trivial and the important are muddled together, and the patient talks with much circumlocution; he is fond of needless system, assumes and parades virtues he has not, *e.g.* an intellectual bias or a devout spirit, and is childishly pleased when anyone praises him. Later, a profound dementia may supervene, but this is not common; it is open to question whether the changes of character just described are necessarily part of a dementing process. It is certain that many epileptics who exhibit some of the most disagreeable features of this sort never become plainly demented, and that many severe epileptics are free not only from dementia but also from these traits. There is ground for regarding this impulsive, pretentious, fawning and snarling way of some epileptics as partly a variable expression of their constitutional predisposition (to which the motor seizures are likewise due), and partly as a reaction to their situation. Consequently it is much less evident, or not evident at all, in those who in spite of their fits live comparatively normal lives.

E. INTOXICATIONS

1. ALCOHOLIC DISORDERS

Alcohol is so permissible and trusted a poison, so easy of access for those who wish to escape from their troubles, that it is resorted to in excess

by maladjusted persons of every type; consequently its effects may complicate or be complicated by the psychopathic anomaly which favoured the taking of the drug, *e.g.* episodic excitement or depression, anxiety, cerebral arterial disease, syphilis, paranoid states, epilepsy, hysteria. The acute effects of a single dose of alcohol are either the well-known phenomena of intoxication, or an excitement (*mania a potu*) sometimes with clouding of consciousness. The excitement is commoner in people with cerebral trauma, arteriosclerosis, epilepsy, or unstable hysterical personality, and in them may lead to acts of violence; rarely it may occur in normal persons who have taken alcohol when they were exhausted or upset.

In chronic drunkards, a dementing *demoralisation* can occur. Their narrowing of interest, superficiality of thought, weakness of memory and moral decrepitude are reminiscent of what happens in many epileptics and some early general paralytics. The crudeness and even brutality of their conduct is in ill accord with their maudlin prating about virtues and their pothouse jollity. The mood of these men can be as labile as their abandonment to it is constant: they pass from rage to weeping, and laugh soon after, with no shame for themselves and no thought for the miseries they put on their families. Such degradation is of course far from being the rule: some chronic alcoholics become only cheap editions of themselves, with their former qualities underlined or smudged rather than defaced; they are perhaps weak and irritable, untrustworthy or lying, but not given to savage fury, nor grossly damaged in judgment and social feeling. Some of them develop delusions, especially of jealousy. They collect, as paranoid people of other kinds do, scraps of alleged evidence which they piece together to prove their suspicions right; complicated delusions of persecution, however, they rarely develop. Sometimes the delusions of jealousy fade as the patient gets more and more facile, but more often they persist as a chronic insanity and are of the greatest danger to the suspected wife; murder is not unknown in such cases. The nature of the delusions is to be attributed in part to the lessened sexual potency of chronic drunkards and to the domestic wretchedness and aversion they often create, as well as to the same causes as in "functional" paranoid states, where such delusions are also common, especially in middle life.

The symptoms of *delirium tremens* would appear to differ in nothing but severity from the essential symptoms of any delirium (see p. 1824). Some observers, however, deny this. The anxiety amounts to terror, mixed oddly enough with euphoria; optic and cutaneous hallucinations are vivid and restlessness can be extreme. There is almost complete sleeplessness, and much disorientation as to time and place, but not as to personal identity. The patient's attention wavers between his hallucinated and his actual surroundings, but can usually be caught and held for a few moments. He is very suggestible, as most chronic drunkards are; pressing on his eyeballs, for example, will very likely make him see whatever one tells him he sees, and he will read aloud from a blank sheet if one wants him to. Among the visual hallucinations may be miniature ones (micropsia), and many illusional perceptions. The content of the hallucinations changes rapidly, and a false perception in one field (*e.g.* a vestibular one) tends to evoke others (*e.g.* of sight, touch, or hearing). Insight is commonly lacking; afterwards there is patchy amnesia for what has happened in the

delirium. The death rate, with adequate treatment, has been about one in seven; and of those who die most of the men are under 40, and most of the women under 45.

In *acute alcoholic hallucinosis* auditory hallucinations of a persecutory kind are prominent and consciousness is not notably clouded. It is rarer than delirium tremens, and is more prone to follow a bout or orgy of drunkenness. The patient is frightened, but not obviously out of his mind; he is correctly orientated and may be able to go about his business for days. Auditory hallucinations are vivid and insistent, after a premonitory phase in which there are sensitiveness to sounds, and roaring, singing, hissing, etc., in the ears. Tormenting voices, sharply localised but seldom fastened upon bystanders, abuse, threaten or discuss the patient: they may say his wife plays him false, order him to kill himself, describe his every movement, especially at private moments in the bath or lavatory, cast up his more shameful secrets at him, shout his thoughts aloud. There may be many voices, of men, women, and children, all talking together and perhaps rising and falling in the same rhythm as his pulse. They are so real that the patient answers them; he may be in doubt about the presence of his tormentors and may shout back insults to see if a blow will follow from the owners of these evasive pursuing voices. Hallucinations of sight and other senses are far less prominent than those of hearing; cutaneous ones, *e.g.* of being sprayed with a cold liquid, are not uncommon. Delusions are usually inconspicuous: they are as a rule attempts to account for the hallucinations, and they commonly fade out of the picture or pass into a chronic persecutory disorder. Flight or acts of violence may result from the patient's fear or anger. Usually it is a matter of only 2 or 3 weeks before the hallucinosis clears up, if no further alcohol be drunk; sometimes, however, a delusional state, more rarely a Korsakoff picture, supervenes in predisposed persons. After recovery, there is little or no amnesia for the events of the hallucinosis. Relapse is to be feared if the drinking goes on.

The *Korsakoff* syndrome is not invariably associated with polyneuritis. Nor, as stated on p. 1825, is it limited to alcoholism; it can follow other severe chemical and mechanical injuries to the brain. In alcoholics it is commoner in middle life, developing either insidiously in the course of chronic alcoholic demoralisation, or after delirium tremens; women are especially prone to develop this syndrome after the delirium. The symptoms have already been described. The disorientation, superficial appearance of clarity, incapacity for initial perception and subsequent recall (extending often to most of the material of memory) yet with retention of some capacity for learning by repetition, along with confabulation, dullness of emotion and initiative, and grossly impaired judgment make a striking picture. Complete recovery is on the whole uncommon, occurring in less than a quarter of all cases. The mortality rate is higher in women and older people, in those with acute onset and with a red-cell count below 3,000,000, or with a rise in the protein content of the C.S.F. It does not correlate with the severity of the peripheral neuritis.

Chronic Delusional States have been referred to above; they are sometimes called alcoholic paranoia, but inappropriately so; jealousy is the commonest and most dangerous feature. Alcoholic epilepsy has been described. It is no more than a symptomatic epilepsy, often atypical; some-

times in unstable hysterical patients it may be brought about through over-breathing when intoxicated.

Diagnosis.—The diagnosis of alcoholic psychoses must depend much more on a history of drunkenness in any patient than on his clinical psychiatric features, none of which are limited to alcoholic disorder. Since, however, alcohol is far the commonest cause of most of the toxic abnormalities described, it can be safely presumed in some cases in which the certain history of addiction is unobtainable.

Differential diagnosis, so far as ætiology is concerned, will turn on somatic findings, including the results of chemical and biological tests. If the form of the disorder is in question, the chief diagnostic difficulty arises with acute hallucinosis and the chronic delusional varieties. A hallucinosis of similar type can occur in schizophrenia and in affective disorders, but in the latter is recognisable by the ideas of self-reproach expressed; the differentiation from schizophrenia is difficult, since in many of the cases the progress of the disorder is towards a chronic schizophrenic psychosis, and one may suppose that in these patients the intoxication had activated, as it were, the same mechanisms as those involved in schizophrenia, or had complicated a schizophrenic illness. This applies also to the chronic psychosis with delusions of jealousy. There is no value in differentiating carefully the clinical varieties of alcoholic psychoses, since they overlap.

Treatment.—Prophylaxis is the main thing. The incidence of alcoholic psychoses in London has fallen to one-third of what it was before the War of 1914–1918; and this may be attributed almost entirely to social influences, of which the increased cost of alcoholic drinks is the most effective. Individual prophylaxis is scarcely to be considered, save as a by-product of psychiatric treatment, since a great proportion of unstable persons are potential drunkards, and in any case we cannot yet tell which alcoholics will become mentally ill through their drinking. Social prophylaxis is so immeasurably better in forestalling alcoholism and the psychoses and degradation that sometimes spring from alcoholism, that deliberate individual prevention is here negligible.

When alcoholism is itself to be treated, independently of its ill-effects upon mental health, the problem is that of any drug addiction. Absolute removal of the drug is essential, yet this cannot be done unless the patient, the treatment, or the environment is exceptional. A suitably exceptional environment can be provided by getting the patient into a hospital or home where he cannot obtain the alcohol he desires, but the other requirements are more difficult to meet. The exceptional patient who after years of excess can put aside alcohol while it is within his reach is as rare as the treatment that can bring him to this state; and when such a change does occur, a great emotional upheaval, *e.g.* bereavement, religious conversion, fear of death, has usually led to it. For the most part, treatment of alcoholism without restrictions upon access to the drug is a failure; the restrictions must at first be imposed from without, not left to the patient's self-control and judgment. He should remain in the hospital or home for a year at least. Psychotherapy is an essential feature of the treatment in those cases in which inner struggles and neurotic disabilities have been the basis for the addiction; it must, however, be conjoined with social and other measures (see p. 1815). Special chemical methods have little or no value.

The grosser mental disorders due to alcohol need hospital treatment. Delirium tremens should be treated as far as possible without hypnotics, which have little effect upon the excitement and sleeplessness unless employed in dangerous doses; if any, paraldehyde or hyoscine should be used. Circulatory failure and accidental self-injury are most to be guarded against. The continuous bath at body temperature is sometimes beneficial; otherwise the patient should be in bed with a minimum of necessary restraint, the company of an experienced nurse, and ensurance of adequate diet—mainly fluids and glucose and large amounts of vitamin B_1. No alcohol should be given. Occasionally lumbar puncture is helpful.

Especial care must be taken against the early discharge from hospital of alcoholics with delusions of jealousy. If they have been certified, they may add a deep resentment on this score to their other grounds of morbid hatred, and there is grave danger that they may, if they resume drinking, attack their wives murderously.

2. Morphinism

Only the effects of this belong among the organic disorders; its causes, and the incapacity of the addict to escape from it, are due to social and intrinsic factors, not to any physical damage. Weak, unstable, unhappy people, *e.g.* many homosexuals, are most likely to become addicts; it is rare to meet an addict who has not shown pronounced psychopathic traits before his addiction began; and few of those who profess to have been seduced into the habit by more or less injudicious administration of morphine for some pain they had, are in that telling the whole truth. Yet it is a wise caution that withholds morphine from all chronic disease that is not hopelessly progressive, and hesitates to prescribe it at all for those whose personality or opportunities make the risk of addiction greater.

Symptoms.—These are not at first noteworthy, unless the patient be seen during the next 2 or 3 hours after he has taken his drug. The symptoms of withdrawal, sometimes severe, are more likely to occur in those whose tolerance has been raised by the habit; they consist of yawning, sneezing, overflow of tears and saliva, fullness in the head, then restless movements, malaise, twitching in the face, tremors, palpitation, indigestion, vomiting, diarrhœa, strangury, sleeplessness, and circulatory upset which may go on to collapse.

It is difficult to judge how far the drug itself is responsible for the demoralisation that is met with in chronic morphine addicts; probably as important in causing it are the psychopathic personality of the addict, and the underhand life he must lead. Laziness and lying are frequent, and the patient may resort to subterfuges, or even crimes, to get his drug. Dementia does not occur; delirium is rare. The physical effects of chronic morphinism are dryness of the skin, hair, and nails, constipation and anorexia, partial impotence, and poor resistance to infection.

Prognosis—This is poor as regards recovery from the addiction. The more normal the patient's personality, the better the outlook. After apparent cure, however, relapse is frequent, and the outlook is then correspondingly worse unless the patient can be stopped from getting the drug. Many morphine addicts also take alcohol, cocaine, and such other drugs as they can get. Suicide with morphine is not uncommon, for obvious reasons. Death

is sometimes the result of cutaneous infections, especially when the patient is grossly undernourished.

Treatment.—This must be in an appropriate institution; general hospitals seldom have the necessary facilities. Treatment at home is bound to be a failure. It should be impossible for the patient, however skilled in stratagems, to get hold of morphine. He should, if possible, contract to stay for at least 2 months. The withdrawal of the drug should be abrupt and total, except in very debilitated patients; "tapering-off" prolongs the distressing period of withdrawal symptoms and gives opportunity for the patient to develop psychopathic reactions and dodges. If the patient's condition demand a gradual withdrawal, this need seldom extend over more than a fortnight. When an abrupt end has been put to the taking of morphine, the rigours of the first 4 or 5 days (after which the worst is over) can be alleviated by sedatives in fairly large doses, copious fluids, warm baths, massage and fresh air; gastric lavage and alkalies help, and for circulatory symptoms caffeine may be given, with small doses of morphine also in very severe cases. After this phase is past, sleeplessness may still be intractable: in giving sedatives or hypnotics for this, barbiturates and paraldehyde, with occasional doses of hyoscine, are the safest, but should be used sparingly, with frequent changes and, it need hardly be said, complete refusal to let the patient know what he is having. Psychological treatment is of great importance, but there is no specific technique applicable to this addiction. To be successful, the psychological treatment requires the co-operation of the patient's family as well as of the patient himself, and it will be wise for him to keep in touch with his physician for years. The great difficulty of getting the drug in this country, because of the vigilance of the Home Office, is an immensely favourable factor after active medical treatment has ceased. It is wise for the patients to eschew alcohol and, of course, all hypnotic drugs.

3. Other Intoxications

Cocainism is very rare in England. The causes and symptoms are similar to those of other addictions, *e.g.* alcohol and morphine. Deliria, hallucinations, Korsakoff syndrome, or demoralisation can occur: in the former conditions microptic and cutaneous hallucinations, *e.g.* of bugs under the skin, are prominent. A paranoid schizophrenic state sometimes comes on, usually clearing up after the drug has been stopped. In treatment what was said of morphinism mostly applies here, though withdrawal symptoms are far less severe.

Bromide intoxication is common, and often unrecognised. It is probably now in England the most frequent cause, after alcohol, of mental disorder due to a drug. All the organic syndromes can occur, usually as complications of a pre-existing disorder for which the bromide has been prescribed. A delirium and a paranoid confusional state or lachrymose amnesic syndrome are the usual forms. In the more long-standing and severe forms cachexia, circulatory failure, and even death may occur. Acne and other physical signs of intoxication or idiosyncrasy may not be evident. Diagnosis rests on the history and the amount of bromide found in the blood, more than 50 mgms. per 100 c.c. being indicative of a considerable intake or retention of

bromide. Treatment consists in complete withdrawal of the drug, promotion of its excretion by giving sodium chloride and fluids in large quantities, and general physical and psychiatric measures.

Barbituric acid derivatives, such as barbitone (veronal) and phenobarbitone (luminal), can in rare cases lead to apparent euphoric dementia, likely to be mistaken for general paralysis because of the ataxia, tremor, articulatory disorder, and other neurological signs. Recovery is the rule when the drug is stopped. Picrotoxin may be needed for acute poisoning. For the addiction itself, essentially the same problems and methods of treatment are in question as with other drug addiction. This applies also to *ether*, *chloral*, and *paraldehyde*.

Mercury and *lead* poisoning may lead to mental disorder (see pp. 376 and 366), *manganese* to a Parkinsonian syndrome with compulsive symptoms (reminiscent of encephalitis lethargica) and a mild paranoid or euphoric dementia; and *benzene* or *carbon disulphide* may cause delirium.

Acute carbon monoxide poisoning in rare instances leaves behind severe mental disorder of the amnesic-aphasic kind, which may not become apparent until several weeks after the recovery of consciousness. More commonly, it results in a clinical picture almost indistinguishable from hysteria; this may take months to clear up, and is in no wise benefited by psychotherapy. Chronic poisoning by small quantities of carbon monoxide causes neurasthenia.

F. INFECTIONS AND EXHAUSTIVE DISORDERS

1. Infectious Toxæmias

Delirium and a Korsakoff syndrome are the more actue, and naurasthenia the milder, signs of mental disorder due to an infectious fever. In many of the cases, however, in which mental disorder is attributed to "sepsis" or other infection, either the mental changes are unconnected with the infectious process or there has not been an infectious process, as is often found when one inquires into an alleged attack of "influenza" and finds it was nothing of the kind. There are three possibilities: the mental changes are mainly due to the infection; they are independent of the infection; they are partly due to the infection and partly to other, usually constitutional, causes. The depression that occurs in and after many infections is usually of the third category mentioned; delirium instances the first possibility; and the second is often exemplified when some non-organic syndrome is put down to "latent sepsis" in the bowel or the tooth socket or some rather inaccessible cavity. It is not that infectious toxæmia is always innocent of doing this sort of psychiatric harm, but that it is far too often charged with the offence when it is blameless.

Wherever a delirium or other mental disturbance of one infection differs from that of another, *e.g.* the delirium of typhoid from that of pneumonia, the difference lies only in the severity and duration of the physical effects of the intoxication and in the peculiarities of the affected person; no mental symptoms specific to any one infection can be demonstrated. Among the individual peculiarities just mentioned must be included a constitutional

predisposition or readiness to respond with symptomatic psychoses to mainly physical ills.

There are a few infections that hardly ever cause mental disturbance, *e.g.* tetanus and diphtheria; others do so by their local cerebral incidence, *e.g.* malaria or encephalitis lethargica. *Tuberculosis*, from its chronicity and its occasional incidence on the central nervous system; has a special position. Its treatment, moreover, especially in the pulmonary form, necessitates an abnormal, unsatisfying life for a time, and this with the toxæmia seems to be responsible for euphoric or anxious restlessness in which erotic tendencies and irritability are often prominent. Spes phthisica is partly attributable to toxic euphoria, in part it is a form of over-compensation for fear.

2. Exhaustion and Inanition

These, especially if conjoined with some shattering experience—an earthquake, an invasion, a bereavement—bring about severe mental disturbance, *e.g.* a twilight-state or a delirium. *Hemorrhage* and cachexia may be responsible for "light-headedness," as in advanced carcinoma, or after a severe operation.

G. METABOLIC, ENDOCRINE, AND VISCERAL DISEASE

1. Metabolic Disorders

Various metabolic disorders can similarly, *i.e.* non-specifically, affect mental health. *Diabetes*, for example, which is especially frequent in families with a predisposition to affective psychosis, may be accompanied by transient phases of depression, anxiety or excitement which correspond to changes in the blood-sugar level, or a ketosis may be ushered in by mild delirium. A diabetic pseudoparesis, with peripheral neuritis, may cause slight difficulty in diagnosis. In children, insufficient carbohydrates may be responsible for anxiety, naughtiness, and other disturbances of behaviour. Anomalous psychic states may be produced in the rare condition of hyperinsulinism, and be mistaken for hysteria or an anxiety state of the psychogenic sort. *Gout* may occur in people predisposed to affective disorder; often a depressive phase precedes an attack. Alkalosis and anoxæmia may each be the cause of mental disturbance of the organic type. In *pernicious anæmia* there may be symptoms, *e.g.* an acute confusional state, referable to the structural changes in the central nervous system, but more often depression occurs without "organic" features; mania can also occur, and in some cases a chronic paranoid condition. The more "organic" the picture, the poorer the prognosis for a return to mental health. Of deficiency diseases *pellagra* is the one most commonly productive of mental disorder. It must be remembered that a long-standing anorexia, of psychogenic origin, or occurring in the course of a chronic melancholia, may itself lead to a pellagroid condition, so that the symptoms of mental disorder will then be those of the original illness plus those due to the deficiency. The clinical picture is sometimes very like that of hysteria; or the usual organic

syndromes may be produced, especially florid confusion with perhaps hallucinations of fire.

In the metabolic disorders just mentioned the physical phenomena are relatively coarse and obvious. It is in some cases proven and in others highly probable that less obvious metabolic disturbances are either among the primary symptoms of "functional" mental illness, or are its pathological basis. The acid-base equilibrium and the electrolytes of the blood, the metabolism of carbohydrate, fat, and protein, and the chemical regulation of the vegetative activities are all, in such forms of mental illness as schizophrenia and mania, subject to changes which have not as yet been used in the pathology or treatment of these conditions, because the findings are not sufficiently constant or specific; it is also likely that our methods of investigation are not delicate enough.

2. Endocrine Disorders

These play a more prominent rôle in the investigations than in the clinical practice of psychiatry. Many endocrine preparations have, it is true, been administered to schizophrenic, sexually perverted, and melancholic patients, either empirically or in accordance with a premature and ill-devised theory, but the good results of all this are negligible. Œstrin treatment of menopausal neuro-vegetative symptoms is a rational procedure. The blind use of the endocrine glands in the theory and practice of psychiatry has had its day.

Exophthalmic goitre is more prone to occur in anxious, nervous people, especially after some sudden shock. The usual concomitants—restlessness, tension, irritability, difficulty of concentration, and liability to sudden changes of mood—may be complicated by a definite mania or depression and, if the disease be severe or advanced, delirium and confusion may supervene. Though such organic syndromes mean as a rule a bad prognosis, they sometimes clear up dramatically after operation. The interaction of constitutional and psychogenic factors with the actual thyrogenic intoxication makes some treatment of the anxiety by psychological as well as other methods desirable in many cases of exophthalmic goitre, either as a preliminary or supplement to partial throidectomy.

In adult *myxœdema* the slowing of mental activity may sometimes be accompanied by a chronic paranoid psychosis, or there may be a phase of excitement with hallucinations; the variety of syndromes that can occur is referable to pre-existing constitutional tendencies and to the varying severity and rapidity of development of the thyroid deficiency. An apparently "functional" syndrome may precede the overt myxœdema.

Juvenile and congenital myxœdema is described elsewhere (see p. 495).

Tetany may be signalised by epileptiform seizures, or there may be a proneness to psychogenic fits; thus the patient may spontaneously overbreathe until a sufficient disturbance of calcium, etc., results in an induced convulsion. Hysterics sometimes use hyperventilation in this way to induce a passing tetany. In severe tetany a resistive lethargy or an excited incoherent confusion may occur.

Pituitary diseases are more often accompanied by mental symptoms that are a comprehensible reaction to the physical symptoms than by organic syndromes; the latter when they occur may be due to increased intracranial

tension. In acromegaly, depression, reserve, touchiness, and irritability are not surprising, though some acromegalics remain cheerful as long as their disabilities are moderate, and sometimes there is a blindness to the disease, a lack of insight, even when it is advanced. In dystrophia adiposo-genitalis a rather childish placidity may be met. In adiposis dolorosa depression may be severe, or hysterical symptoms may develop. Simmonds's disease may be accompanied by depression, severe anorexia, reaction to the psychosexual disturbance, and, in the later phases, by organic syndromes due to the cachexia. Similarly, disorders of pituitary function have been found in some cases of "anorexia nervosa." In Cushing's basophil syndrome depression and other mental disturbances can occur: we have seen a severe paraphrenia develop during the course of the illness.

Addison's disease is accompanied by a neurasthenia of which for a time the physical basis may be quite overlooked (as may also occur in myasthenia gravis); in the later stages delirium has been known to occur.

Sexual epochs may in women be associated with mental disorder of the organic type, *e.g.* some psychoses of pregnancy and the puerperium. During pregnancy plain psychosis is rare, but hysterical symptoms, depression, and anxiety are fairly common, especially if the mother is reluctant to have another baby; a gross psychosis may, however, break out during the latter months of pregnancy. The organic mental syndromes may develop along with polyneuritis, eclampsia, or chorea gravidarum. Termination of the pregnancy is called for on account of the mental condition when there are symptoms of organic psychosis which are likely to get worse, a history of suicidal attempts or infanticide in connection with previous pregnancies and a depression again in this one, or if on other grounds there is a clear risk of suicide or other untoward result of the mental illness, should pregnancy continue. The decision is often a very difficult one, requiring an expert knowledge of psychiatry for the careful appraisal of ætiology and prognosis essential in every case. The question must turn mainly on the therapeutic value of terminating the pregnancy, so far as the mother's mental state is concerned, as well as upon the stage of pregnancy reached.

In the puerperium "functional" psychoses often develop in predisposed women; if there be septicæmia as well, a confusional state or a delirium, followed by a period of neurasthenia, may occur. In many cases the delirious puerperal psychosis clears up in a week or two; the more endogenous varieties have sometimes a less satisfactory outcome than their form and onset suggest. Infanticide may occur in a puerperal psychosis, especially if the mother has, while pregnant, felt resentful at having a baby or been troubled by murderous preoccupations, *e.g.* obsessions. Psychoses of lactation are rare, and seldom of the organic type. Menstruation is apt to be associated with depression, irritability, and languor in many women, especially during the few days before the period begins; there are no menstrual psychoses, but the liability to suicide and to psychopathic reactions is somewhat higher at this time. Puberty and the climacteric are periods of stress during which schizophrenic and affective disorders may occur. The effects of castration are dependent on the age at which the gonads are removed: intellectual development is unaffected, but the emotional and conative activities of those castrated in adult life may be impaired. Neurasthenic symptoms are frequent, and in women anxiety symptoms may appear.

3. Visceral Disease

This may be directly responsible for mental disorder of the organic type. Thus *cardiac* disorders predispose to an anxiety, which at night may take the form of mild delirium, with restlessness, terror, disorientation, and auditory and sometimes visual hallucinations. With improvement in the circulation, the mental symptoms disappear, or remain only as a moody unrest. Reference has already been made to arterial hypertension (see p. 1829). The connection between *alimentary* disorders and neurasthenic states is well attested, and is striking in children. Jaundice may be accompanied by severe depression, but seldom leads to delirium, save in the case of acute yellow atrophy. *Uræmia* may disturb consciousness greatly, in the form of any of the organic syndromes, from a twilight-state to a euphoric dementia; a Korsakoff condition can occur, but is infrequent.

H. MENTAL DEFICIENCY

As already stated, there is nothing in principle to separate these from other forms of cerebral impairment save that they occur at an earlier stage of life. As with mental disorder, they shade into normality so that no man can say where stupidity ends and feeble-mindedness begins. Again, as with mental disorder, the same clinical picture may be due to a variety of causes ranging from heredity to trauma. They are, moreover, delimited rather by social than by other criteria, and they are not definitely associated with any constant pathological findings. In that they are capable of only limited improvement when well established, and that the intellectual functions are more obviously damaged than any others, their similarity to dementia is easily seen. They are not by any means cases of purely intellectual defect; they represent, it is true, one extreme on the scale which has people of great intellectual ability at its other end; but they are also examples of a general impairment of mind, affecting the emotional and conative functions, and often associated with a more general impairment of the whole organism, which may be seen in its physical structure. Since the milder forms are indistinguishable (except on an arbitrary reckoning) from what may be termed normal stupidity, it is difficult to use rigorously the official definition of mental defect, as a condition of arrested or incomplete development of mind existing before the age of 18 years, whether arising from inherent causes or induced by disease or injury; but the description is serviceable. It should be recognised that, just as "psychosis" differs from "neurosis" only in a rough social sense, turning on the need for special care; and "neurosis" from "normality" only in respect of the limitations the former imposes on one's daily life as a social organism, so does the distinction between normality and feeblemindedness, and between gross or certifiable deficiency and the lesser forms, turn on the social adaptation of the person in question. To complete the points of similarity there is recognised a "moral defectiveness," which has its parallel in some kinds of "psychopathic personality." The effects of encephalitis lethargica, parenchymatous

syphilis, and thyroid deficiency upon the mental state and development at different ages, or the varying results of amaurotic familial idiocy in the infantile and the delayed juvenile form, illustrate how important is the stage of growth or maturity at which damage is done.

Ætiology.—The common division is into primary and secondary, though an alternative distinction has been proposed between those who represent the lower extreme of normal variation (the " subcultural " group) and those in whom a gross structural pathology is discoverable. The primary or hereditary group is a large one, making up approximately three-quarters of all cases of mental defect. This is an estimate arrived at by independent workers, but likely to be changed as we acquire better methods of determination and subtler views of the interplay between environment and heredity. The grosser the deficiency the less important the hereditary factor, except in some rare well-defined anomalies, such as amaurotic idiocy. Familial concentration of a given form of defect is specific for each clinical type. Dominant inheritance is more evident in the families of simpletons than of idiots. An incompletely dominant single factor or a combination of several genetic factors may be responsible. The mode of transmission of amaurotic familial idiocy and of phenylketonuria is recessive ; that of epiloia dominant.

The environmental causes are prenatal (*e.g.* mongoloid idiocy), congenital, or infantile (*e.g.* birth injury to the brain, meningo-encephalitis, hydrocephalus, cerebral syphilis). Various poisons and deficiencies may be responsible, as in the well-known instance of cretinism, as well as certain malformations of the cerebral tissue, *e.g.* microgyria and porencephaly, and of the cranium, *e.g.* oxycephaly. Sensory defects, as in a deaf-mute, may greatly impair mental development. It is possible that some cases of schizophrenia beginning in the first few years of life are indistinguishable from mental defect and are diagnosed as such ; in more general terms, it may be said that the mechanisms commonly implicated in the adult illness schizophrenia may be those chiefly affected from the beginning in some cases diagnosed as mental defect.

Pathology.—In many cases there are no significant findings ; this is particularly the case with high grade defect. It is probably impossible from the histological appearances to infer the extent of hereditary or exogenous causation. Developmental anomalies, such as general hypoplasia and macrogyria may, however, be mingled with evidences of a past lesion, as in porencephaly or hemiatrophy, or with signs of a disease actually present, as in amaurotic idiocy, cerebral lues, and tuberose sclerosis.

Symptoms.—The customary classification is into idiots (who are too defective to be able to guard themselves against common physical dangers like falling into the fire), and imbeciles and feeble-minded persons (who need to be looked after because of their incapacity to manage their affairs or to profit by instruction). Imbeciles cannot earn their living ; the feeble-minded cannot get on in an ordinary school, but may learn a good deal in a special school and be able to earn a living. The criterion is in each case mainly a social one ; the same is true of " moral defect," *i.e.* mental defect coupled with strong vicious or criminal propensities. Although these terms are defined in an Act of Parliament, they are vague and of administrative rather than medical use. At attempt has been made to render

them more precise by psychometric means: the customary tests for mental age are applied, and if the subject's intelligence-quotient $\left(\frac{\text{mental age}}{\text{actual age}} \times \frac{100}{1}\right)$ be less than 20, he is called an idiot; if it be between 20 and 50, an imbecile; if between 50 and 70 feeble-minded. It must, however, be recognised that though mental defect is mainly a matter of intellectual capacity, it is not solely this, and that intelligence tests, however valuable and trustworthy, cannot give a complete indication of the degree of mental defect. Even the intellectual defect may be uneven, showing much more in some tasks than in others, and it would be an error to suppose that a mentally defective person with a mental age of, say, 9½ years is mentally in the same state as a normal child aged 9½ years.

The *physical* symptoms are chiefly due to lesions of the central nervous system: birth trauma may have led to paralysis, spasticity, athetosis; or there may be evidence of an inflammatory condition of the brain and its membranes, as from syphilis. The whole clinical picture may be greatly coloured by the motor disturbance, *e.g.* continual rocking and twisting movements, grimaces, and abnormal posture. The special senses may be affected, as the result of an independent anomaly, *e.g.* coloboma, misshapen ears; or from a common cause, *e.g.* interstitial keratitis, the retinal changes of amaurotic idiocy. It is dubious whether the "stigmata of degeneration," such as a "Gothic" palate or a Darwinian tubercle, occur any more frequently among defectives than in the rest of the population: at all events, there are none that can be used diagnostically, except in the case of mongoloid idiocy. There are, however, some correlations between somatic anomalies and mental defect. Thus, there are more physical defects among these people than in the average population, and this becomes more evident as one looks lower in the scale of mental defect, in which skeletal and cardiovascular anomalies may fairly often be found, sometimes, but not always, due to thyroid or pituitary disorders. The mongoloid variety is described below.

The *mental* symptoms are lack of intelligence and of the normal exercise and control of primitive tendencies. This may be extreme, as in idiots, who cannot be taught to feed themselves and keep clean or who can only just recognise their companions and make their elementary needs known—they are, indeed, much less intelligent than an animal. Imbeciles are usually incapable of learning and remembering any but very simple matters. They may, however, be able to do automatically what they cannot understand or put to independent purpose: thus, "idiots savants" are especially clever at doing mental arithmetic, recalling dates and other such operations. What imbeciles manage to learn they cannot utilise in any but the most familiar circumstances. Abstract concepts are too hard for them, and their judgment is as poor as their grasp or awareness of what is relevant in any situation. Though in many ways suggestible and accessible to flattery, they may be obstinate and egotistical, and readily fall into antisocial courses, *e.g.* prostitution, vagrancy, crime. Crude sexual offences or murder may be committed as lightly as some minor deception. The personality of imbeciles varies widely: some are docile and kindly, others rough or deceitful and vindictive. It depends much on their upbringing. It has been found that in satisfactory conditions only about 8 per cent. of defectives show antisocial or

troublesome behaviour. But though the deviations of personality may not lead to delinquency, it is common to find in mentally deficient persons defects of temperament and character, as well as of intelligence, which are reflected in social inefficiency. This is most important in the feeble-minded, who have intelligence enough to learn an occupation; whether they can earn their living by it will depend on their character and the way they have been brought up.

Many persons who are high-grade defectives, when measured by formal tests, are not taken to be such because of their social adaptability, their fluency and capacity for keeping their head above water as long as economic and other stresses are light. There are instances of people classed as mentally defective during childhood, because of their backwardness in school and their low score in tests, who later in life amass money by their own efforts, or even hold a responsible position. A majority of high-grade defectives, however, live dependent and often troublesome lives; at most they do simple repetitive work. Many of them are unstable creatures, whose psychopathic personality may be sufficiently antisocial for the term "moral deficiency" to apply to them. Hysterical trends may show themselves in crude phenomena, *e.g.* convulsions, counterfeit insanity or fantastic lying; and religious and artistic pretensions may take in gullible followers and even lead to the founding of ephemeral movements.

Defectives are prone to disturbances of mood, sometimes arising out of awareness of their inferiority and its social consequences. Sudden outbursts of excitement may show similarity to manic or catatonic hyperkinetic states; they may be accompanied by a paranoid hallucinosis, mainly auditory, which clears up with startling rapidity in a day or two. In respect of these psychotic episodes, defectives are like epileptics and juvenile encephalitics, in whom a cerebral impairment has likewise occurred before the attainment of maturity. Some of the morbid phenomena, especially in idiots, are very similar to the disorders of motility seen in schizophrenics, because, it may be assumed, the same bodily mechanisms are implicated.

The *mongoloid* type of idiocy is characterised by striking physical features. Probably the outcome of intra-uterine conditions, it is most frequent in last-born children in a large family, or in children born of elderly mothers; parental syphilis may occasionally be the cause. In many cases the brain-stem and cerebellum have been disproportionately small, and other signs of maldevelopment have been reported. It is likely that hereditary factors of a recessive nature also play a part. The condition is usually present from birth; physical growth is slow, and has stopped by the time the child is fifteen. Defective growth of the skull, leading especially to abnormalities of the base and the orbit, are responsible for the peculiarities of cranial shape. The pituitary gland has been reported as showing an increase in eosinophil cells and deficiency of basophil cells. The appearance of these usually happy idiots and imbeciles is rather suggestive of a Mongol or of a fœtus. The skull is small and round, and the junction of occiput and back of neck flat; an epicanthic fold across each inner canthus, narrow tilted eye-slits and lids without lashes, red cheeks, fissured and often protruding tongue, stubby depressed nose with nostrils looking forward, irregular late-appearing teeth, coarse hair on the scalp, small facial bones and occasional neurological anomalies, such as nystagmus, make the head of every mongoloid a disagreeable but ready

index to his disorder. That the disorder is a general one the rest of his body testifies; his limbs are lax and over-mobile at the joints; he has broad, clumsy feet and hands, with short fingers and a crease running straight across the palm, protuberant belly and low stature; and perhaps a congenital cardiac lesion. The similarity in a few respects to juvenile myxœdema, and the occasional concurrence of the two conditions sometimes make differential diagnosis difficult; not all of the signs here mentioned need be present in any one case. On the mental side, there is a liveliness and amiability not often seen with so much intellectual defect: the patients like music and little jokes of a primitive sort; they will imitate gestures, but seldom learn to speak properly with their rough harsh voices.

The forms of deficiency due to *thyroid insufficiency* and *cerebro-macular degeneration* are referred to elsewhere (pp. 1844 and 1624). *Epiloia* is the name given to the rare condition in which tuberose sclerosis of the brain, adenoma sebaceum and tumours of the kidney and heart may be associated; epilepsy is common, and there are gross mental disturbances. *Gargoylism* is a rare chondrodystrophy, with hepato-splenomegaly and mental deficiency. *Phenylketonuria* may be recognised by the characteristic metabolic disturbance. It is a hereditary disorder, due to a single autosomal recessive gene.

Diagnosis.—Recognition of gross mental deficiency calls for no skill. The degree and kind of impairment, however, and the somatic variety or cause have to be worked out in every case. The latter problem—a minor one, except in the case of juvenile myxœdema and syphilis—is to be settled by careful physical examination and inquiry into the history. The former is a matter of assessing intelligence and social aptitude.

The assessment of intelligence is nowadays a matter of giving the patient tests which have been standardised on average samples of the population. What is average or normal at a given age is therefore known, and the defective child's performance can be compared with this. The most popular and serviceable tests are modifications of those put forward by Binet and Simon in 1908. As these may give a rating that depends unduly on the child's educational opportunities and facility in language, and may not indicate special abilities, *e.g.* in mechanical matters, many other tests have been worked out which supplement or, in certain cases, replace the Binet scale. A child under the age of 5 cannot be satisfactorily dealt with by the Binet tests, which moreover have only limited value for measuring the intelligence of adults. It is difficult to agree about what in a normal child must be regarded as the limiting age at which he becomes of adult intelligence; it is generally taken as 14 or 16 years. In all tests the emotional state of the subject is a factor that influences his performance. The emotional reactions to being tested must be taken, along with responses to more familiar situations, *e.g.* at home or at school, as evidence of the soundness or instability of the child's personality; by such criteria must be judged the social development of the patient, his fitness for living in the community or being put under lasting surveillance and control.

Treatment.—PROPHYLACTIC.—Eugenic measures are desirable for the rare hereditary conditions, like amaurotic idiocy, and in the case of those imbeciles and feeble-minded in whom genetic rather than environmental causes have been responsible for their maldevelopment and who are capable

and desirous of procreating—idiots do not procreate. Voluntary sterilisation for eugenic reasons has been recommended by a Departmental Committee, but has not yet been explicitly sanctioned by law. Birth control, therefore, is the eugenic measure to be advised in cases in which defectives seem likely to transmit their defect; unfortunately few such defectives can be relied on to observe contraceptive precautions effectively. Segregation may indirectly serve the same end. Well-managed parturition and treatment of parental syphilis are the only other practicable ways of forestalling defect.

Educational and social.—Much improvement may be attained by the training of defectives: it is work for experts. Where there are special disabilities, *e.g.* of the senses, or of such capacities as reading and writing, attention to these may lift the child out of the class of mental defectives altogether. Whether the child lives at home or in a colony or institution will depend not only on the degree of his intellectual and social deficiency, but also on the adequacy of his home circumstances. There are many kinds of provision for the care of the 300,000 defectives in England and Wales, ranging from special schools and statutory supervision to mental hospitals; 40,000 defectives are in institutions and nearly 35,000 are under statutory supervision. Well-run colonies serve to socialize many defectives hitherto vicious or violent, who can then go out and live more or less usefully in the community. Some, however, prove intractable, especially those who have epileptic fits.

Physical.—The bodily disturbances, *e.g.* contractures and paresis, call for orthopædic treatment, which sometimes indirectly benefits the mental state. The treatment of the forms due to thyroid deficiency or syphilis is described elsewhere.

AFFECTIVE DISORDER

This is of three types:

1. Manic excitement and hypomania.
2. Melancholia and mild or neurasthenic depression.
3. Agitated depression and anxiety state.

There is in each case a major and a minor form. Each is related to a more or less characteristic personality, and for each the cause of occurrence may be chiefly environmental or chiefly hereditary. Combinations are frequent (mixed forms), or there may be successive appearance of the different types, often with an interval between the attacks. A benign outcome or periodic course is the rule for the major forms, but not for the minor, which often tend to become chronic. This is partly because the environment can have more influence, whether for good or bad, on the course of the minor than of the major, more explosive and sweeping, forms. It would be a very convenient thing if endogenous cases could be sharply differentiated from psychogenic ones, as in the Kraepelinian scheme, but it cannot be done.

Ætiology.—INTRINSIC.—Heredity is the most constant single cause. Research has been mainly into the major manic-depressive cases. The genetic factor is weakly dominant. It may be that more than one gene is concerned, but this is hard to tell, because the predisposition to an affective disorder may be latent in persons who have not been subjected to the stresses

that would make it manifest, and consequently the usual Mendelian figures are not obtained. The present state of knowledge is illustrated by studies on manic-depressive twins, among whom 69 per cent. of those monozygotic (*i.e.* with identical heredity) were alike affected with the disorder, while the corresponding figure was only 16 per cent. for the dizygotic pairs (*i.e.* with dissimilar heredity). In the 31 per cent. of monozygotic twin pairs who were not alike in respect of mental illness, the difference must have lain in the environment, thus showing the relative importance of external factors in causing the inherited tendency to become manifest. Although not manifest as illness, the inherited tendency may express itself in bodily and mental constitution.

The bodily habit that is found in a majority (not the overwhelming majority) of those with affective psychoses is called "pyknic." It is best seen in men after the age of 30. It is characterised by large visceral cavities (head, thorax, belly), a tendency to fat on the trunk, slender shoulder girdle and extremities, stocky build, a broad face on a short massive neck, thick receding hair and, later, baldness, venules on the cheeks, and a disposition to arthritis, gout, diabetes and especially arterio-sclerosis. As this John Bull build is so common in mentally healthy people, it cannot be regarded as a precursor of mental illness, but only as an indication that some of the constitutional and genetic causes, or biological requirements, for affective psychoses are present.

The same is true of the mental constitution or personality. Here there are several groups, shading off on the one side, by way of cyclothymia and other intermediate forms of mild disorder, into definite affective psychosis, and on the other into normal and stable personality. There are those with a pervading gloominess, pessimism and feeling of insufficiency that spoils their lives; others who are for ever anxious, keyed-up, wondering whether something has gone wrong or will go wrong, and whether it is their fault—careworn worrying creatures; while a third group is made up of the lively, enterprising, confident, sociable people, whose euphoria is patent. Irritability may be found in any of these groups, especially the second and the last. Contrasted or different features are often found mixed in the same patient. The most striking characteristic of the personality of manic-depressive patients is their ready responsiveness and lability of mood; they fluctuate with their surroundings, and in many instances pass suddenly and with small occasion from one mood into another far removed from it.

The signs of affective illness may appear in childhood, though major outbreaks of mania, depression or agitation are rare before puberty. When these occur, the phases are usually brief and the environmental influences strong. Milder forms are often regarded as normal, since night-terrors and other fears, mischievous gaiety and sulky gloom are all familiar enough in children; it is the degree, occasion and persistence of the affect which must decide whether it is morbid.

The psychological crises of puberty are only occasionally affective—chiefly self-reproachful depression or agitation—but during adolescence the illness becomes more frequent; it seldom, however, calls for mental hospital care. Each menstrual period may be accompanied by depression or restlessness, usually coming on about two days before the period. In the

third decade of life the number of cases steadily rises, and there is another peak in frequency between the ages of 45 and 55. The latter, "involutional," cases show the influence of age strikingly, so much so that they are often considered as separate disorders.

There is little to choose between the curves of age incidence for morbid depression and morbid anxiety of whatever degree; for mania the frequency is highest before the age of 30, as also for affective illnesses with a strong confusional flavour. Pregnancy is frequently accompanied by depression and agitation; psychological factors are mainly responsible. After childbirth, though there be no septicæmia, affective illness can occur, running a typical and often lengthy course.

The female climacteric is a time when anxiety usually mounts, and is accepted as an ineluctable effect of "the change." It may become definite illness, persisting even for two or three years. It is doubtful whether there is a specific connection between the endocrine causes of the menopause and so-called climacteric insanity; the melancholia then coming on is like the melancholia of five or ten years later, or the melancholia of middle aged and elderly men in whom the endocrine changes are not the same. The influence of sex as a whole is obscure. Women have this illness more than men, though the manic form is relatively more frequent in men. The reactivity is often greater and the syndrome less clear-cut in women.

There are geographical differences, sometimes thought to be racial, in the incidence, but the little that is known points to environmental rather than intrinsic causes for this. It has been suggested that affective psychoses are commonly linked up with high intellectual gifts; another says they have affinity with mental defect. The former statement has much better support than the latter, but both probably are fallacies depending on the material selected for study.

EXTRINSIC.—*Physical.*—Chronic toxæmia and acute infections, especially influenza and pneumonia, can be responsible for the illness. Various drugs help to heighten the anxiety to a morbid degree, *e.g.* alcohol in certain circumstances, insulin, or hyoscine. Cerebral trauma may provoke an attack. The list of physical factors could be much added to, but it must be borne in mind that wherever a distinctive, rather than incidental, physical cause can be found, the condition passes over into the category of organic psychoses. The most difficult cases in practice are those in which there is a question of cerebral arterio-sclerosis or exophthalmic goitre; the affective disorders indisputably due to these two diseases may be quite indistinguishable from others for which there is no such organic basis. The problem here is clinical rather than fundamental; since vascular, cerebral, endocrine and autonomic functions are particularly concerned in the mechanism of emotional change, certain disturbances of the physical apparatus will necessarily be accompanied by many of the psychological phenomena of these emotional changes. The depression of paralysis agitans and the anxiety of coronary disease are of the same order. The notion that coitus interruptus and other sexual practices produce anxiety is unfounded, but they may contribute to it by psychological means.

Psychical.—A recent misfortune may be the cause: of such, there is a great variety, ranging from commonplace to tragic. Any calamity to which human beings are liable may provoke an affective breakdown. Sometimes

it is induced by the insanity of a close relative. However trivial it seems to outsiders, the event that has precipitated an affective attack has been felt as a catastrophe by the patient; there are no records of great and sudden happiness causing an affective psychosis. The nearest approach to a specific connection between the precipitating happening and the type of affective illness is seen in the anxiety disorders which follow a terrifying experience such as exposure to shell fire and bombardment from the air; morbid depression following bereavement, financial setbacks or degradation is an understandable response, it is true, but to ascribe the type of response directly to the nature of the experience is specious, since on another occasion it may be with hilarious mania that the calamity is met.

Moreover, the experiences of a lifetime will have determined what calamities are most felt; they need not be calamities in other people's eyes at all. Experiences, spread over years, are the common extrinsic cause of the more chronic neurotic forms of affective illness: this applies least to chronic hypomania. In these chronic conditions the patient's own behaviour has so much to do with what happens to him, as it were, from outside that to separate extrinsic from intrinsic is very hard.

Pathology. — The *physiological* changes are characteristic only of emotional disturbance, not of morbid emotional disturbance; and therefore they are not of diagnostic value. They consist in lability of blood-pressure and pulse-rate, abnormal motility of plain muscle, especially in the alimentary tract, carbohydrate disturbances, variations in either direction of the rates of salivary and other secretions, and decreased psychogalvanic activity. The changes are variable from patient to patient and are not always discoverable. More significant are changes in basal metabolism, weight, sleep and menstruation; loss of weight is the rule during the illness. Irregularity of menses and then amenorrhœa often occur. Hypercholesterinæmia, rise in the blood iodine content, changes in the K/Ca ratio, and diminished cellular respiration have been alleged, not as yet conclusively.

The *psychological* changes, in spite of great external differences, have the following in common: the morbid phenomena are in accordance with the prevailing mood, though not wholly derivable from it; thought is less purposively directed to impersonal ends than it would normally be, but more purposively to personal ones; there is a small number of topics of preoccupation in each patient, but his ways of arranging and embellishing them can be many; the whole body (or parts of it) often receives much of the patient's attention, because of more or, it may be, less feeling in it (hypochondria, depersonalisation); misconstructions abound, with consequent ideas of self-reference and persecution as well as misidentification; and there is a feeling of inner tension, unrest and excitement, however apathetic or care-free the patient's demeanour.

The seemingly greater quickness and capacity of manic patients has not been confirmed by psychomotor, intellectual and association tests; hypomanic patients sometimes, however, do better than in their normal state. This can be compared to the effects of increasing doses of alcohol. Patients with affective disorder are more irritable and excitable than is normal. Time appreciation may be grossly disturbed: personal time seems to pass very differently from clock time; time may seem to stand still; no future is conceivable. Perplexity may be conspicuous, and explanations of this

in terms of Gestalt psychology, conditioned reflexes, and toxæmia have been proffered.

The effects of experience in bringing about this illness cannot be explained in terms of a logical and coherent system, unless one accepts the premises of that system and infers what cannot be observed. Consequently, as there are several such psychological systems, there are several explanations. They state the conjectured ways in which instinctual energy or libido may become misdirected because of environmental conditioning, frustration and loss. It is possible to eschew such conjectures and at the same time to see the conditioning, the threats, frustration and loss that have understandably brought the patient to an excess of sadness, excitement or fear.

Symptoms.—SYMPTOMS OF MANIA.—There is excitability of mood and movement. The *mood* is mostly one of jollity, rather infectious, but likely to become boring or overbearing; occasionally it turns to anger and resentment. It is labile; tears will flow readily on some trivial occasion, to pass into laughter in a twinkling.

Thinking is apparently rapid. There is flight of ideas, with successive words and phrases loosely connected only by similarities of sound or chance associations. Consequently, the patient wanders from the point; whether he can come back to it depends on the severity of his condition. Jokes, self-praise, flighty comment on his surroundings, and facile optimism make up the tenor of his exuberant conversation. Nevertheless, the number of topics he touches on in the course of the day is often more limited than if he were in normal health: he reverts to a few matters over and over. He may criticise himself, with cynical bitterness or humour, as he criticises others; he may talk a lot about bodily disturbances, *e.g.* his varicose veins or his sore throat. His mood and expression are consonant with what he says. He is distractable, herein seeming at the mercy of his sensations and of every small detail, whether it be inside himself or, as is more common, connected with things about him. Judgment is impaired.

Delusions are less common than *distortions* and misstatements. People are wilfully called out of their names, events misrepresented, bodily sensations exaggerated, and accusations of ill-treatment or persecution irresponsibly preferred and sometimes long persisted in. The more confused and excited the patient, the more likely to be deluded and even hallucinated. Most of the seeming hallucinations are *façons de parler* or illusions; sometimes the patient is, as it were, pretending or acting the part of a hallucinated person.

Activity is exaggerated, and in severe cases incessant. Its object may change from moment to moment, but sometimes the main end is kept pertinaciously in view. The patient, if tactlessly thwarted, gets angry, sulky or violent. He feels very strong, and seems untiring. He has many schemes, of an optimistic cast, and, in the course of putting them into action, may be extravagant, inconsiderate or interfering. Sexual excesses or drunkenness may occur and bring much harm, especially when the patient is a young woman. Troubles with the police arise through silly pranks or self-confident exploits.

Sleep is brief but deep. In the early and mild stages the patient looks exceptionally well, but after weeks or months of over-activity and little sleep he looks exhausted, with sordes on his lips, hoarse voice, drawn skin and perhaps less total activity but many unfinished little movements. Food is

welcomed in the mild stages; when the activity is great, the patient does not give himself time to eat, but plays with his food or is continually diverted to something else. Sexual desire is at first heightened but potency less.

The symptoms vary widely in degree. Mild hypomania may be an enviable time of well-directed expansive energy, unencumbered by some habitual restraints; gross mania may be a delirious, hallucinatory condition, with incoherent talk and little free activity.

Symptoms of Depression.—In the early stages or milder forms, the patient finds concentration and recollection difficult, he has less interest and pleasure in life, he feels that this world is unreal and himself changed, he dreads effort or responsibility.

The *mood* is one of grief and misery, looking in every direction for material to feed on. The past supplies peccadilloes or graver lapses; what is wretched in the present is dwelt on inordinately; the future is foreseen as hopeless ruin. Anxiety is mixed with it, often in extreme degree. Weeping is less common in the extreme forms. The patient's expression usually conforms to his affect.

Thinking is more difficult. This " retardation " in thinking shows itself as incapacity to deal quickly and purposively with impersonal topics, while brooding on personal matters goes on, with a press of inner activity, a ceaseless roundabout of painful thought. The making of decisions is dodged. Conversation may become meagre, even monosyllabic, though some patients are ever ready to tell their troubles. The content of their thought is sombre—the product of ruthlessly unfair examination of their frailties and misfortunes. Some criticise themselves remorsefully or with cynical detachment; some bewail their losses; others abandon themselves to resigned and world-shunning despair. There are many varieties of misery, and melancholia knows them all—as many varieties as can be made from the experiences, character and imagination of a human being. Consequently they reflect the moral, economic or hygienic standards of what is good and bad that are imposed on us by modern society and our particular education.

Delusions occur in proportion to the depth of affect; they are the extreme form of the doubts or preoccupations just mentioned. Patients often fluctuate between uncertainty and conviction about their troubles even during the same day or the same conversation. Insight may be good and judgment sound, when the affect is not overwhelming. The delusions are the product of the depression, which is primary; they are not its occasion, though often adduced as that. Most of them concern the future as well as the past; anxiety is prominent. Wickedness to be visited with damnation; secular crime to be punished in this world; loss of property that will mean starvation and beggary for one's family; mortal or corrupting diseases—these are the common substance of delusions and are often commingled. For example, some patients blame themselves for having caught venereal disease which will expose them to the loss of their job and of their hope of salvation, exclude them from decent society, and do loathsome damage to their bodies; no evidence, no argument shakes the erroneous belief. The delusions may be grandiose in that the patient affirms himself the chief of sinners, no one has ever been as wretched or wicked as he, he alone has done the unpardonable sin; or they may be of a minimising sort—nobody cares about him, he is of no account, let him go into a corner to hide, people despise him. This last

belief is often understandably associated with ideas of reference or persecution —people make contemptuous gestures or remarks as he passes, they set detectives to watch him, they tell each other how bad he is. He accepts this almost always as his desert, though occasionally there may be overt resentment. Apart from this resentment, his beliefs derive understandably from his affective state. There are, however, features that betoken undercurrents at variance with the professed attitude or delusions. Thus many depressed patients, professing humility, are importunate in their demands on those around them.

Such hallucinations as occur are in keeping with the patient's affect and are of much the same nature as the delusions, though expressed more in perceptual terms. People are making derisive remarks, his body gives off foul smells, food has a different and disagreeable taste—it is often the mode of expression rather than of subjective experience that decides whether these are hallucinations or delusions. This is notably the case with bodily preoccupations, when, for example, patients report their food to be stagnating in their belly, their skin dull or fetid, their eyes impaired, their head empty. Much of this depends on depersonalisation, in which the body as a whole feels bereft of life and feeling, and emotional deprivation or emptiness is translated into bodily experience. In mild forms of depression there is no question of delusion or hallucination, and often no recognisable content to the gloom; the patient cannot say why he is sad. In the more chronic forms a settled and partly justified conviction about ill-health, present troubles, and the dark future prevails; the ideas may be obsessional and partly divorced from the prevailing affect.

Activity is limited, thus contributing to the "retardation." The more severe the depression the less does the patient do, unless the concomitant anxiety makes him restless. It is possible, however, for a patient to be depressed without "retardation." In typical cases facial expression is rather fixed and movements delayed, as though done against resistance; more or less complex activities, dressing, say, or writing a letter, take unduly long. The most extreme form is stupor or lack of all spontaneous activity; it is seldom absolute. Patients rarely become wholly indifferent to cleanliness in defæcation and micturition.

Suicide is the greatest danger in depression. Whereas manic patients thoughtlessly do themselves harm or get into a fight but do not try to get hurt, depressive patients are often bent upon doing away with themselves. The risk is not proportionate to the degree of depression; many very retarded and melancholy patients make no attempt, while in depersonalised mild cases a fatal outcome is not uncommonly brought about thus. There is consequently much risk during the phase of improvement—often more risk then than during the preceding severe "retardation." Deliberate self-mutilation is rare.

Sleep is bad—hard to come by, light and unrefreshing. The *appetite* is bad too: food may be constantly refused for this reason. Commonly also the patient eats too little because of feelings of fullness and other discomfort in the abdomen, or because of delusions about his bowels or his food. Mild constipation is common, but is often given much exaggerated importance by the patient. The *weight* diminishes, chiefly, but not by any means wholly, because of insufficient intake of food. Daily fluctuation in the general condition, with improvement towards evening is common. The skin may be dry

and sallow, and in some severe cases pigmented, as it is in pellagra. Menstruation may lessen or cease; sexual desire is much less.

Here, too, there are wide variations, between the mild "neurasthenic" and the grossly deluded melancholic who craves death. There is every gradation between the two extremes, and a single case may during its course exhibit them all.

SYMPTOMS OF ANXIETY.—The *mood* ranges from uneasiness to panic-stricken terror. It may be an abiding or a recurrent state. Though chiefly turned to the future, as fear must always be, it rests on past experience, often painful and largely repressed, and it reverts to the past to account for the troubles in store. Herein, as with rationalisation and some other psychological devices, there is evident a strong desire to make things understandable in a causal nexus—a tendency to be found not only in patients but also in those who observe them. The patient's expression varies with the strength of his fear.

Thinking is troubled, the disorder showing itself in speech somewhere between frightened dumbness and the voluble talk that seems designed to cover up embarrassment and disquiet. The patient can seldom follow a train of thought for long without a limited number of preoccupations forcing themselves in. How far this interferes with daily life or set tasks depends on the amount of anxiety, as does also the impairment of judgment and insight. The content of thought is as manifold as in depression, every normal matter of human concern enters into it. Fears centring strictly on a few special topics, *e.g.* the fear of being run over in the street, may be to the fore; the fear of insanity is particularly common.

Delusions are frequent in the grosser forms, which are most strikingly though not exclusively seen in patients of late middle life. They may say that their bowels are stopped up and their bodies about to rot; their enemies are waiting to tear them to pieces; their families will be tortured; their names abhorred for ever. Hell, they are certain, awaits their souls though their bodies cannot die; time stands still and no redemption is possible. There are many delusions less extreme than these mainly hypochondriacal and nihilistic ones; *e.g.* beliefs that employment will be unobtainable, or that the patient will be victimised for having had such an illness. Hallucinations can occur: at the height of fear every sound and sight and smell may be misinterpreted as meaning some pain to come; but most of this is illusional colouring of actual percepts. Depersonalisation is common with all degrees of anxiety.

Activity is much disturbed. There may be sudden attacks of panic in which the patient rushes blindly out into the open, or aimless wandering, ceaseless agitation, with movements especially at the small joints—wringing of the hands, rubbing the face, picking at sores, pulling out hair. Starting many tasks and finishing none is as characteristic of anxiety as of mania. Anxious people are distractable: their eyes follow a trivial movement—a fly walking on the window-pane—though they only comment on it when some interpretation that chimes with their mood can be fitted; their ears are sharp for hints of alarm. During an attack of anxiety with strong somatic repercussions (*e.g.* vaso-vagal attack) activity may be completely interrupted—so-called collapse—while the patient, terror-stricken, expects his death; alternatively he may run for air or help. Very agitated patients may

lie or sit in semi-stupor, with starting eyes and parted lips, incapable of speech unless under some strong stimulus.

Suicide is uncommon in those with episodic, highly somatic attacks of fear, and in those with chronic mild hypochondriacal anxiety, but not infrequent in the grosser forms and in those mingled with depression.

Sleep is bad: in the mild forms the patient may be afraid to fall asleep because of his horrifying dreams and the terror into which he suddenly awakes.

Sudden highly somatic episodes of anxiety, vaso-vagal attacks, are common: the patient feels his heart palpitating, his bowels turning over within him, he sweats, his limbs tremble, his mouth is dry, he feels he will fall or collapse or die; he turns pale, his pulse-rate changes, usually becoming more rapid, his blood-pressure rises, he may want to open his bowels or pass his urine. When anxiety is long-standing and severe, such attacks are rare. It is possible for parts of this general affective disturbance to be isolated, and to occur with little conscious anxiety, as in muco-membranous colitis, effort-syndrome, aerophagy, neurotic indigestion, enuresis, impotence, ejaculatio præcox, psychogenic asthma, hyperidrosis. The factors determining such special emphasis on one or other system are partly physical (some organic defect or innate functional anomaly) and partly psychological; in depression a comparable problem would be weeping or constipation. In anxiety thyroid enlargement can occur; weight falls off; menstruation is irregular or ceases; the deep reflexes are very active.

Diagnosis.—Typical cases are easy to recognise. The common errors of diagnosis lie in: (1) Missing organic disease (*e.g.* general paralysis, cerebral arterio-sclerosis); or the converse (*e.g.* mistaking the more expansive manic patient for a general paralytic). (2) Forgetting how mixed the symptoms of mania, melancholia, and anxiety may be, so giving rise to atypical pictures that may be mistaken for schizophrenia, if too superficial an examination or too static and rigid a diagnostic criterion be used. (3) Forgetting the influences of age, general personality, and milieu on the content of a patient's mind, *e.g.* his having lived among spiritualists may lead to deceptively fantastic statements. (4) Expecting to be able to diagnose solely on presenting symptoms, without regard to previous history and constitution; the reverse is also to be avoided. (5) Expecting diagnosis always to lie between distinct entities which could not possibly be mixed together in the same person, as though hysteria were incompatible with affective psychosis, or both of these with schizophrenia; in fact, they often are mingled. This is not to make light of diagnosis, which gives the psychiatrist much knowledge that he cannot gain from study of the individual case before him.

Nothing in the mental state of a patient with affective disorder enables one to exclude an organic basis such as general paralysis or cerebral arterio-sclerosis. This decision must turn on the physical findings. The problem becomes simpler when signs of dementia supervene. (See p. 1825.)

From schizophrenia, diagnosis depends on a picture of the whole illness, on the presence of characteristic thought-disorder, incongruity of affect and bizarreness of behaviour, as well as on the previous personality and constitution, rather than on any positive features of affective psychosis; the remoteness and unconvincing manner of the schizophrenic, so hard to describe but

almost conclusive when recognised, may help. Later, when complaints have become empty and repetitive to the point of stereotypy, and catatonic symptoms mix with the anxiety, diagnosis is easier. As between schizophrenic and manic excitement, the setting in which the excitement occurs is almost more important than the *prima facie* symptoms. In young people schizophrenic features may often be found without their being of much significance; in the elderly what seem to be catatonic features may rest on an organic cerebral basis. The more easily one can get in touch with the patient, enter into his mood and understand what he says and does, the more is it an affective, not a schizophrenic disorder. The range of benign affective phenomena is wider than a textbook description can convey.

There is no need to try to diagnose affective psychosis from psychogenic depression, cyclothymia, anxiety neurosis, neurasthenia, or involutional melancholia; these are only subdivisions of it, in which the age, reactivity, severity, or chronicity of the condition is being stressed. Periodicity is sometimes made the hallmark of affective psychosis; this historically interesting point of view is hard to apply, because so many patients have only one definite attack in their lifetime, and because periodicity can be striking in other conditions, such as obsessional disorder and schizophrenia.

From obsessional disorder the diagnosis may be difficult when there is localised anxiety or depression with sharp content and good insight; so closely alike are the conditions, that eminent authorities would include obsessional disorder also in the manic-depressive group, thus disposing of the diagnostic problem. It is best, however, to keep them distinct, and to discover in a particular case whether the characteristic subjective rejection of the obsession occurred at its first appearance; often the anxious or depressive patient at the beginning has welcomed the thought which accords with his affect, though later he struggles against it and may disclaim it. Genuine obsessions, however, are common in affective psychoses.

Course and Prognosis.—The varieties of outcome and sequence are many. They depend on the balance between particular intrinsic and extrinsic causal factors in each case, and on the extrinsic factors which are brought to bear on it in the form of treatment. The more typical the illness, the surer the recovery in favourable circumstances.

A history of definite affective psychosis in a parent or grandparent points to recovery from the attack, but it is unsafe to infer the course of the illness from hereditary data alone. A well-adapted personality and a pyknic build, a history of similar illness followed by complete recovery, a fairly sharp and fairly recent onset, and precipitation by external troubles which will not be likely to continue are all of them points to the good. Advancing years make the prognosis poorer, but a first attack of involutional melancholia, if there be no vascular disease, eventually clears up in two-thirds of the cases. Bodily symptoms are often the best indication of coming recovery. Improved appetite and regularity of the bowels, cessation of anxiety attacks, clearing of the complexion, increase of weight and return of menstruation may be noted, even before any increase of activity and long before any admission of feeling better can be got from the patient.

A first attack of excitement or anxiety will seldom be the only one; of depression it may. Periodic depression and anxiety is less likely to cease in middle life than periodic excitement. The occurrence of hallucinations or

delusions is in itself of little consequence prognostically. A transition from anxiety to depression or mania, and from mania to depression, or *vice versa*, is commonly gradual. Only in predominantly reactive attacks can one surmise how long the illness will last, or when another attack is to be feared. After recovery complete insight into what happened during the illness may not be attained, especially by resentful manic patients, melancholics who are sensitive and suspicious, and agitated patients who feared personal harm.

Generalised somatic disturbances, *e.g.* loss of weight, especially if acute and brief, are of good prognostic import, other things being equal. The more the somatic preoccupations or symptoms are diffused over a period of time and localised to one system, the poorer the prognosis; this, however, does not apply so much to children as to adults. Hypochondria and depersonalisation suggest a long illness, as do nihilistic delusions (*e.g.* denying that one's bowels are opened at all), and, to a far less extent, admixture of hysterical or schizophrenic features. The more the psychogenic causes have been obviously operative for a long period, the greater the tendency to chronicity. In the more chronic forms or after a series of attacks, there may be impaired initiative and judgment, irresoluteness, dullness, and social deterioration—none of them conspicuous. Puerperal and pregnancy psychoses have a good outlook. The milder forms of anxiety and depression, if not already chronic, respond well to treatment, especially to psychotherapy.

Death may occur from suicide, insufficient food, and intercurrent disease, especially pneumonia. Sometimes it is inexplicable on such grounds; a wasting disease, reminiscent of pellagra, carries them off.

Treatment. — PROPHYLACTIC. — Genetic prophylaxis is occasionally possible, as when two persons with definite affective disorders marry each other and are advised not to have any children. Rules of thumb do not apply in this matter; it is wrong to tell a patient he should marry or not marry, procreate or not, unless one has been able to weigh the dubieties of our genetic knowledge, the pedigree of the patient and all his transmissible qualities with an informed and cautious judgment.

Individual prophylaxis is not practicable until after symptoms have appeared which bring the patient to the doctor; social prophylaxis, mental hygiene, and child guidance have not yet been proved to have permanent value in staving off or mitigating affective illness except in the matter of depressive suicide. In so far as one finds environmental factors (*e.g.* heavy responsibility, unemployment, or sexual frustrations) important in inducing an attack, advice on these matters may be helpful; it may be practicable by psychological and social treatment during the healthy interval to do much good in this way. But some cases, in which intrinsic factors seem all powerful, are proof against such measures, and in any case it is not easy to persuade the patient when he is well again to put himself for a long time in the doctor's hands.

TREATMENT OF THE ACTUAL ILLNESS.—It is convenient to consider separately the acute major forms, and the minor more chronic ones.

For the former, treatment is directed to safeguarding life, relieving distress, and providing the best conditions for the emotional disturbance to subside; the situation is like that in tuberculosis or typhoid fever. Exhortations to "pull yourself together" are as out of place as advice to take a

voyage or an argument about the delusions. If the attack is sufficiently severe to unfit the patient for ordinary duties, treatment at home is probably inadvisable. Although in such attacks all argument is futile and active psychotherapy harmful, yet the loss of relation between current experience and emotion is never absolute; there is virtue in separating the patient from real trouble and distressing associations, reassuring him, giving him firm, kind management. The essential combination of these, and especially the last, is rarely obtainable at home. The patients, however boisterous or suicidal, usually recognise their need of treatment and are willing to enter hospital voluntarily. They should not transact any business if it can be helped; their judgment may be too much disturbed, they lay up trouble for themselves. Continuous narcosis sometimes seems to curtail an attack; ephedrin and acetylcholine have also been reported as doing so. The former treatment, *i.e.* narcosis, demands experience and care, No treatment cuts short an attack regularly or dramatically enough to justify any set conclusion about its efficiency in this regard.

Prolonged baths—for 8 or 10 hours daily at a constant temperature of 96° to 98° F.—have much value in allaying restlessness, whether of the manic or the anxious kind, especially the former. They have the further merit of diminishing angry contact with other people, permitting fairly free movement and lessening dirtiness, besides promoting sleep.

Drugs are indispensable. The fear of habit formation should not prevent hypnotics being given when there is persistent insomnia. Barbiturates, phenobarbitone or paraldehyde often suffice: it is well to ring the changes, to prescribe the barbiturate in divided doses, and in each case to diminish the dose without the patient's knowledge. For severe anxiety bromides, opium (*e.g.* as papaveretum) and hyoscine may be helpful; the risks of the two latter are obvious. As to bromides, the risk is intoxication, which makes the patient worse; estimates of the bromide content in the blood and clinical scrutiny should prevent this. Continuous narcosis is valuable, and in some cases convulsant therapy cuts short an attack. Both these methods must be used with caution and reserve, because of the risks, which may be disproportionate to the advantages. Food must be given in adequate quantity and kind. Artificial feeding, preferably by nasal tube, may be necessary because otherwise the patient would die of starvation. The presence of acetone in the urine and a falling weight curve are strong indications that nutrition must be attended to promptly. A good nurse may sometimes, by unusual patience and sense, get over an obstinate refusal to take enough food and drink, but often nothing prevails against it. Apart from hydrotherapy, rest in bed, fresh air, attention to the bowels, and other measures of general hygiene are desirable.

Suicide is of the first importance. Prevention of it can be better ensured by close knowledge of the patient and his day-to-day condition than by mechanical precautions, but if he is bent upon it, these may be unavoidable. It is possible to make them unobtrusive without nullifying them. Certain it is that excessive use of bolts and bars can defeat its own ends, and excessive supervision aggravate a patient's misery, his fears, or his resentment. Two good rules are: (1) to discredit the maxim that those who talk of suicide never commit it, and (2) to remember that most suicides are surprises. Convalescence from melancholia is a risky time.

Occupational therapy is good, as soon as the patient can be got to co-operate; but it is not rational treatment to pester a melancholic, to encourage the fretful restlessness of the agitated, or to give the manic patient more things to muddle himself with and destroy. Still, it is often surprising to find how soon, under tactful guidance, these patients will enter into ordered activity of a more or less simple sort, and how helpful it can be to them. During the stage of improvement the same is true of recreations and social activities. Patients should not leave hospital till recovery is assured, unless it is obvious that the hospital surroundings and the absence from home and work are an actual cause of their persistent anxiety or dejection.

To revert to the *milder* forms, which tend more to become chronic. Here manipulation of the conditions in which the patient lives at home and at work may be conjoined with psychological treatment, both depending on an appraisal of the causes of his illness. There is nothing distinctive (though much that takes account of the individual patient's needs) in the psychotherapy and social treatment called for (see pp. 1815–1818); danger signals must be recognised as they occur. Zeal must give way to the real needs and resources of the patient, which are often not appropriate to a drastic or very lengthy treatment. Simple measures of inquiry, explanation and reassurance, together with small environmental changes, may have much effect. A fixed regime imposed in detail by the doctor is helpful; this becomes more and more necessary as the affect dwindles in long-standing cases. Hypomania does not usually respond to causal treatment of any kind; it seems to run a largely autonomous course. Anxiety may yield very satisfactorily to patient psychotherapy.

SCHIZOPHRENIA

Definition.—The forms of illness under this name are so diverse that many efforts have been made to distribute them, so far in vain. What is common to them all is a detachment from the world without, and a breaking up of normal psychological connections within. The personality is not integrated as in normal people; thinking, emotion, and conduct are discrepant and morbid, yet there is no impairment of formal intelligence such as is found, for example, in organic dementia. The obsolescent name "dementia præcox" is not a synonym for schizophrenia, but a reminder of its recent history. At the end of the last century a large number of patients in mental hospitals were found to have begun their illness before they were 30, and to have passed ultimately into a deteriorated state that looked like dementia; their illness was closely studied, delimited, and called "dementia præcox." When the same clinical picture, however, came to be found in cases that had not such an outcome or onset, the latter criteria were waived in favour of a descriptive analysis of the actual symptoms, and along with this larger conception came the new word "schizophrenia," which betokened a more psychological approach, and a more elastic and generous notion of what might be included. Theories of causation, psychopathology, and clinical boundaries are implicit in any view of what "schizophrenia" really is; consequently, it is still possible for two experts to disagree about what should properly be included under this name, yet over the diagnosis and prognosis of any particular patient they will attain a measure of agreement and

certainty surprising to those who know the condition only from reading or limited experience.

Ætiology.—INTRINSIC.—The intrinsic factors are very important. Studies of the incidence in twins and in the members of a family demonstrate a hereditary factor in a majority of cases. If one of a monozygotic pair of twins be schizophrenic, the other is also in 70 per cent. of cases. The frequency of the illness among various relatives of patients indicates that it is not transmitted as a simple dominant, nor indeed as a simple recessive; probably more than one recessive gene is responsible. It has been suggested that people of definitely schizoid personality are heterozygotes for the genes concerned, actual schizophrenia requiring that the genes be present in homozygotic form; this is as yet conjectural, though some investigators find about as many schizoid psychopaths as schizophrenics among the brothers and sisters of schizophrenic patients.

The constitutional features that betoken an innate predisposition to this illness are more of the psychological than the physical kind. The bodily attributes have been said to be an "asthenic" (weedy and lank), "athletic," or "dysplastic" build; but, since these are found in much the same proportion among healthy people as among schizophrenics, there is little to be said for them here. It is, however, certain that "pyknic" build (see p. 1844) is uncommon among schizophrenics. More significant, however, are the features of personality, commonly called "schizoid"; they are to be found in a large number of cases, though not by any means in all. The patient is reported to have shown slight peculiarities from his earliest years; he has been quiet, shy, and solitary, a "model child," given more to day-dreaming or abstract speculation than to ordinary interests and activity; sometimes he has been unduly submissive and sentimentally affectionate, or touchy, suspicious, obstinate, and resentful of advice and control. A single "typical" schizoid personality is a myth. It is, moreover, to be stressed that a "frozen" description of the schizoid varieties of personality does not do justice to the true state of affairs: characteristic deviations from the conventional norm of behaviour can always be understood better if the patient's way of dealing with his circumstances is viewed historically as a biography of individual tendencies and experiences, rather than described as a bundle of traits. By paying heed to the development of faulty as well as healthy habits of response, the psychiatrist can often see the march of events that led up to the patient's illness, and escape too artificial a sundering of inherent tendencies from the external happenings by which these tendencies have been evoked and given shape and substance.

EXTRINSIC.—The illness sometimes breaks out after childbirth or an acute infection. None of the efforts made to inculpate some specific infection have succeeded, nor does intoxication in general seem to play any considerable part in the causation of schizophrenia. The same is true of cerebral trauma. There are, however, many instances of a chronic schizophrenia supervening on an intoxication, and of schizophrenic symptoms, especially of the catatonic sort, appearing in the course of an organic disorder, such as G.P.I. or encephalitis lethargica. In these, the same structural and functional systems must be supposed to have suffered impairment as in the "endogenous" forms of schizophrenia, and it has been particularly urged that in the chronic paranoid conditions that may follow an acute alcoholic psychosis, it is really

a matter of schizophrenia that happens to be associated with alcoholism, if not partly activated or released by it. It is further to be remembered that at least one intoxication, namely, with mescalin, produces a mental disturbance that is in some respects similar to schizophrenia, and that any chronic hallucinosis comes in time to look very like a long-established schizophrenia, because the possibilities for abnormality of any human mind are few, the deprivation symptoms almost uniform, and our methods of clinical examination imperfect. Endocrine disorders, especially of the gonads, have been held responsible, but satisfactory evidence is lacking, except in a few cases which can scarcely be representative.

Recent mental stress may sometimes be the starting-point of an attack, but in a considerable proportion of these cases the reported overwork, disappointment in love, or other painful experience, is found to have been a product of the already existing illness, or the last of a long series of disturbing events. No recent experience is ever sufficient to account for the illness without regard to intrinsic causes. Nor is any remote experience either. No matter how searchingly the patient's life be resurrected and analysed, it is scarcely ever possible to discover that anything happened to him which would have led to his adopting a schizophrenic way of shunning daily life unless he had been somehow disposed to it from the beginning; although, of course, much may have happened to him that has strengthened and fostered the disposition.

Among contributory factors, age and sex are noteworthy. An onset after the age of 40 is uncommon. In three-quarters of the cases that later exhibit the characteristic chronic syndrome, the illness begins between 15 and 25. The condition may become overt in children before puberty. Men are more often affected than women—in the proportion of 113 to 100, according to the largest available statistic; the matter is dubious, however, because of the different standards of diagnosis used.

Pathology.—PHYSICAL.—Histological changes in the brain are not characteristic; it is doubtful if they are even frequent. A cellular loss in the third and fifth layers of the cortex, with lipoid accumulation, has been found, but it occurs in many other conditions. Many claims about cerebral pathology, and the chemical and physiological changes in schizophrenia have now been discredited, so that all findings in this difficult field have come to be matters of suspicion. Variations in the same individual may be wide. Recent investigations have purported to show:—a disturbance of the acid-base equilibrium towards the acid side, with a diminished excitability of the respiratory centre to carbon dioxide; lowered rate of oxygen consumption; polyuria; diminished gastro-intestinal motility; poor response to epinephrin; abnormal heat-regulation; decrease or sluggishness of total blood-volume; and slowing of the arm-to-carotid circulation time. These findings have not so far been controverted; they represent disorders of metabolism and regulation which may be partly a concomitant of the characteristic mental disorder, and partly an effect of it, *i.e.* they may be essential physical disturbances in the illness, or may be secondary to the abnormal, often inert life the patients have led since they became ill. There is no ground for supposing them causal.

Some inferences have been drawn from the similarity of catatonia to the extrapyramidal syndrome that can be produced in animals by bulbo-

capnine; the argument from analogy cannot be pushed further than to say that certain functional systems are available in the brain, which are sometimes involved in schizophrenia, as they also may be in poisoning or in encephalitis lethargica, G.P.I. and other diseases.

Very significant are the well-attested metabolic findings in the rather rare cases of cyclical catatonia. In these the nitrogen balance varies periodically; with alternating phases of retention and over-excretion, corresponding to the mental change from excitement to stupor or *vice versa*. By means of thyroxin a thorough emptying of the patient's nitrogen store can be brought about and subsequent nitrogen retention prevented, thus leading to clinical improvement. The correlation between metabolic happenings and clinical condition in these patients is now established.

PSYCHOLOGICAL.—The large and inconclusive literature on the psychopathology of schizophrenia is of five main kinds, namely:

(1) Minute description of the phenomena observed, and abstraction from them of general principles of disordered function.
(2) Experimental study, chiefly quantitative (*e.g.* psycho-galvanic).
(3) Studies of artificial hallucinatory psychoses (*e.g.* mescalin intoxication) and parallel experiences.
(4) Comparative study of animals, children, poets, primitive people, etc.
(5) Intuitive or speculative interpretation.

It will be obvious that these methods overlap and that they differ widely in acceptability and usefulness. The findings of almost all can sound plausible, when stated in general terms; discrepant or abstruse, when stated in detail. Their exposition touches on the most intricate problems of normal and morbid psychology, and therefore is highly technical and unsuitable here. A working hypothesis for clinical purposes is that in schizophrenia there are inherent faulty habits of reaction, whose severity and persistence depends largely on education and other external circumstances. These faulty reactions are characterised by a deficiency in the function of synthesis, so that there is an inco-ordination, "intrapsychic ataxia," as it were, a splitting up of the mental life, which justifies the name "Schizophrenia." Thereby the whole psychic life of the patient, cognitive, emotional, and conative, is changed in a way that is alien to normal understanding. We can observe the change but cannot enter into it or describe it adequately in terms of our own experience, as we mostly can depression, manic excitement, hysteria, or obsessions. It shows itself also as a turning away from the contacts and realities of daily life, a preference for what the mind can supply from its own stores, however morbidly, rather than for the current experience that the outer world affords.

Symptoms.—Schizophrenia may be regarded for clinical purposes as a form of maladaptation in which there are certain characteristic defects of inner harmony and consistency in behaviour, thought, and emotion. These are rarely seen in childhood, but from puberty onwards they may appear in varied combinations (often in persons who for years have been introspective and unsociable). There is discrepancy between mood and utterance, disturbance of conduct (briefly summed up as catatonic or hebephrenic), self-absorption and incapacity for sustained thinking along normal lines. A guarded or artificial demeanour may conceal these essential features, whereas they may be conspicuous in a florid or "deteriorated" case. Hallucinations

and delusions may fill out the picture; affective or other morbid types of reaction may complicate it.

The onset is not always abrupt. There is often a long history of preliminary symptoms in which it is arbitrary to decide where personality has merged into illness. Complaints of headache, weakness, anxiety attacks, loss of appetite, and dysmenorrhœa may have accompanied slight oddities of behaviour, such as rudeness or apparent absence of mind and indecision. The patient may have felt an alarming change in himself, in his capacity to think and feel normally, and been notably depressed and anxious. Ideas of persecution or of exaltation may occasionally escape him, or he may have become stilted in his talk and shown other affectations and mannerisms. The more gradual the onset—and in many cases it has spread over many years—the more unlikely is it that it will have been recognised as morbid.

The commonest or basic symptoms are: (1) Disorder of thinking. (2) Emotional incongruity. (3) Hallucinations. (4) Disturbed impulses or conduct. From these can be derived most of the other symptoms, such as delusions, feelings of influence, autism, catatonic phenomena, anomalies of speech, negativism, and the rest.

The *disorder of thinking* is a characteristic and central feature. The patient cannot command the whole range of an act of consecutive thought; he misses the point, fastens on details and brings in irrelevant associations which are correct in themselves, but which divert him from the main end of his original process of thought; consequently his thinking is incoherent, rambling and jumbled. He brings together the most far-fetched topics, so that the connections are sometimes so superficial as to be empty of meaning, and at another time profoundly influenced by symbolism and highly individual values. The usual logical sequences are ignored: cause and effect are interchanged; temporal, spatial, verbal, and accidental relationships are unduly turned from abstract to concrete, treated as grounds of identity, played with or flouted. Things linked only by analogy and chance association are taken to be the same. The condensation of several conceptions in one, or transference of a set of attributes to some inappropriate object, may become a matter of course, so that only the closest knowledge of the patient and his surroundings will enable the psychiatrist to follow his meaning. It is not necessary, however, that such extreme incoherence be evident in the patient's talk; he may not show any at all when speaking, or may suddenly obtrude a startling lapse from normal ways of thought which he then ignores, justifies or explains away. Inconsistent thoughts can be present together in a way impossible for normal people; and the same object or notion can appear to him in several interchangeable guises, each of which would normally exclude the others. The patient himself is often aware of his disordered thinking, and may describe it: he feels his thoughts are suddenly taken out of his mind, other thoughts, foreign to him, are put into his head, his mind is not his own, his thinking is suddenly interrupted, some external power controls it.

The thought-disorder is illustrated by the following characteristic remarks of patients: "There were bats and bees coming through the window; of course that was because my brother-in-law kept teasing me. He said I had bees in my bonnet." "If I should return during my absence, keep me here until I come back." "I have a lot of forced thoughts. My thoughts

are all drawn-out words, they ought to be pin-pricks. There is an unnatural stoppage in my thoughts, too. . . . I have heard voices say ' He is conscious of his life.' . . . To get my feeling back to normal I feel like changing motor-cars into battleships, to be superior to them."

This disorder may only be demonstrable when the patient gets on the topic of his delusions; in other matters he may seem quite sensible. It is not essentially different from what normal people experience during states of altered consciousness, *e.g.* in dreams, or when falling asleep; the schizophrenic, however, has it with clear consciousness, so that a listener often feels that the patient is making fun of him in giving such transparently absurd answers with an air of knowing exactly what he is about. Some chronic well-preserved schizophrenics make their living as comedians, the audience much enjoying the allusive, half-comprehended nonsense, with its background of innuendo and symbolism. Autism, *i.e.* immersion in his own fantasies and preoccupations, may account for much of the oddity and detachment the patient shows; it accounts also in part for his " negativism," in that he resents any stimulus that interferes with his day-dreams.

Delusions arise mainly out of the thought-disorder. They are often bizarre; they may occur to the patient with a suddenness of conviction that puts them beyond all argument; and they are egocentric in that they commonly bring indifferent happenings or people into a special relationship with the patient—*e.g.* he suddenly knows that when his cousin yesterday said he had been reading about Napoleon's divorce of Josephine, it was a subtle way of telling the patient that his wife was committing adultery with this cousin, whose name is Joseph. The delusional ideas may not be firm conviction, but fleeting notions, readily given up, and based upon some casual instance of the thought-disorder; sometimes they are schizophrenic ways of saying something commonplace—*e.g.* the patient declares his wife has poisoned him, but when he is further questioned says airily that he means she gives him ill-cooked food which is bad for his digestion.

Fixed delusions are, however, common, and are usually of a paranoid complexion; they may develop out of more or less ephemeral ideas of reference. They are often intermixed with hallucinations. The patient gets into a state of mind in which he feels there is meaning in everything, something is going on behind the scenes, he is perplexed by all this, and mystified, it has to do with him in some uncanny way. Presently, he begins to " see through it all," sometimes he gives it some religious or cosmic significance, especially if he has much anxiety as well—the Last Judgment is at hand, he is to be responsible for the regeneration of the whole world. The delusions are not always enacted on so grand a stage; there may be homely fancies about neighbours who whisper and sneer, or about some vulgar bogy like the Jesuits or the Jews or the C.I.D. Often, the patient complains that people work on his mind, hypnotise him, influence him for his own good, set about to drive him mad or ruin him. Delusions of grandeur may be linked up with these paranoid ones (*e.g.* he is being persecuted because he is the Messiah), and may be likewise pedestrian or lofty, according to the patient's previous education and interests, the severity of his disorder, the copiousness of his fancy, and the amount of normal mental function still in evidence. Here, as elsewhere in psychiatry, the symptoms are a mixed outcome of impaired or perverted function on the one hand, and of normal

function on the other, the latter either reacting to and modifying the disorder, or obtaining freer play through it. If, for example, a patient feels his thoughts being controlled by some external influence, and he has queer tinglings in his body, his conviction that he is being hypnotised, and that some one is playing an electrical instrument on to him, must be regarded as a normal attempt to find the cause of an almost inexplicable happening. The delusions are sometimes about past events, which are falsified retrospectively, *e.g.* the patient relates details of his having been a changeling or a predestined hero. Delusions about bodily transformation or disease are frequent, and may be complicated and bizarre.

Patients often do not act in accordance with their delusional beliefs, especially when these are fleeting or chronic; they may, for example, be friendly towards a nurse whom they believe to be persecuting them cruelly. But this is, on the whole, unusual in the early or acute stages of the illness: a patient will then act on his beliefs violently or in terror; he may go to the police or be driven to suicide.

Constantly the matter of a patient's delusions will be found to be intimately dependent on his experiences, his emotional attachments and sufferings, his struggles and frustrations; it is impossible, however, by any such analysis and derivation of his delusions to account for the fact of their occurrence, *i.e.* for the patient's choice of this way of dealing with the experiences in question. The same is true of the general thought-disorder: *e.g.* interruption or "blocking" of the train of thought may take place only when some emotionally weighted topic, some complex, is touched on. This accounts for the place where "blocking" occurs, but not for the "blocking" itself; that, like the other fundamental disturbances of function in schizophrenia, eludes a wholly psychological explanation.

Intellectual defect does not occur. There is usually no clouding of consciousness. Intellectual laziness or evasion is often conspicuous; the patient may repeat questions in a musing way, or profess ignorance. Orientation and memory are not, as a rule, diffusely impaired, though hallucinations, delusions, and lack of interest may interfere with them, and consciousness may be disturbed in stupor or excitement. Many a patient who has long borne the appearance of gross dementia will suddenly show that his intelligence is still a sharp instrument: drugs, *e.g.* sodium amytal or insulin, and intercurrent disease or shock can thus dramatically reveal how little ground there is for calling this illness a dementia. Schizophrenics often do the unexpected. Amnesias, and deliria, when they occur in schizophrenia, may be hysterical; obsessional and hysterical symptoms, like anxiety and depression, are compatible with schizophrenia, and are often an intimate component of the illness.

The speech and writing of the schizophrenic betray the extent of his thought-disorder. Stiffness, pedantry, fantastic euphuisms, words of his own coining, queer symbols and grammar, stereotyped repetition, and infantile twists like speaking of himself always in the third person may be conspicuous features of the patient's use of language. There may, of course, on the other hand, be little or nothing outwardly amiss in his conversation and writings. In florid or chronic cases the patient may talk in an unnatural voice, or without any modulation. Writing may be set forth as though it were painting, and the converse: in subject and matter the patient's insanity

may be patent, but his treatment of his matter, however odd, is seldom odder than some forms of modern art, and it cannot, therefore, be called typical of the illness. These anomalies of symbolical representation are as open to psychological explanation as are the delusions mentioned above; the neologisms, for example, can be analysed up to a point; and these phenomena have enriched our knowledge of the psychopathology of schizophrenia.

The *emotional incongruity* is the chief, but not the only, sign of disturbed affect. Often the patient himself notices in the beginning of his illness that he is less moved by habitual affection, or even feels hatred towards a parent he has loved. The strongest and rarest of human passions are not infrequent in this illness: ecstasy, mystic communion, despair, horror, agony of death, limitless abandon, apotheosis, salvation, are approximate names for these exceptional states that are probably indescribable in the current language of normal people. Apart from these, and much the commonest of the affective changes, is apparent emotional shallowness: the patient receives moving news without any sign of being touched by it, or his response is perfunctory; he smiles or looks bored when talking of a recent tragedy in his own family. This shallowness and incongruity of affect is, however, not to be taken at face value. What the patient says, and what he means with his words, may be very different; so may what we say be very different from the meaning the patient attaches to it. It is unsafe to assume that the patient's words have reference to what is mainly going on in his mind at the moment, or that his outward expression is a trustworthy index of his emotional state. Violent emotional outbursts—of anxiety, rage, love, misery—can certainly occur in a patient who has lately seemed empty of all affect. The schizophrenic patient is undoubtedly different from normal people in his emotions, but not in so negative a way as his seeming apathy and lack of affective rapport would suggest. His attitude towards the same person may change quickly, in accordance with conflicting or opposite tendencies in himself; this ambivalence is often understandable in the light of his earlier history. Sometimes the illness leads to a blunting of ordinary reserve, a lack of reticence, or a levelling down of the gravest matters, so that frivolous or cynical indifference and imperturbability are signs of the patient's morbid condition.

Hallucinations are not so frequent as superficial examination of patients might suggest; many of the patient's assertions about queer sights and sounds are not the expression of vivid perceptions but of passing fantasies, imagined more plastically than is normal; this is particularly true of many of the so-called visual hallucinations, or of cases where the unreal perceptions occur in several senses together. Hallucinations are nevertheless extremely common and persistent in schizophrenia: auditory ones occur most often, diffuse somatic ones not infrequently, those of smell, taste and sight more rarely.

The " voices " are sometimes so closely linked with the thought-disorder that it is difficult to tell whether the patient is relating what he has heard or what he has thought. He may show the intermediate stages between the two, declaring that people repeat his thoughts or that everything that passes through his mind is spoken aloud inside his head; his actions are described publicly, he cannot go to the lavatory without shameless comments. What the voices say may be abuse or encouragement, trivial repetition or threats and commands; this content can usually be accounted for by the psychiatrist,

when he knows the patient and his history well. The voices may come from strange places, *e.g* from inside the patient's own chest or abdomen, and are then often accompanied by curious somatic hallucinations, indicative of morbid attitudes, both physiogenic and psychogenic, towards parts of the body. The latter often occur independently. Queer sexual feelings, or distortions and impossible growth of various organs, may be reported. They are usually bound up, as any schizophrenic symptom is likely to be, with delusional and emotional components, which are partly derived from the patient's experiences and psychological development. The visual disturbance, like the gustatory, is more often illusional than hallucinatory, *e.g.* people's faces look fiendish or artificial or transfigured.

The *actions and bearing* of the patient are often characteristic. Abruptness or lack of grace in movement may be seen early ; it can be indistinguishable from the fidgety self-conscious hobbledehoy stage of adolescence. The patient may pull faces at himself in the mirror, or may be unaware of his grimaces. Asymmetrical movements of expression, twitchings, mannerisms, queer rituals and tic-like gestures are to be met with. The meaning of the patient's movements can usually be worked out, but after they have been present for long their sharpness is rubbed off, as it were, and the empty stereotyped movement at last gives little clue to what was once a significant emblem of experience and feeling. The movements often seem to become automatic, like the " verbigeration " of empty phrases in the patient's speech. Negativism, talking and acting beside the point, and bizarre escapades may be seen at any stage of the illness.

There may be a suspension of movement, or the reverse : akinesis or hyperkinesis. Both may occur in the same patient, who may lie for weeks or months in a catatonic stupor, from which he suddenly emerges into swift action. He may carry out some impulsive action and then promptly return to bed and stupor ; or he may become wildly excited and imperil his life by his blind and raving activity. During catatonic stupor, patients may adopt strange postures, *e.g.* holding their head off the pillow all day, pursing their lips. They may be indifferent to cleanliness about fæces and urine, or actively dirty in this regard. Waxy flexibility is rare, but many patients are automatically obedient so that they keep up an imposed posture.

The variety of schizophrenic anomalies of conduct is too great to be described here. They must not be assessed absolutely, but always in relation to the setting in which they occur. Then they have meaning in the individual case, and are not merely so many examples of " ambivalence," or " mutism," or " negativism." It is, however, true in this matter also that understanding the content of an anomaly does not make its occurrence likewise understandable. Much of the schizophrenic's conduct is so close to certain disorders of movement in organic disease of the central nervous system, that somatic mechanisms may be assumed to have suffered damage in this condition. There are three main things to be done with any schizophrenic symptom : (1) to search out its psychological origins, and its meaning for the patient in his present situation ; (2) to link it up with the other functional disorders that he shows ; and (3) to consider its background of physical structure and function. It is not always practicable to attempt all three, nor is it as yet possible to do them well, but none can be ignored without detriment to a full analysis.

Often the most significant yet intangible effect of the illness is upon the patient's *personality*. After florid symptoms have died away, or when there are no definite symptoms at all, a change in the patient's ways is remarked by his intimates. Not only is he outwardly different—more "peculiar," less understandable and predictable, rather shut-in upon himself, remote, with queer values and impulses—but in many cases he is also aware of this change, and may complain of an inner perversion of himself, a loss of that unity which we take for granted when we say "I," or "me." Insight in schizophrenia, in this respect and more generally too, may be penetrating and just, as many self-descriptions attest. There may also be varying degrees of impairment up to gross lack of insight.

None of the *bodily symptoms* are characteristic of this illness, though many occur. Besides the somatic complaints and preoccupations already mentioned, patients, especially if young, show vegetative anomalies. Thus, vasomotor disturbance may take the form of cold bluish extremities, exanthems or œdema. Seborrhœa is common. Abnormal growth of hair occasionally occurs in women. Loss of weight in the acute stages, and fatness in the chronic condition, interruption or irregularity of menstruation, and fluctuations of temperature may also be observed, especially in catatonic cases; of the schizophrenic states, stupor is the richest in demonstrable bodily changes. Fleeting neurological signs, *e.g.* pupillary anomalies, may be found. In states of acute excitement attacks of unconsciousness may occur, but epileptic seizures are very rare.

VARIETIES.—There are three main forms—catatonic (with acute outbursts); hebephrenic and simple (early onset, chronic course); paranoid (fairly late onset, delusional). They are not exclusive categories, and it is usually profitless to try and apportion a doubtful case to one or the other. They do not correlate closely enough with outcome to be of much use clinically.

In *hebephrenia*, the least common variety, delusions and hallucinations are inconsiderable, but abnormal conduct is to the fore: the patient may be silly and mischievous, abruptly eccentric or inert and without initiative. The illness may progress without acute episodes (dementia simplex), or be interrupted by phases of excitement or obvious insanity, which subside, leaving the patient worse than before. In *catatonia*, the most favourable variety, the symptoms are plain even to the layman: akinetic or hyperkinetic states may appear and subside quickly, sometimes for good or for several years. There are usually, also, characteristic disorders of thought and emotion, which may clear up when the stupor or the excitement does. In the *paranoid* form, generally rather late and insidious in its development, but less damaging to the personality than the hebephrenic, partial systematisation of the delusions is common in the earlier stages, but may be later swallowed up in the general thought disorder and deterioration (dementia paranoides). The more bizarre the delusions, the more likely is affective emptiness to replace gradually the initial resentment and distress, but sometimes the patient passes into a chronic paranoid state, obviously schizophrenic to the psychiatrist, but compatible with ordinary life outside an hospital. Hallucinations and luxuriant delusions may, however, be conspicuous in the paranoid form (paraphrenia and dementia phantastica).

Diagnosis.—The chronic and advanced cases—"typical dementia præcox"—that abound in mental hospitals, are easy to diagnose, but

early or inconspicuous cases often extremely difficult. The chief positive points to look for are: characteristic thought-disorder, a qualitative change of affect, and other evidence of "intrapsychic ataxia," as well as feelings of being under external influence. Catatonic symptoms are of limited diagnostic value, because of their frequency in organic and symptomatic psychoses. More important than any single feature is the impression of the case as a whole, the development away from normal interest and response to the real world, and the establishment, instead, of "autistic" self-satisfactions so that the patient's personality is twisted awry, as it were, and withdrawn from easy contacts.

From organic syndromes—syphilis of the central nervous system, alcoholic psychoses, disease of the cerebral vessels, encephalitis lethargica, etc.—the differentiation turns on the physical findings, more than on the mental state: a schizophrenic syndrome may appear in an organic condition, because the brain, as Kraepelin said, is like an organ whose stops give out the same sound, whoever works them. Often it is not a matter of deciding whether the syndrome is organic or schizophrenic, but whether, being schizophrenic, it has a discoverable somatic basis or not. Alcoholic delusional states are an instance of the complicated relationship that may be found (see p. 1838). If, after consciousness has become clear again, the other phenomena of toxic confusional psychosis persist, then schizophrenia is the more probable diagnosis.

Diagnosis of schizophrenia from an affective syndrome is difficult, because both are often combined in the same patient. Some of the significant points have already been referred to (see p. 1859). Catatonic excitement differs from mania in that the speech and acts of the latter are intelligible as expressing a general affect and are conformable to the situation in some measure; the onset and cessation are not so abrupt as in catatonic excitement; and there are usually characteristic features which make the distinction easy. Melancholia becomes suspect when delusions are repeated without the appropriate affect, and there is a readiness to project responsibility for the illness, to complain of external influence. The inertia of the depressive is not so complete as that of catatonic stupor, nor so likely to be abruptly broken through. States of severe agitation are not always easy to distinguish from schizophrenic excitement, but a more frequent problem is that of deciding whether some bodily fear or conviction of disease is schizophrenic or not. Whether in regard to a preoccupation or a delusion, the chief point to consider is the appropriateness of the affect to the alleged hypochondriacal notion; the more bizarre the bodily change described, the more likely to be schizophrenic. Depersonalisation is sometimes at the bottom of these somatic complaints; what is significant is not the depersonalisation, but the way it is elaborated and regarded by the patient.

Hysteria can offer great difficulties, largely because hysterical mechanisms are so often operative in schizophrenia. Plain motor or sensory disturbances commonly give less trouble than hysterical dissociation, stupor, and pseudo-dementia. The previous history, the relationship of the outburst to a particular set of happenings, the behaviour in the intervals, the demands upon the attention or response of bystanders must be taken into account. The mistakes and oddities of the hysterical pseudo-dement may be theatrical, in accordance with his ignorant notion of what insanity is like; the deliriously dissociated

hysteric does not identify correctly the people around him, as the schizophrenic usually does, even when in a dream-like state; the hysteric who is acting some imagined scene does so without discrepancies or gross interpolations, whereas the schizophrenic is seldom so consecutive and persistent. The degree to which the patient is being influenced by his immediate surroundings is, however, the chief guide, apart from definite schizophrenic features.

Obsessional states offer difficulty when the patient is in doubt as to whether his alien thought or impulse comes from within his own mind or is imposed upon him. If he shows indifference as to the occurrence and content of the compulsive ideas, it is suggestive of schizophrenia; but careful examination of the development of the symptom, and the patient's attitude towards it, permits a clear diagnosis in most cases. Complicated rituals, odd obsessions and chronicity make an obsessional illness look very like schizophrenia; as does intoxication of an obsessional patient by bromides. Obsessions may develop into schizophrenic symptoms (see p. 1888).

Prognosis.—Schizophrenia is always a serious condition. Though some recover, the tendency of this morbid change is to do permanent damage to psychic life. In the individual case, however, pessimism is not justified. It is certainly never possible in the early stages of the illness to be certain that recovery is out of the question.

Heredity is a poor guide to the prognosis, except in the rare cases in which an identical twin of the patient has for some years had a schizophrenic illness, or in which one parent is schizophrenic, and the other has schizophrenic relatives; even then it is difficult to prognosticate with assurance regarding the present attack. If one parent has had an affective illness the prospects of recovery are brighter, but this can better be assessed from the patient's own bodily and mental constitution. If he is of pyknic build, the outlook is much better. Similarly, the patient who has for years tended more and more to withdraw from his surroundings, to be careless of social requirements, to lie late and live alone, given up to day-dreaming and eccentricity—such a one should he become overtly schizophrenic, has a poorer chance of doing well than the active, suspicious and impulsive man, or the self-conscious, introspective worrier who similarly falls ill. A narrow and rigid previous personality makes deterioration more likely than if there had been wide interests and possibilities of adaptation.

The more abrupt and stormy the onset, the better the outlook. This is one of the most reliable guides. When the onset has followed upon a recent painful experience, and the content of the patient's talk and his behaviour refer to this, or when a physical damage appears to have provoked the symptoms (*e.g.* influenza or head-injury), the outlook is rather better than when the provoking factors are obscure; but this is by no means always the case. If the attack occurs during puberty or adolescence, prognosis must be cautious, because of the difficulty of distinguishing between the transient upsets of this period of adjustment, and the progressive schizophrenia that may then show itself plainly. The earlier history is of great help.

The nature of the symptoms is not a safe guide. Very severe departures from normality may clear up, yet an outwardly mild condition be of grave omen. Symptoms such as stereotypies of movement and speech, which indicate that the illness has been going on a long time, and that there is a

general narrowing and fixity, are grave; as are also hebephrenia, and a long-drawn-out stupor, with negativism, impulsive violence and vasomotor changes. The more manic or depressive features, the better. Previous attacks, with an interval of normality between them, are prognostically favourable. If the patient first falls ill after 30, he will scarcely go downhill in the tragic way young people sometimes do. He may develop fixed delusions, which are often rigid and encapsulated, so to speak, and therefore he may be able to return to ordinary life, with reservations; or it may be that his morbid beliefs absorb all his mental powers, and compel institutional life. The more the psychiatrist can discover healthy modes of response in the illness itself, as well as in the previous personality, the happier the outlook. Many patients, after an attack, do not return to work, but have narrower interests, and less spontaneity than before; they are more easily tired, and may be hypochondriac, or show other symptoms thought to be "neurotic." Such patients have sometimes made a poorer recovery than others who return to work and can meet most social demands, though careful inquiry reveals definitely schizophrenic sequelæ in their thinking and emotions.

The simplest rule is that an abrupt onset of the illness, an adequate cause for its occurrence, and a well-adapted non-schizoid personality are the criteria of good prognosis. Sensible early treatment may avert disaster.

Treatment.—PROPHYLACTIC.—This, whether eugenic or individual, is limited and uncertain. Even if effective, it can reach only a minority at present, and its effectiveness is a matter of faith. Probably child guidance and other measures of mental hygiene do good in averting potential schizophrenia, but no one can be sure of this. Such treatment aims at diverting the child into social activities and keeping him out of situations in which he will be mortified or otherwise troubled emotionally. However wordily or abstrusely the prophylactic treatment be described, it is essentially a matter of trying to make an unusual child into an average one, or making his surroundings unusual to suit him.

TREATMENT OF THE ACTUAL ILLNESS.—There is no one treatment of the disorder that has manifest superiority over any other. Painstaking attempts at readjustment of the patient's outlook and behaviour by means of psychotherapy (not psychoanalysis), occupation, games, etc., are the most systematic and rational way of making a permanent change for the better. The co-operation of the patient is here necessary, and also the help of a social worker desirable, who may do much to modify and arrange the patient's circumstances in the interests of his mental health, *e.g.* getting him suitable occupation, and schooling his relatives in a sensible attitude towards him. Such treatment is not practicable for those acutely ill, but for the mild, the convalescent, or the imperfectly recovered case it is of great value. By means of it many patients can be discharged from hospital before they have settled into apathy, or become unresponsive to the claims of the external world; it is better not to keep a schizophrenic patient in hospital waiting for complete recovery, but to get him back into ordinary life as soon as possible, provided conditions there are not too adverse for him, or he too abnormal to cope with them.

Treatment in a psychiatric clinic or mental hospital is usually necessary at some stage of the disorder, and must be decided chiefly by the severity

and social risks at the time. For the large number who become permanently in need of institutional care, much of the deterioration formerly customary may be averted by the energetic use of occupational therapy and recreation which make the patient's life less sterile.

There are few conceivable ways of altering a human being that have not been tried in this illness. Many of them have been those believed to be efficacious in other illnesses; some have been intended to shock the patient somehow. Of the former may be mentioned endocrine preparations (in large doses), transplantation of gonads, removal of supposed septic foci, induction of fever by malaria, etc., injection of human serum, manganese salts, production of aseptic meningitis and continuous narcosis. Of the latter, *i.e.* shock-methods, many of the procedures of a bygone time are examples; the whirling chair, precipitation from a height, immersion in ice-cold water, and so forth. The most recent methods which entail a profound and alarming disturbance are those which use insulin or a convulsant (see p. 1819). Though the direct emotional effects of such treatment are not negligible, metabolic changes are no doubt chiefly responsible for the clinical effects seen. Insulin has more value then the convulsant method. It should be employed only in hospitals fully equipped and staffed for the purpose. The treatment is most effective in cases which would have a good prognosis for the attack if treated by other methods. It is not a panacea for schizophrenia, but may shorten an attack in suitably chosen cases.

The details of treatment, whether in hospital or at home, must be individual; even in such matters as the allaying of excitement no uniform procedure, *e.g.* continuous baths, or narcosis, can be a routine measure. When excitement is extreme, disturbances in water metabolism and loss of salts may be combated by giving 5 per cent. saline intravenously, 300 c.c. every other day, alternating with forced fluids. During stupor, general measures for ensuring adequate food (in some cases feeding by tube), cleanliness and evacuation of urine and fæces must always receive attention. It has been found that various chemical agents, such as carbon dioxide inhaled in a 30 per cent. mixture with oxygen, and sodium amytal, will temporarily interrupt a catatonic stupor; this finding accords with the chemical metabolic changes reported in the condition, but its therapeutic value is slight.

PARANOIA AND ALLIED STATES

The words "paranoia" and "paranoid" are used loosely by many. Kraepelin gave paranoia its modern meaning, describing it as the endogenous, insidious development of a permanent and unshakable delusional system, with complete preservation of clarity and order in thought, will and action. If the illness cleared up, if it showed symptoms of an organic, affective or schizophrenic syndrome, or if it was provoked by external happenings, it could not be paranoia. Thus delimited, the condition is exceptionally rare; so rare, indeed, that there is no use in having such a category. Moreover, cases that Kraepelin himself called paranoia have since become obviously schizophrenic. There is now no profit in thinking of paranoia, or paranoid states either, as syndromes in their own right, so to speak, and of the same order as schizophrenia or affective disorders. They are on the

same subsidiary level as stupor, hypochondriasis, anxiety and depersonalisation. When met with, they must be distributed according to the accompanying symptoms and the general trend of the illness; and their prognosis and treatment must be assessed accordingly.

Besides the paranoid beliefs and attitude referred to in previous sections, there are a number of instances of this unhealthy relationship between the patient and his surroundings, which are mild in their outward form, easily understandable in the light of the patient's history, and fairly responsive to treatment. Sensitive and shy people are often troubled by doubts and shame as to their physical or moral worth; and, by projection, attribute to others the dislike or contempt they do not acknowledge in themselves. This occurs in youths who masturbate, and suppose others to remark it, and in old maids who believe men to be pursuing them; but there are many varieties of shame and desire, besides the sexual, which lead to such ideas of reference or persecution. The development of paranoid reactions of this sort is usually plain. So is that of the querulous, resentful type of reaction, *e.g.* in the man who believes himself done out of his rights and who becomes a persistent litigant or writer of memorials. Before judging such a man psychopathic, the extent of the injustice he has suffered must be compared with the degree of his resentment and his relevant conduct. Commonly the injustice is found to be fanciful or trifling, and the man's sense of grievance immoderate, so that he comes to believe there is a veritable conspiracy to wrong him, and devotes most of his time to useless appeals or threats. He may persuade his wife or his children of the justice of his complaints, inducing delusions in them, *i.e.* folie à deux, etc. Many such patients, however, never become deluded: they are contentious about their wrongs, and waste years, perhaps, in proclaiming them or seeking redress, but they are well aware how other people regard them, and what has actually happened. Many claimants of compensation, "grousers," "old soldiers" and unstable adherents of more or less cranky movements, are to be placed here. There is no sharp dividing-line between these psychopathic people, and the more or less normal, often socially precious, leaven who detest injustice and are willing to do much to defeat it. Some deaf people become paranoid, misinterpreting what they cannot hear plainly, and construing it into a jeer or an insult.

HYSTERIA

In hysteria, symptoms of illness are represented by the patient for the sake of some advantage, without his being fully conscious of this motive. The form of representation will vary widely according to the circumstances that have provoked the illness, the patient's experience of what the symptoms are that he is trying to represent, and his somatic resources. These factors, presently to be discussed, bear on the hysterical symptoms that simulate physical disease. But it is impossible to restrict hysteria to this physical form. The illness that is represented by the hysteric may be a mental one; moreover, it is not possible to consider hysteria without regard to the mechanisms of its occurrence which manifest themselves in the personality and are mainly psychological. Hysteria is the most psychogenic of all illnesses. Its recognition is therefore a double problem: (1) exclusion of

what may be called " genuine " illness, *i.e.* of a recognised morbid pattern ; and (2) discovery of an adequate motivation. To ignore either of these requirements is to court error, since hysteria may occur along with physical or mental disorder, elaborating upon it and mimicking it, and, on the other hand, some physical diseases give rise to symptoms indistinguishable in their form and apparent psychological mechanism from those of hysteria.

Ætiology.—A hereditary factor is probable in many cases. Thus, a group of hysterics who were pathological liars were compared with the average population in respect of the proportion of their brothers and sisters who were in mental hospitals : it was five times as many ; and of the parents of the group, a sixth were psychopathic. From these and similar figures it is not possible to tell the mode of transmission or the nature of what is transmitted, but only to infer a hereditary factor. The occurrence of hysterical mechanisms in children, and their frequency in healthy adults, especially after calamities or in unendurable conditions, such as may occur in war, suggest, however, that hysteria is potentially present in most people and that environment is more important here than heredity. The combination of heredity and environment may result, long before actual illness occurs, in a *hysterical personality*. This is not found in all patients who show hysterical symptoms, but nearly all people of hysterical personality show hysterical symptoms. Many of the features of this personality are socially obnoxious, but other features are not, and it is wrong to use " hysterical " as a depreciatory epithet for a set of qualities that one dislikes. These people are unduly responsive to the situation they are in, especially if by their excessive response they can fulfil wishes of which they are hardly aware, or evade what is painful in the situation, instead of meeting it and disposing of it adequately. Unsatisfied with their own capacities, they seek to cut a better figure than their endowment warrants, and are constantly posing and pretending. This, like all their behaviour and aims here described, is not done with full consciousness, but with a more or less sincere ignorance or ambiguity of purpose ; it is not a question of deliberate deceit, of studied histrionics or malingering. In thus responding to situations and turning the response to some inadequate end, the hysterical person is characterised by a lack of inner stability and of constant standards of behaviour, and also by a lability of affect and an exuberant fancy. The fantasies normal in childhood are here seen in physically mature adults, who, like children, can temporarily live their fantasies, absorbed in this unreal compound of past experiences and longings, yet not so wholly divorced from their real surroundings as might appear. In an attenuated form, this is evident when they almost unwittingly manufacture some situation, according to their needs—literally " making a scene "—and enter into it emotionally with a rapidity and fervour impossible for more stable people. Egotism and untruthfulness (pseudologia phantastica) may be pushed to the point of delinquency. There may be a longing for prestige, sympathy, love, or some other emotional relationship, which leads the hysteric to behave in a way strikingly out of keeping with his demeanour on other occasions ; the inappropriateness of his behaviour even at the time may be obvious to a detached onlooker, but is not always so. Many of these people can use illness or well-acted fantasies of illness to satisfy their hardly conscious needs ; they may also gain their ends by forgetting what it would be painful

to remember. Here again the onlooker may find it hard to tell how genuine or complete is this forgetfulness, but the question is of little moment compared with discovery of the motive for the hypomnesia. The much-stressed suggestibility of hysterics is a notable aspect of their responsiveness to situations and of their especial responsiveness to a person with whom they develop an emotional relationship, often unrecognised by themselves as such. The emotional attitude of a hysteric towards other people is often influenced by sexual factors. Hysterical personality is believed to be much commoner in women than in men, and may be associated with psychosexual immaturity. Coquetry and frigidity are not uncommonly allied in hysterics; there may be much flirting and sexual excitation, but not actual coitus: it is, however, juster to say that the sexual lives of hysterics show instability and inadequacy than to specify any particular aberration.

Hysterical personality can be recognised before puberty; in younger children, however, it must be extreme to be recognised, because of the great frequency of hysterical mechanisms then (*e.g.* behaving as though fantasies were real, counterfeiting illness, somnambulism). Some of the grossest instances of hysterical behaviour have been recorded in girls not yet adolescent, cf. the Salem witches. Much of the work of Child Guidance Clinics is taken up with the treatment of hysterical tendencies, not perhaps taking the form of definite symptoms but plainly evident in the child's personality.

The precipitating factor for the onset of hysterical symptoms is usually a situation, emotionally charged, out of which the patient's symptoms will bring him more or less overt, but unacknowledged, gain. This gain need not be material and obvious, and may run directly counter to such accepted values as health and ability to work. One of the plainest instances of a partial unsubstantial gain is that created by an accident, and the resulting claim for compensation; hysterical symptoms flourish in such a soil, and are usually influenced for the worse by repeated medical examinations. Hysteria occurs among soldiers under active service conditions, and can readily be fostered in them by injudicious measures. It is not infrequently a sequel of the acute panic or stupor which may in some men be the effect of intensive bombardment and exhaustion during active warfare.

Pathology.—This is almost wholly a matter of psychopathology. It is true that disseminated sclerosis and many other organic diseases of the brain may be accompanied by hysterical symptoms, but the association is not a constant one. The psychological changes can usually be traced further back than the happening that provoked the illness; often they are the continuation of normal tendencies of childhood that have been fostered and extended by ill-judged upbringing. The hysterical symptoms that appear as motor or sensory phenomena show the patient's readiness for the translation of experience into bodily symbols; this is a special instance of the universal tendency for somatic representation of experience, converting it into action. It is the facility and exaggeration, not the existence, of this "conversion" mechanism that is characteristic of hysteria. What is thus translated or "converted" into physical terms has been something painful and unacceptable; the partial exclusion of it from consciousness, "repression" of it, is therefore understandable; in its physical, symbolic form it is tolerable and may even be prized. Identification with other people is responsible for the frequent imitation of symptoms and for the epidemics of

hysteria. Suggestibility, with its characteristically quick formation of habits of somatic response, is another way of describing the phenomenon. Clearly the mechanism need not be limited to the production of physical symptoms, though bodily structure and local weaknesses may conduce to this. There can be hysterical phenomena, such as the dissociation seen in fugues and so-called splitting of personality, which are instances of the exclusion of recent and remote painful experience from clear consciousness. The wishes and fears that deviously attain outward expression as hysterical symptoms do not derive solely from the recent past, though much of their strength may come from it. It must be admitted that there are some hysterics in whom this psychopathology cannot be demonstrated, and that such cases are among the most intractable.

Symptoms.—These may be divided into: (1) sensory; (2) motor, including fits; and (3) quasi-psychotic.

The symptoms can be like those of any conceivable affection of which the patient has a notion. The cruder his notion, the less will his symptoms be like those of the simulated condition, but after he has been demonstrated to a class or repeatedly examined he may better his notion, and consequently his symptoms come closer to those of organic disease. Or, if he has had opportunity of seeing insanity, his pseudo-insanity may smack less of the stage than it otherwise usually does. The range of hysterical symptoms is so great that to describe them all in detail would take inordinate space, and there is no need to do so.

The *sensory* or, more properly, the *perceptual* symptoms include clavus and globus hystericus, blindness, deafness, and anæsthesia. The two former are so common in all sorts of mental disorder, especially those accompanied by anxiety, that they are of little specific importance in hysteria; inquiry as to their presence will often in these suggestible, rather hypochrondriacal patients lead to their occurrence. The difficulty in swallowing reported by hysterical women may be associated with a strong disinclination to eat—anorexia nervosa; it should not be confused with depressive anorexia or that of pituitary cachexia. Any cutaneous disturbance of sensation that the patient has a notion of can be presented, *e.g.*, anæsthesia, either mono- or bi-lateral, or of stocking and glove distribution, and analgesia of any part. The anæsthesia seldom corresponds to any nerve trunk, nerve root, or spinal segment, unless the patient has had special opportunities of knowing. With an anæsthetic hand objects may be identified, and any test which the patient does not recognise as referring to this disability he will perform satisfactorily. Such tests are not a means of "catching the patient out" as though he were a malingerer, but of ascertaining whether the symptoms express only his notion of some illness. The tests for a malingerer, it is true, amount to the same thing, though one assumes the malingerer to be clearly conscious of his purpose; consequently any distinction between hysteria and malingering must depend on the observer's impression as to the patient's honesty and self-knowledge; certainly it cannot be decided by tests. The tests for blindness (*e.g.* using a stereoscope with a supposedly blind eye), deafness (*e.g.* effect on pulse, respiration and psychogalvanic reflex of exciting remarks addressed to the patient), and for other forms of perceptual defect all depend on the physician's greater knowledge of what should or should not accompany the symptoms of which the patient complains; they are not intended to dis-

cover hysterical "stigmata" or characteristic anomalies. The ovarian and other hyperæsthetic spots, the pharyngeal anæsthesia and the concentric limitation of the field of vision formerly used diagnostically, were all products of suggestion or, as in the last instance, phenomena that may occur in normal fatigue, in hypochondria and in certain cerebral lesions.

The *motor* symptoms are paralyses, pareses, spasms, contractures, and tremors. Hysterical paralysis or paresis never affects individual muscles, but always movements. By various devices it can be shown that the patient can still use the affected muscles, as long as he does not know that the movement in question requires their use. The paralyses affect chiefly the left side of the body, are common in the legs (preventing proper walking or standing), and often occur in limbs or other structures that have earlier been the seat of an organic disability, *e.g.* trauma or paresis. If the paralysis be flaccid, no loss of tone or of reflex response is found, and the patient, through his ill-informed notions of what should happen, behaves otherwise than a patient with organic paralysis would—*e.g.* if asked to rise from the supine to the sitting posture without using his hands, he keeps his paralysed leg flat on the bed. If the paretic part be kept stiff, the antagonists will be found to come into action first when the patient is asked to perform the movement he says he cannot; and if the movement has to be made against resistance, sudden removal of the resistance reveals how much of the apparently tremendous effort was going into associated irrelevant or antagonistic movements. Passive movement to overcome the spasticity or subsequent contractures cause the patient to be more upset than could be accounted for by any pain he may complain of. The varieties of abnormal gait are numerous; many of them fantastically elaborate and, from the look of them, exhausting. Not only the musculature of the limbs may be affected but of the trunk (leading to curvatures and odd postures) and indeed any voluntary muscles, *e.g.* of the tongue, larynx, pharynx or eye. In hysterical aphonia the voice may sink to a whisper, or there may, more rarely, be complete mutism; the voice can, however, be used normally for coughing and similar purposes. The aphonia often comes on after some local inflammation that has caused hoarseness, or after a fright. Stammering, usually of the exaggerated kind, may also occur. Spasm of the external ocular muscles, leading to a convergent squint, may accompany a spasm of accommodation. Ptosis and blepharospasm sometimes occur. Many of the tics and spasms that used to be thought hysterical are now recognised to be often physiogenic, *e.g.* residual symptoms of encephalitis lethargica and chorea; spasmodic torticollis, for instance, is far less often psychogenic than used to be thought. When a spasm or paresis has long been maintained, trophic disturbance may follow: blueness and œdema, shiny skin, fibrosis of periarticular structures, and similar effects of rigidity and disuse. Tremor is most often seen in patients with a spastic paralysis, but may occur independently, as in many of the war cases. It is variable in degree and rhythm, and usually disappears when the patient's attention is turned from it; this does not apply, however, to some very long-standing cases.

Hysterical *fits* commonly occur in patients with obviously hysterical personality. They may be little more than a fainting-attack or an outburst of temper, significantly like the tantrums of an ill-behaved child. Often, however, they are more differentiated than this, and diagnosis from an epilep-

tic fit may be difficult. Sometimes the fit grows out of a tremor induced by fright or anxiety, as in many war-hysterics, or it may express some emotional state, such as great pain, anger or erotic excitement. Occasionally the patient shows plainly by her expression and movements that the fit is erotic; it may be a typical orgasm. The "classical" four-phase fits which Charcot described were artefacts of the clinic; they do not happen now.

Sometimes the patient's fit becomes very like an epileptic one after he has spent some time at a neurological clinic, or he may be an epileptic who also has hysterical fits. Some hysterics, by overbreathing, induce an epileptiform convulsion, which can be abruptly terminated if an injection of calcium chloride or gluconate be given. They may pass from one such fit into another, so that the condition suggests a status epilepticus. The unconsciousness that often appears to accompany a hysterical fit is seldom as complete as it looks; neither is the subsequent amnesia. There may, however, be a delirium, corresponding to the emotional upheaval. Patients very rarely hurt themselves seriously in the fit, however violent, or have a fit when alone or asleep. The length of the attack and its degree often depend on the audience; the more the bystanders try to restrain the movements, the wilder do the kicking, struggling, biting, shouting, panting, spitting, etc., become and the longer they go on. There is neither the pallor nor the cyanosis, the regular sequence nor the subsequent headache and sleepiness of epilepsy; urine is not passed nor the bowels opened; reflexes, including the corneal response, are unaffected, and the end of the fit may be abrupt.

The *quasi-psychotic* symptoms are stupor, twilight-state, pseudo-dementia, and fugue. In the stupor, seen typically in harassed weary soldiers under bombardment, the patient lies motionless, taking food like a twelve-months baby, non-resistive, sometimes incontinent of urine or fæces, and without any predominant emotional tone. It is of brief duration if the exciting circumstances cease to prevail. In less acute forms there may be a sullen resistive akinesia, or a condition lasting even for years, with an occasional break; this is a rare form. The confusional or delirious states may accompany a fit or represent an important emotional experience, *e.g.* some sexual episode. They are often histrionic, and represent wishes of a religious or grandiose sort; or the patient may behave as though he were an animal or a child. Sometimes they occur during the night, and in a somnambulist state the patient repeats some past happening, or may do complicated work. This is closely akin to the hysterical fugue, in which there is not so much a clouding as a narrowing of consciousness, a "dissociation." In the fugue the patient says he has forgotten some or all of his life before a certain date, and later he may profess to remember nothing of what has happened during the fugue. There is, in short, a double set of memories, which may alternate, and since the patient's own identity is commonly included in the repressed and temporarily forgotten material, he may be said to have two personalities, and sometimes three or four. Actually there are no cases in which it is strictly correct to speak thus of multiple personalities; it is only a matter of different aspects or fragments of the one personality. In the fugue the patient may live out some fantasy or—as more commonly happens—simply says that he does not know who he is or where he lives. Nearly always a hysterical fugue with gross amnesia turns out to have been a means of evading some predicament, and it is well to keep in mind in such cases that the patient may have

broken the law or otherwise exposed himself to disgrace and punishment. The amnesia is seldom as complete as the patient states. Fugues may occur as a hysterical mechanism in an organic psychosis; we have seen a man with arrested general paralysis who had been prominently and in detail reported as a case of multiple personality which responded to psychotherapy.

"Pseudo-dementia" covers the large group who behave as though insane. It may occur, as in the so-called Ganser syndrome, in prisoners awaiting trial. Whatever the circumstances, its motive is escape from a disagreeable situation. It is likely, however, that it is mainly those with a predisposition towards severe mental illness, especially schizophrenia, and the high-grade defectives who have recourse to this kind of hysterical behaviour. It sometimes comes on after brain injury. The patients' behaviour corresponds necessarily to their notion of insanity, which is usually far enough removed from anything the psychiatrist knows as such. Occasionally, however, it is very near the buffoon-like conduct of some schizophrenics. The patients say that they do not know their own age, affect not to understand simple remarks, give absurd answers which nevertheless indicate that they know the right answer (*e.g.* by inverting the correct order of the figures in a sum). When asked about some simple matter, they look as though they were making terrific efforts to remember (herein behaving differently from the schizophrenic). The most characteristic thing is the disparity between the patient's alleged deficiencies and his general alertness: he says he does not know anything about his own past, he cannot read or spell or do the simplest arithmetic, and yet he may be behaving quite naturally and adapting himself to the situation in a way which would be inconceivable if he had actually so advanced a dementia.

Some hysterics go to great lengths in their representation of ideas of illness. They will allow themselves to be put among grossly insane people, or submit to repeated operations, such as amputation. Self-inflicted injuries, *e.g.* keeping wounds and sores open, are not uncommon (cf. dermatitis artefacta). In some such cases masochistic tendencies can be recognised, but by no means in all. Suicidal attempts are not infrequent. They often have as their purpose revenge, the satisfaction of some spite, and the patient may leave behind a lying, fantasy-coloured letter, indicting someone. Frequently the suicidal attempt is in the nature of a theatrical demonstration, done in such circumstances as make it unlikely to be fatal; and if the patient kill herself, it is more through bad management than intention.

Diagnosis.—It will be plain from what has been said that diagnosis must be both negative and positive—negative, by excluding any organic cause for the symptoms; positive, by finding motives and relating the symptoms to them. Neither method is alone sufficient, because of the occasional concurrence of structural disease with psychogenic symptoms. As to the former, *i.e.* the negative method, it is unnecessary to enter here into all the differentiating points. Many of them have been mentioned in the foregoing description of symptoms, and all turn on the disparity between what experience tells us would occur if these symptoms were of organic origin, and what the patient knows about such matters. Consequently a doctor who has hysterical symptoms is extraordinarily difficult to diagnose, in this negative sense. The method of arriving at a diagnosis by suddenly taking the patient unawares, and seeing if his symptoms persist, is to be deprecated; it antagonises him. Likewise undesirable is the procedure of see-

ing whether one can suggest new symptoms to the patient, *e.g.* an anaesthesia; it can be both misleading and harmful. Neither is the hysterical nature of a symptom to be judged solely by whether it can be removed by suggestion; for some organic symptoms are temporarily got rid of thereby, and many hysterical symptoms are not. An intimate knowledge of the range of symptoms of physical disease is much more useful to the physician than an equipment with special tests and lists of differences between "functional" and "organic." It is not only a problem of neurology but of the whole of medicine, since the hypochondriacal tendencies of many hysterics lead them to complain of visceral symptoms; usually, in doubtful cases, the symptoms are those which might well occur in the earlier stages of some physical disease. It is, however, in neurology that the most difficult cases of all arise, *e.g.* in disseminated sclerosis, carbon monoxide poisoning, cerebral vascular disease or encephalitis lethargica; here there is more likelihood of the organic disease being overlooked than of its being wrongly diagnosed. The patient's previous personality, any provocative situation or emotional disturbance, the previous occurrence of organic signs, *e.g.* transient diplopia, and the age of the patient must be considered. Hysterical symptoms appearing for the first time in middle or later life in someone whose personality has been stable, are probably not solely psychogenic. If the symptoms diminish when little or no attention is paid to them, they are more likely to be hysterical.

Course and Prognosis.—This depends mainly on the patient's personality and social setting, and on the treatment employed. A long history of hysterical traits prior to the illness, a continuance of circumstances favourable to the symptoms, and inadequate or excessive treatment are all unfavourable. This is, however, an illness that sometimes confounds prediction, patients recovering when many adverse factors have been operative and the symptoms have been present for years. In children the prognosis is fairly good if treatment can be undertaken promptly; it is best if the hysteria is monosymptomatic and has come on after a fright. In all cases in which the situation which provoked the illness persists, the outlook is bad; for example, in the compensation cases, for which no medical treatment is of any avail—for obvious reasons—until the litigation is settled once for all. Similarly, during war, psychotherapeutic successes are often dazzling while the hysterical soldier is under treatment in hospital, but the symptoms come again when he must return to duty. There are many varieties of outcome, chronic invalidism being the commonest. A few patients later become schizophrenic, and a few become involutional melancholics. The prognosis in respect of the patient's hysterical personality is more important than that of his hysterical illness; it is, however, no more to be assessed by rules than the general future of any human being's life and personality. Patients do not necessarily tend to become anti-social; delinquency is certainly a likelihood in some hysterical people, but bravery and self-devotion may be conspicuous in others.

Treatment.—Too much treatment is worse than too little. Injudicious physical or psychological treatment of hysterics often makes their symptoms worse and their illness intractable. Recondite methods should be eschewed by all but experts. Common sense is as important as psychological understanding; and social usefulness more to be aimed at than removal of symptoms or attainment of self-knowledge. In short, it is not the hysterical illness or

the mechanism of repression and conversion that calls for remedy, but the patient's inadequate way of dealing with difficult situations. Consequently, the whole treatment must aim at the patient's return to ordinary conditions of life as soon as possible, and at a re-education of his ways of meeting difficulties. To this end it is profitable to go over with the patient the situations, emotional disturbances and motives that led up to the illness, and to do this without implying moral judgment or social indifference—certainly without teaching the patient one's psychological theories. It is a matter of general psychotherapy (see p. 1816); and it may entail a far-reaching analysis of the patient's past life, her emotional development and her instinctual tendencies. It is questionable, however, whether anyone without special psychiatric experience is wise to enter lightly upon this way of benefiting the patient. For, on the one hand, he may be misled into a wilderness of fantasy masquerading as once-repressed, now-recalled psychic trauma; and, on the other, he may be at a loss how to deal with the attachment and dependence upon him which the patient will come to show, and which may in fact be the chief influence in bringing about her precarious recovery. A great deal may be achieved—perhaps as much as by more thoroughgoing methods—if the physician, himself mature and with impartial insight into the psychological motivation of the symptoms, leaves aside in his dealings with the patient any very detailed inquiry into the causes of the illness and the purposes it served; and, instead, directs her towards a better social adaptation, by advising her to avoid when possible the situations that, as he sees, favour the production of symptoms, getting her into a disciplined way of living, and stepping in with explanation, support and advice whenever fresh difficulties arise. His success in getting rid of individual symptoms at the beginning may be an important factor in establishing the necessary relationship with the patient. Such a line of treatment is not heroic, it is scarcely even rational, in the sense of being causal, but it avoids some of the commonest blunders and may be strikingly successful. For this, or indeed any treatment, admission to hospital is not essential; but it will help when there are adverse factors in the patient's situation and, of course, will be essential if there be such symptoms as self-injury, suicidal attempts, pseudo-dementia, or gross paralysis. The danger of the patient's picking up new symptoms in hospital should also be weighed. Isolation is usually inadvisable.

Many of the symptoms of hysteria will not wait upon general treatment, but demand energetic intervention. Anorexia, for instance, cannot be allowed to go on to an avoidable inanition, nor a paralysis to the stage of contracture; a mute patient, or one who is deaf or blind or ignorant of his own identity, offers such practical obstacles to almost any kind of treatment that the symptoms must be tackled and disposed of early. For this purpose suggestive measures are valuable and appropriate physical treatment may be called for, *e.g.* supervision during feeding, or even tube-feeding in anorexia nervosa, physiotherapy for paralysis, voice-exercises. Suggestive measures need not take the form of hypnosis; suggestion in the normal waking state has many advantages over hypnosis, though those expert in the latter are sometimes very successful in their treatment. Suggestion, like almost every form of treatment of hysteria, has pitfalls, and its triumphs, like those of every other method, sometimes prove vain, but in the hands of a physician who is at once confident and cautious, this method may result in a satisfactory

recovery. If, in using suggestion, such physical devices as faradisatio an be avoided, it is better to do so. As a means of demonstrating that the illness is not due to local disease, however, such methods sometimes take their place in a detailed plan of treatment. Motor and sensory symptoms can usually be got rid of in one or two sittings if the physician is patient, determined and confident in the use of persuasion and suggestion.

The choice of occupation, the settlement of any social cause of illness (*e.g.* claims for compensation), and the obtaining of a healthy attitude—neither complaisant, much-enduring nor harsh—on the part of the patient's relatives and friends, are all important factors in treatment. The hysterical reactions to injury call for special mention because of their frequency. Though often of transparent motivation, they are not by any means to be regarded as outright malingering; for the patient's feeling of illness may be sincere, his symptoms distressing, his anxiety typical, and his irritability and insomnia symptoms that he would gladly get rid of. But they are none the less psychogenic. It is often assumed that so far as an illness is psychogenic, it must be treated only by psychotherapy. This is false theory. There are few mental disorders in which psychotherapy alone produces such small benefit as in the hysterical conditions due to the compensation or pension situation that may follow an injury. Putting an end to the situation early and the resumption of ordinary activity as soon as any physical injury has been repaired are the most potent measures in the earlier stages. Even if the symptoms have been present a long time, the ending of disputes about claims and the return to ordered routine and regular occupation achieve more than do frequent medical interviews. Psychotherapy is then an adjunct, not an essential feature, of the treatment. Marriage should never be recommended as treatment for hysteria; the superstition about this has resulted in lamentable troubles, especially for the person the hysteric marries. This is not to say that every hysteric is to be dissuaded from marrying; there are more things than treatment to be considered then. Married hysterics, however, should not be recommended to have a child. Contrary to popular notions, pregnancy and puerperium more often aggravate than benefit hysteria. Moreover, hysterical women are not usually satisfactory parents, and commonly induce psychopathy in their children.

ANXIETY STATE

As already stated, the emotional syndrome so called is part of the group of affective disorder, in which depression and manic excitement are also included. It is there described. It would be indefensible to put into a special category all the forms of mental illness in which anxiety is conspicuous, for it can be severe in the most diverse conditions, ranging from delirium tremens to schizophrenia. The outwardly mild form, tending to chronicity and often largely psychogenic, responds well in the less advanced stages to psychotherapy; it is therefore important that its recognition should not be delayed because of a doubt as to physical disease. Yet often the correct diagnosis is overlooked while the patient is being investigated or treated for some local disorder. This arises partly because of the quasi-physical signs of fear which he may show—dizziness, tremor, nausea and

vomiting, indigestion, diarrhœa, shortness of breath, palpitation, a sense of oppression in the chest, rapid pulse, flushing, sweating, frequent passage of urine, etc. It is still more due to the patient's anxiety turning on his health, especially his physical health, and leading him to ask for more and more medical opinions, X-rays, laboratory investigations, etc., the favourable results of which, however, do not allay his worry. Over-cautious advice as to regime, based on a possibility that there may be some early physical disease, can be harmful to the patient's mental health in that it restricts his normal life, and may constantly recall and reinforce his anxiety. The converse error of mistaking some early symptoms of physical illness for hypochondriacal anxiety is equally to be avoided. Physical investigation of doubtful cases is, in short, indispensable, and should be prompt as well as thorough. When it fails to confirm the presence of a physical disorder the patient should not be treated as though he will still be in danger of the physical illness unless he takes special precautions in diet, exercise, etc. This is well illustrated by such a condition as effort-syndrome, where care taken to avoid any damage to the heart intensifies the illness. The patient should be fully investigated on the psychological side and treated accordingly; this does not mean that he should be treated only by psychotherapy. The discovery of a possible psychological cause for the symptoms does not prove that there is not also a physical cause for them, but it makes it less likely. The converse is also true. For ætiology, diagnosis, prognosis and treatment see section on Affective Disorders.

OBSESSIONAL DISORDER

Definition.—In this condition the characteristic feature is that, along with some mental happening, there is an experience of subjective compulsion and of resistance to it. Commonly the mental happening (which may be a fear, an impulse, or a preoccupation) is recognised, on quiet reflexion, as senseless; nevertheless it persists.

Ætiology.—INTRINSIC.—The hereditary factor is strong. A third of the parents of obsessional patients, and a fifth of their brothers and sisters, have themselves shown pronounced obsessional traits; the proportion is in each case higher if all forms of mental abnormality be included, since both schizophrenia and affective illnesses occur with more than average frequency in families of obsessionals. The abnormal personality of the parents is probably also potent as an environmental cause. Very many obsessional patients have for years before they became ill shown a rather characteristic mental constitution: they are excessively cleanly, orderly and conscientious, sticklers for precision; they have inconclusive ways of thinking and acting; they are given to needless repetition. Those who have shown such traits since childhood are often morose, obstinate, irritable people; others are vacillating, uncertain of themselves, and submissive. "Obsessional" traits occur, however, in many people who never become mentally ill, and in many who become mentally ill otherwise than with an obsessional disorder. Consequently these traits cannot be rigidly held to be the forerunners or non-morbid counterpart of obsessional illness.

EXTRINSIC.—The influence of strict, morose, cruel, overconscientious, or obsessional parents has just been mentioned. It is difficult to weigh its

importance; certainly in some cases it plays no part. There is nothing specific in the situations which supply the content of an obsession: they might equally well have preceded hysterical symptoms, for example, in a person so predisposed. Nevertheless, the fright or pain which once accompanied a particular experience, or a long series of experiences, must not be overlooked in working out the multiple causes of some obsession psychologically related to this experience.

Encephalitis lethargica and a few other cerebral diseases may produce typical obsessional symptoms in persons previously free from demonstrable tendencies in this direction.

Pathology.—Apart from the difficult instances in which lesions of the brain are accompanied by obsessions, this is at present wholly a matter of psychopathology. Some elements of an obsession are universal human attributes: all little children tend to ritualise and repeat; all human beings are at times uncertain of the rightness or sense of what they have done; they try to avert trouble by symbolical acts and other magical devices, whose effectiveness they may question (*e.g.* superstition); many normal people, moreover, have mild obsessions that do not bother them (*e.g.* scruples). The manifest struggle going on in the obsessional patient may be restated in terms of hypothetical instinctual tendencies. Such attempted explanation cannot be verified; and it is more useful to pay heed to the repression, displacement and substitution which lead to symbolic representation of emotionally significant earlier experiences, and to the protective mechanisms by which the patient tries to ward off the painful and overwhelming obsession, with the result that he develops complicated rituals and similar devices which may be mistaken for the essential symptom. The transition from obsessional to schizophrenic is easy to understand psychopathologically, since in both some contents of consciousness are separated from the main stream.

Symptoms.—Obsessions are conveniently classified as: 1. ideas or images; 2. impulses; 3. phobias; and 4. rumination. These overlap constantly.

Among obsessional *ideas and images* are tunes, phrases, mental pictures of a disagreeable sort (*e.g.* of a mutilated corpse), and obscene associations (*e.g.* every cranny reminds the patient of a vulva). Obsessional *impulses* are often of a suicidal or aggressive character: the patient may feel an urge to kick people in the street, to push his friend over a cliff, or to throw himself under a passing train. In many other cases, however, they are less alarming; *e.g.* impulses to swear loudly in church, or to laugh at a funeral; or more of an intellectual sort, such as an impulse to count and manipulate numbers senselessly or to avoid typing any word with a given number of letters or beginning with a particular consonant. *Phobias* are closely bound up with the other varieties of obsession: thus, the patient who has an impulse to plunge a knife into his friend's or his own neck has an understandable phobia of knives; the patient who is troubled by obscene thoughts whenever he looks at a naked statue develops a phobia of museums. Not all phobias can be so accounted for; they may rest on some forgotten alarm, and take a queer form, such as a phobia of lavatories or of one-legged men. It is loose usage to give the name "phobia" to every case in which an individual develops fear that is excessive or inexplicable; the essential features of an obsession, already mentioned, should also be present. Fears of dirt or infection are very common phobias: they are symbols of moral, usually sexual, taint, and they

lead to much washing, etc.; thus, a patient who has blamed himself for masturbation may be constantly washing his hands, or following a complicated ritual of touching nothing with his bare hands for fear of contamination. Often the rituals and defensive precautions seem grotesque when compared with their ostensible purpose, as in the case of a patient who is perpetually putting himself to the greatest trouble in order to ensure that he never steps on a worm inadvertently; much of the grotesqueness disappears when it is discovered what the worm symbolises for him. Ludicrous as his behaviour may seem, it is often tragic in the distress, and indeed ruin, it may cause him. Another phobia is that which has fear as its object, *i.e.* the patient is afraid of any situation in which he may feel fear; some such patients do not leave their homes for years, because they fear they may have an attack of agoraphobia once they get outside. Obsessional *rumination* usually takes the form of endless questioning or search. The patient has to ask himself "Why" with pointless insistence about all manner of problems beyond his or anybody's grasp; or he has to keep casting round in his mind after some forgotten name or word which he could easily do without. Religious scruples sometimes fall into this category, as when a penitent is continually running to his confessor with some venial trifle he has come upon in his interminable self-questioning and doubt.

Obsessional patients are in most cases depressed; their illness is a depressing one. Besides this secondary depression, however, there is frequently an association of a more intimate kind, in which depression—or mania—is the essential or the main part of the illness, and the concurrent obsessions seem to be symptoms of this affective disorder. In such cases the obsessional illness is very often cyclical in its course. Anxiety is a common accompaniment of obsessions; in phobias it is most conspicuous. The anxiety is inseparable from the patient's struggle against the subjective compulsion which is so alarming to his feeling of integrity in self and mind, such a shock to his belief that he is a free agent. Schizophrenic symptoms may be in the offing, or actually present, when the obsessional ideas are of the magical kind, *e.g.* the patient feeling that the effect of his obscene thoughts upon others may be averted by some gesture, or when his rituals are carried to bizarre lengths, *e.g.* having to save the last drops of his urine because of some recurring doubt. Depersonalisation may occur in the course of an obsessional illness.

Diagnosis.—If the essential features, *i.e.* feeling of subjective compulsion and immediate resistance to this, be kept in view, it is seldom difficult to distinguish between obsessions, on the one hand, and delusions, hallucinations, ideas of reference or self-reproach, feelings of being influenced and schizophrenic stereotypies, etc., on the other. The only difference between obsessions and many schizophrenic phenomena towards which the patient retains insight and which he regards as alien to him, lies in the nature of the compulsion he experiences: in obessions it is subjective—he feels that it comes from within his own mind, whereas in the schizophrenic phenomena he feels that it comes from without, it is imposed upon him. It is a difference, however, that may be obliterated, *i.e.* what was once obsessional may become schizophrenic, but this is an uncommon outcome when the obsessional disorder is definite and well-established. In differential diagnosis it must be remembered that obsessions may occur in the course of almost

any mental illness in a person of obsessional tendencies, and that the psychological mechanism for the production of obsessions, like that for hysterical symptoms, is present in almost everybody in varying degree. Consequently, an illness is not to be regarded as obsessional unless obsessions are the chief symptoms.

Course and Prognosis.—The outlook for recovery is worse if obsessional symptoms have been present since childhood, if they now fill up most of the patient's time, and if he is weakly resigned to his illness. The best outlook is when the obsessional illness comes on suddenly in a person who has not had conspicuous obsessional traits or who has had previous benign attacks. A cyclical course is not uncommon. The situation is ominous when the ritual gets more and more systematised and remote from what previously occasioned it. The development along schizophrenic lines, already mentioned, is more to be feared in such cases and in those with bizarre obsessional thoughts; the great majority of gross obsessionals, however, do not become schizophrenic or anything else than obsessional. About half the cases recover from an attack, which may, however, last for a year or even more. Many people are subject to brief attacks, lasting only a few days, and largely due to fatigue or physical illness reducing their mental health. Intercurrent happenings influence the course of the illness, *e.g.* some men were free from symptoms during their period of war-service, with its routine and lack of responsibility or need for decision. The content of the obsessions is of little use prognostically. Old age is not in itself an adverse factor, but attacks in childhood suggest a strong constitutional bias and are therefore unfavourable on the whole. Few obsessionals give way to anti-social impulses, *e.g.* to suicide, homicide, delinquency. It is true that obsessionals who are also depressed may kill themselves, and that obsessionals who are irritable and angry may injure others; but obsessionals rarely yield directly to an impulse they have resisted, or need to have "irresistible impulse" urged in extenuation of a crime. Sexual offences and perversions are rarely obsessional.

Treatment.—Patients should be encouraged to continue at their occupation and not to test themselves, or try to overcome their obsession, by repeatedly putting themselves in a situation in which it will occur. So long as their impulses are not likely to get them into trouble, they should be encouraged to give way to them, rather than to "fight." The physician must aim at getting a patient well by putting an end to his anxiety and struggle; if that is not wholly attainable, the patient must be educated to deal with his obsessional tendencies by acknowledging their existence, their psychological origins, and their harmlessness in those very respects in which he thought them most harmful, *e.g.* obscenity. Frank recognition of obsessional tendencies, which everyone has in some degree, is an important step in learning to control them. In some patients the obsessional attack is so cyclical and almost self-limited that a brief rest and general care are all that is needed. In others, whose affection is chronic, recovery is out of the question, but advice about the management of their lives, varying according to their individual circumstances, helps them greatly. These patients, so prone to rumination and endless questioning, often clamour to be psychoanalysed. There is no evidence that psycho-analysis, however prolonged, benefits them more than methods that are not so exigent of time and money.

Obsessional children usually respond well to changes in their human environment, advised after the physician has inquired into the family and school situation; temporary separation from an obsessional parent or treatment of the latter often proves remarkably beneficial for the child. Discussion of his problems with the child (especially if they centre round secret sexual play) is an important adjunct of such treatment, just as it would be with an obsessional adult.

EDWARD MAPOTHER.
AUBREY LEWIS.

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